



Health Protection Report

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Outbreak of respiratory infection on a cruise ship

On 27 July the Kent Health Protection Unit (HPU) was alerted to an outbreak of respiratory infection among passengers on the Black Watch Fred Olsen Cruise sailing in the Baltic between 15 July and 1 August. The ship had 756 passengers and 329 crew on board. Most of the passengers are elderly. Seven passengers were transferred from the ship that day and five were admitted to hospital in Stockholm. Over the weekend, about 40 passengers on the ship reported a range of respiratory symptoms and some were treated with antibiotics by the ship's medical centre. Environmental samples were taken while the ship was in port in Stockholm on 27 July and the use of the pools and other risk facilities on board was suspended for the remainder of the cruise. The cruise was terminated early and arrived in Dover on Monday 30 July

On arrival in Dover, the ship was boarded by a team led by Kent HPU, including representatives of Dover District Council, Eastern and Coastal Kent PCT, Kent Environmental Microbiology Services and the HPA Centre for Infections. Further sampling was carried out before superchlorination and heat treatment of the ship's water systems was carried out.

Twenty-four passengers with respiratory symptoms provided urine samples, 16 of whom also gave nose and throat samples for virological testing before they disembarked. Two of these passengers were transferred to hospital in Ashford, Kent (a further two were admitted the following day, one in Ashford and one in Margate). All are elderly, aged 70 years or more.

Of the five patients admitted to hospital in Sweden, two have been reported as positive for legionella by PCR, and one was positive by *Legionella pneumophila* urinary antigen detection. All 24 urine tests carried out in the United Kingdom (UK) by the Ashford NHS laboratory were negative for *L. pneumophila* urinary antigen and six viral swabs have tested negative for flu A and B by PCR at the Southampton HPA laboratory. Further tests are now being conducted on these specimens for detection of other respiratory viruses and other bacterial infections, including non-serogroup 1 *L. pneumophila* infection.

All patients in Sweden are responding to treatment. Four patients remain in hospital in the UK, two are recovering and two are being treated for pneumonia.

Preliminary results from Sweden indicate that low levels of *L. pneumophila* sg1 and sg2-14 were detected in samples taken from the shower in the cabin of one of the hospitalized cases and low numbers of *L. pneumophila* sg2-14 from the shower in the cabin of another patient. The results of the water samples taken in England are awaited.

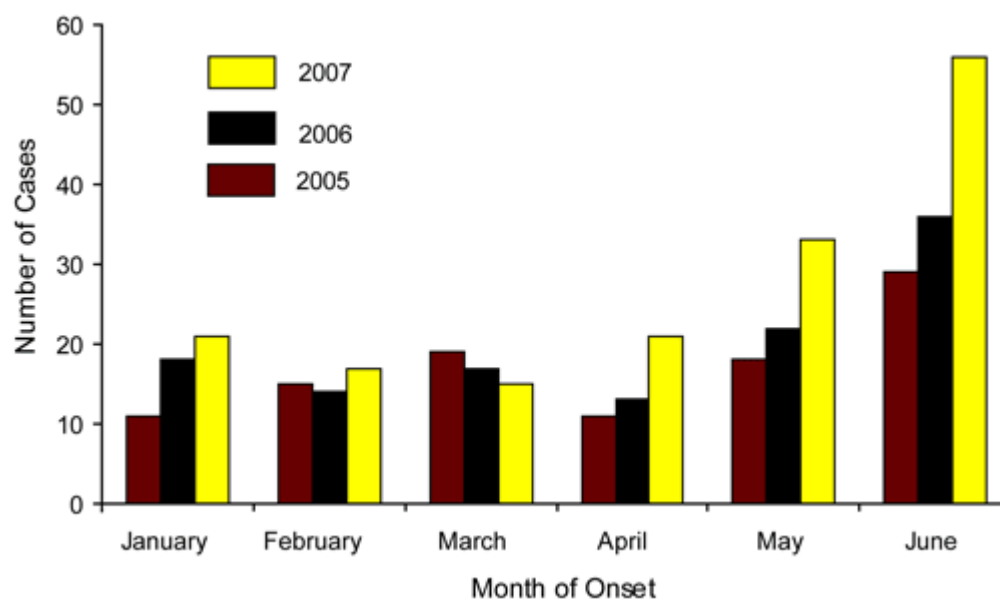
Information is being collected from Sweden about on-shore excursions made by the cases and their use of the spa pools and other water facilities on the ship before they became sick. Microbiological information is also being sought through the City of Stockholm public health department.

All disembarking and embarking passengers have been informed of the incident and provided with advice and information on legionnaires' disease, should they become sick. The ship has now begun its next cruise and spa pools will remain closed until sampling results are known and further advice is given by the HPA to the ship's engineers.

National increase in cases of legionnaires' disease

The number of cases of legionnaires' disease reported to the Health Protection Agency with date of onset between January and June has shown a rise in 2007 compared with the same period in 2005 and 2006 (figure). One hundred and sixty-three cases of legionnaires' disease were detected in the first six months of 2007, compared with 120 cases the year before and 103 cases in the same period in 2005. The seasonal increase in cases normally begins in spring and peaks between August and October each year. Five hundred and fifty-nine cases were reported to the HPA's National Surveillance Scheme for legionnaires' disease in residents of England and Wales for 2006, the highest number reported since the scheme began in 1980. Over 200 of these cases occurred in August and September and are being investigated for links to the very warm weather experienced in 2006, and possible climate change effects on the ecology of the disease.

Figure Cases of legionnaires' disease in residents of England and Wales : January to June 2005 to 2007



Reports to the HPA include cases acquired both in the United Kingdom (UK) and overseas. To date, 57% of all reported cases in 2007 were contracted in the community, 3% were hospital acquired, 6% were associated with travel in the UK and 34% with travel abroad. The proportion of community cases relative to the other cases has changed since 2005. In that year 41% were community acquired compared with 47% in 2006 and 57% so far in 2007. As in previous years, cases in 2007 have been reported from all regions, with some community clusters detected and investigated for common sources of infection. So far clusters have been reported from the West Midlands, the South East, the North East and London. One hospital

outbreak in the East of England involving three cases, one of whom died, was also investigated. The overall case fatality rate for 2007 is currently 11%.

The high number of cases detected over the past few years is likely to be associated with an increased awareness of the disease, an increased use of rapid testing methods to identify the disease and possible consequences of the rise in sustained warm weather patterns. However, the weather patterns since June this year have been very different to the summers of 2005 and 2006. It is therefore not clear whether the high number of excess cases detected in the UK in the last two summers will be repeated this year.

National outbreak of Vero cytotoxin-producing *Escherichia coli* O157 infection, England and Wales: June to July 2007

Routine local follow-up of cases of Vero cytotoxin-producing *Escherichia coli* (VTEC) O157 infection by Environmental Health and Health Protection Agency (HPA) staff in north west England revealed that two apparently unlinked cases reported exposure to the same coriander and lemon chicken wrap which was purchased from different branches of the same national supermarket chain on 26 June 2007. Both cases became ill on 29 June and no other known risk factors for VTEC O157 were reported by either case. A local outbreak control team (OCT) was convened on 5 July.

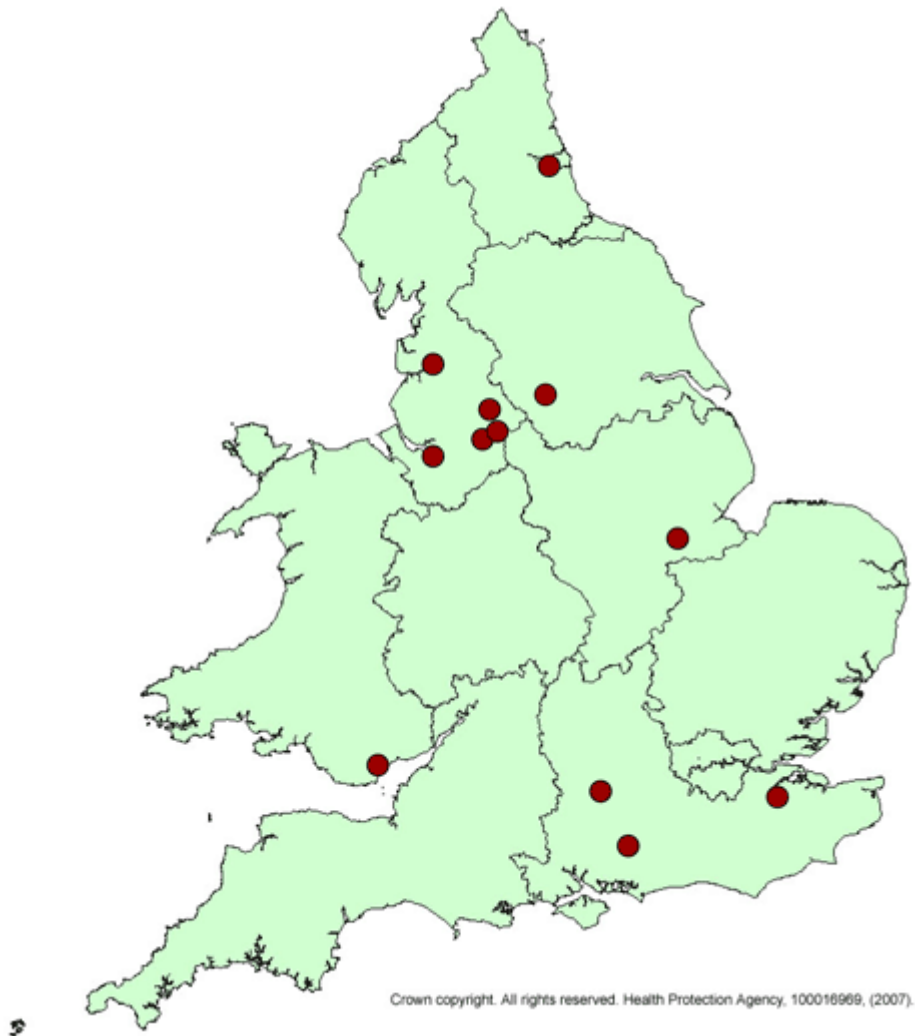
A third case, who ate a coriander and lemon chicken wrap from the same chain on 26 June and fell ill on 2 July, was reported in the north west on 6 July. It was established that the lemon and coriander chicken wrap was supplied by a food production unit in Milton Keynes. Two and a half thousand wraps were produced daily and distributed nationally. The Environmental Health Department at Milton Keynes, the Food Standards Agency (FSA) and the supermarket chain were informed. The product was withdrawn voluntarily by the company at 6pm on 6 July, and additional control measures for manufacturing processes involving fresh herbs were instigated. Environmental investigations, including sampling of lemon and coriander chicken wraps from the supermarket chain, were initiated on the 6 July. Isolates from the three cases were referred to the HPA Centre for Infections (CfI) Laboratory of Enteric Pathogens (LEP) for confirmation and subtyping and were identified as *E. coli* O157:H7 phage type (PT) 8 possessing genes for vero cytotoxins one and two (VTEC O157 PT8 VT1+2).

Active case finding through the HPA Local and Regional Services (LaRS) began on 9 July. Health Protection Units were asked to report any recent cases of *E. coli* O157 in their area who had eaten a chicken wrap from the major supermarket chain and to ensure that isolates from such cases were sent to the LEP at CfI. A fourth case, resident in the south east of England who became ill on 30 June, was identified by this means and a national OCT, with representation from the HPA, the FSA, and the Environmental Health Departments involved, was convened on 10 July to review the epidemiology and make recommendations for control.

Milton Keynes Environmental Health Department conducted detailed investigation of processes and records in the food production unit and traced back the products used in the wrap. Fifteen ingredients were used to make the wraps and investigations focussed on those unique to the product. Raw ingredients, finished wraps and water used in processing were tested on 11 July, and food production equipment screened. These samples were sent to the HPA London Food, Water and Environment laboratory for testing (culture and PCR) and food handlers from the food production unit were requested to submit stool samples. The supermarket chain also sampled several hundred raw materials and finished products from the food production unit. The samples were subsequently forwarded to the HPA for re-testing (culture and PCR testing) in HPA food and water laboratories. All samples tested were negative for *E. coli* O157 by both culture and PCR.

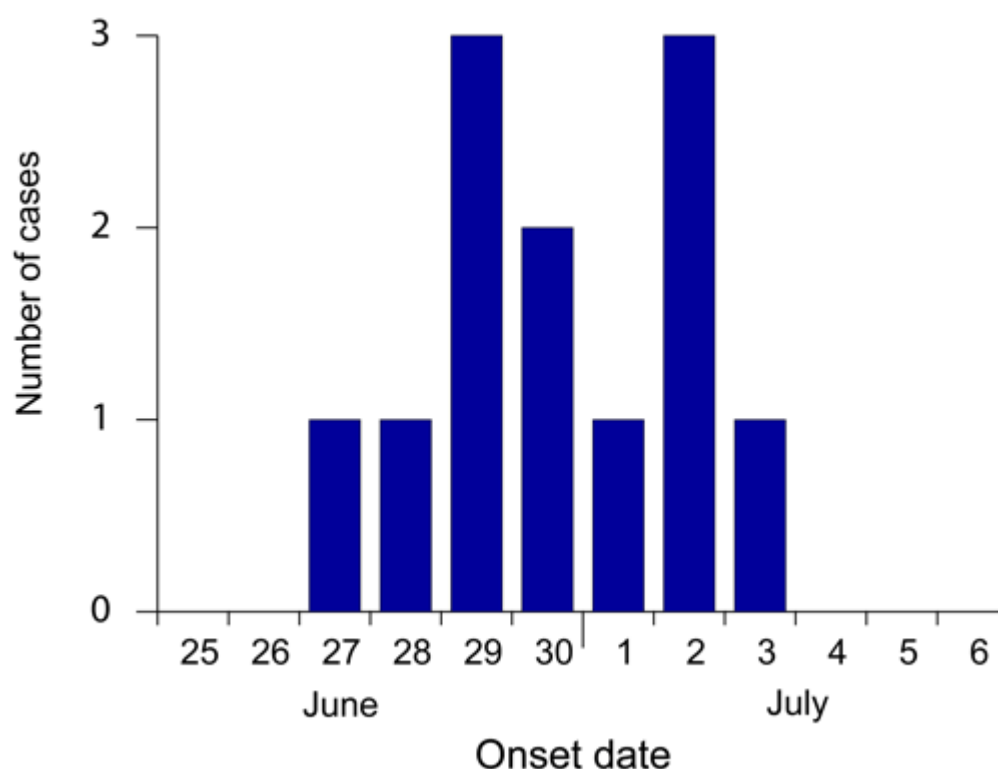
Active case finding identified 12 cases of *E. coli* O157 infection who reported the consumption of a lemon and coriander chicken wrap from the same national supermarket chain prior to illness. These cases ranged from 17 to 50 years of age (median 28 years) and three quarters were female. Cases were reported from five NHS regions and from Wales, with most cases reported from North West and South East England (figure 1).

Figure 1 Geographical distribution of cases (N=12)



Onset dates ranged from 27 June to 3 July, with an epidemic curve suggestive of a point-source exposure (figure 2). Illness length for eleven patients ranged from five to 16 days (median seven days) and three of eleven cases (27%) were known to have been admitted to hospital as a result of their illness.

Figure 2 Epidemic curve (N=12)



An urgent enquiry through the international surveillance network Enternet did not identify any additional cases other than those in England and Wales.

To provide further discriminatory power and to assess the extent of the outbreak, Pulsed Field Gel Electrophoresis (PFGE) was applied to these isolates in addition to all VTEC O157 PT8 VT1+2 isolates received by the LEP since 20 June 2007. Isolates from cases associated with secondary transmission, onset prior to 20 June or linked to foreign travel were excluded. To date, 49 isolates from humans have been screened and 12 were found to possess a PFGE profile unique to this outbreak. An additional case, known to have consumed a lemon and coriander chicken wrap prior to onset, was infected with a similar but distinguishable strain of VTEC O157 PT8 VT1+2.

An unmatched case-control study was undertaken to test the null hypothesis that infection was not associated with the consumption of coriander and lemon chicken wraps from a single national distributor. Cases were defined as “residents of England and Wales with a laboratory-confirmed VTEC O157 PT 8 VT1+2 infection, notified to Health Protection Units (HPUs) since 20 June 2007. Asymptomatic controls were recruited through systematic sequential dialling, based on the cases' telephone numbers. Cases and controls with a history of recent foreign travel or contact with individuals with gastrointestinal symptoms were excluded. Sample size calculations suggested that 10 and 20 eligible cases and controls respectively would need to be interviewed successfully to provide sufficient power (80%) to detect a difference at the 95% level. Cases were asked about exposures in the five days before illness. Controls were asked about exposures in the three weeks before interview – a period which included cases' exposure period.

Between 12 and 14 July, 19 cases and 40 controls were interviewed successfully, of whom eight and 39 were eligible for inclusion in the analysis, based on the application of exclusion criteria and the results of PFGE profiling. Cases were more likely to report the consumption of lemon, coriander and chicken wraps from a single national supermarket chain (Odds Ratio (OR) 46.40; 95% Confidence Interval (CI) 5.39-infinity; P=0.0002) or the consumption of chicken sandwiches, rolls, baguettes or wraps, bought outside the home and containing

coriander (OR 15.46; 95% CI 1.28-846; P=0.03). When these factors were included in a multivariate logistic regression model only the consumption of lemon, coriander and chicken wraps from a single national supermarket chain remained significantly associated with being a case.

This outbreak was identified through a common exposure reported by a number of patients and analytical epidemiology confirmed an association between this exposure and illness. Furthermore, molecular typing data demonstrated that, with the exception of one case, patients who reported this exposure were infected with a unique strain which was not observed in patients with contemporary VTEC O157 PT8 VT1+2 infections who did not report this exposure.

The fact that the organism was not isolated from any raw ingredients, product or processing equipment tested suggests that this outbreak occurred as the result of a single contamination event which had passed by the time the outbreak came to light. The epidemic curve adds weight to this hypothesis. The supermarket chain and the manufacturer acted swiftly to identify the possible cause and put additional controls in place, reducing the chance of further transmission. Analytical epidemiology, even when applied to a relatively small number of cases, can provide evidence where contamination of ingredients may be transient, or the organism has not been, or it unlikely to be, identified in a food product.

The investigation and response to this incident involved integrated working between HPA Local and Regional Services, Laboratories and Centres with hospital Trusts, Local Authority colleagues and the FSA.

Advisory Committee on the safety of Blood Tissues and Organs – vacancies for Chair and up to 19 Members

The Department of Health has recently decided to establish a new advisory non-departmental public body, the Advisory Committee on the Safety of Blood, Tissues and Organs (ACSBTO). The Committee will advise the United Kingdom (UK) Government and the Devolved Administrations as well as UK Health Departments on the most appropriate ways to ensure the safety of blood, cells, tissues and organs for transfusion/transplantation. Its remit will include providing advice on the microbiological safety of gametes and stem cells. There are vacancies for a Chair and up to 19 members to take up their posts in the autumn.

The Committee will meet four times a year in London. Additional days may be required for sub-committee work or for *ad hoc* meetings. Members are not paid a fee, but can claim travel and subsistence, at rates set centrally.

Further information is available on the Appointments Committee website at http://www.appointments.org.uk/view_vac.asp?ID=1675. The closing date for applications is Monday 27 August 2007.

Respiratory

Laboratory reports of respiratory infections made to Cfl from HPA and NHS laboratories in England and Wales: weeks 27-30/2007

Data are recorded by week of report, but include only specimens taken in the last eight weeks (i.e. recent specimens)

Table 1 Reports of influenza infection made to HPA Centre for Infections, by week of report: weeks 27-30/2007

Week Week ending	Week 27	Week 28	Week 29	Week 30	Total
	8/07/07	15/07/07	22/07/07	29/07/07	
Influenza A	2	–	1	2	5
Isolation	–	–	–	–	–
DIF	–	–	–	–	–
Four-fold rise in paired sera	–	–	–	–	–
PCR	–	–	1	–	1
Other	2	–	–	2	4
Influenza B	1	–	1	–	2
Isolation	–	–	1	–	1
DIF	–	–	–	–	–
Four-fold rise in paired sera	–	–	–	–	–
PCR	–	–	–	–	–
Other	1	–	–	–	1
Influenza (untyped)	–	–	–	–	–
Isolation	–	–	–	–	–
DIF	–	–	–	–	–
Four-fold rise in paired sera	–	–	–	–	–
PCR	–	–	–	–	–
Other	–	–	–	–	–

*DIF = Direct Immunofluorescence.

†'Other' = 'Antibody detection - Single high titre' or 'method not specified'.

Table 2 Respiratory viral detections by any method (culture, direct immunofluorescence, PCR, four-fold rise in paired sera, single high serology titre, genomic, electron microscopy, other method, other method unknown), by week of report: weeks 27-30/2007

Week	Week 27	Week 28	Week 29	Week 30	Total
Week ending	08/07/07	15/07/07	22/07/07	29/07/07	
Adenovirus*	33	26	32	24	115
Coronavirus	–	–	–	–	–
Parainfluenza†	9	6	5	6	26
Rhinovirus	4	1	1	–	6
Respiratory Syncytial Virus (RSV)	6	4	8	7	25

*Respiratory samples only. Excludes diagnoses made by electron microscopy (EM)

†includes parainfluenza types 1, 2, 3, 4 and untyped.

Table 3 Respiratory viral detections by age group: weeks 27-30/2007

Age group (years)	<1 year	1-4 years	5-14 years	15-44 years	45-64 years	≥65 years	Unknown	Total
Adenovirus*	12	21	12	48	17	3	2	115
Coronavirus	–	–	–	–	–	–	–	–
Influenza A	–	1	1	–	1	2	–	5
Influenza B	–	–	–	1	1	–	–	2
Parainfluenza†	6	11	–	4	4	1	–	26
Rhinovirus	5	1	–	–	–	–	–	6
Respiratory Syncytial Virus (RSV)	22	2	–	–	1	–	–	25

*Respiratory samples only.

†includes parainfluenza types 1, 2, 3, 4, and untyped.

Table 4 Laboratory reports of infections associated with atypical pneumonia, by week of report: weeks 27-30/2007

Week	Week 27	Week 28	Week 29	Week 30	Total
Week ending	08/07/07	15/07/07	22/07/07	29/07/07	
<i>Coxiella burnettii</i>	–	–	–	–	–
respiratory Chlamydia sp.*	4	9	4	4	21
<i>Mycoplasma pneumoniae</i>	9	6	13	8	36
Legionella sp.	13	27	21	17	78

*Includes *Chlamydia psittaci*, *Chlamydia pneumoniae*, and *Chlamydia* sp detected from blood, serum, and respiratory specimens.

Table 5a Reports of legionnaires' disease cases in England and Wales , by week of report: weeks 27-30/2007

Week	Week 27	Week 28	Week 29	Week 30	Total
Week ending	03/06/07	10/06/07	17/06/07	24/06/07	
Nosocomial	–	–	–	–	–
Community	5	17(1*)	13(1†)	11	46
Travel Abroad	7	10	7	1	25
Travel UK	1	–	1	5	7
Total	13	27	21	17	78
Male	10	20	14	17	61
Female	3	7	7	–	17

* Non-pneumonic case(s).

† 2006 case(s).

Seventy-seven cases of legionnaires' disease were reported with pneumonia and one with non-pneumonic infection; 61 males aged from 32 to 85 years and 17 females aged from 25 to 74 years. Forty-six cases had community acquired infection. Six deaths were reported in five males aged from 59 to 78 years and F 64y.

Thirty-two cases were travel associated: Spain (10), United Kingdom (7), Bulgaria (3), France (2), one from each of China, Cyprus, France/Spain, Greece, Italy, Kenya, Malta, South Africa, Tunisia , Turkey.

Table 5b Reports of legionnaires' disease cases by region of report in England and Wales: weeks 27-30/2007

Region	Nosocomial	Community	Travel Abroad	Travel UK	Total
North East	–	–	1	1	2
Yorkshire & Humber	–	5	4	–	9
East Midlands	–	3	1	2	6
East of England	–	5	1	–	6
London	–	12	–	–	12
South East	–	9(1†)(1*)	3	2	14
South West	–	–	3	–	3
West Midlands	–	8	6	1	15
North West	–	3	4	1	8
Wales	–	1	2	–	3
Total	–	46	25	7	78

* Non-pneumonic case(s).

†2006 cases.

HIV/Sexually Transmitted Infections (STIs)

- ▶ HIV in the United Kingdom : data to the end of June 2007
- ▶ New diagnoses of HTLV infection in England and Wales: 2002 to 2006
- ▶ HIV Drug resistance in the United Kingdom: data to end of 2005

HIV in the United Kingdom : data to the end of June 2007

The current *HIV New Diagnoses Quarterly Surveillance Tables (data to the end of June 2007)* are now available on the HPA website to download:

http://www.hpa.org.uk/infections/topics_az/hiv_and_sti/hiv/epidemiology/hars_tables.htm

The tables include data on reports of new HIV and AIDs diagnoses and deaths among HIV-infected individuals to the end of June 2007 in the UK (excluding Channel Islands), with breakdowns by exposure category, country and SHA of diagnosis, age at diagnosis, ethnicity, and children born in the UK to HIV-infected women .

A full quarterly summary is not appearing in this issue of the *Health Protection Report* as much of the data will be covered in the forthcoming HIV and STI Annual Report in November.

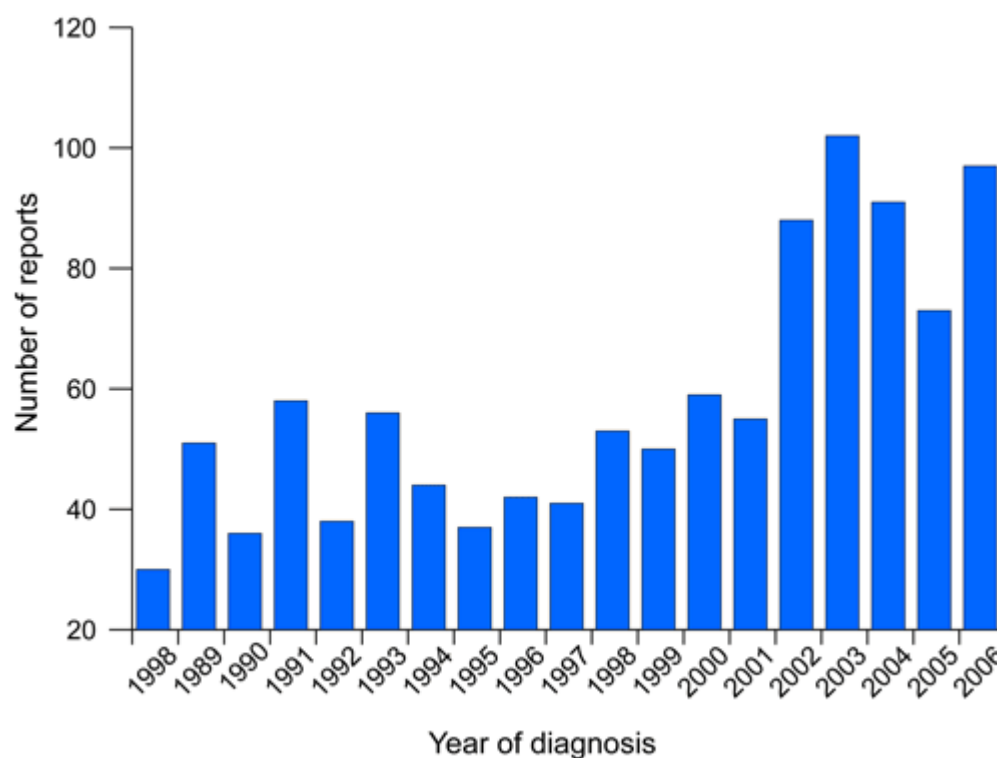
New diagnoses of HTLV infection in England and Wales: 2002 to 2006

Reports received by the end of June 2007

The Health Protection Agency's Centre for Infections undertakes the surveillance of Human T cell lymphotropic virus (HTLV), a retroviral infection. HTLV types I and II are transmissible through breast feeding, sexual contact, and blood transfusion, with HTLV-II particularly associated with injecting drug use in Europe . HTLV-I is endemic in the Caribbean, Japan , South America, and parts of Africa with HTLV-II found among some native American groups. An infected individual's lifetime risk of developing disease is low (less than 5%). Clinically, HTLV-I infection may cause adult T cell lymphoma (ATLL), HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP) and other inflammatory conditions [1]. There is some evidence that HTLV-II infection is associated with neurological and lymphoproliferative disorders [2].

Surveillance of new diagnoses of HTLV infection in England and Wales began in the late 1980s (figure 1), and was enhanced in 2002 by the routine follow-up of all laboratory reports through clinicians [3]. Additionally, in August 2002, the National Blood Service (NBS) introduced testing of all blood donations for HTLV in England and Wales, with reports of any infections identified passed to the routine surveillance scheme.

Figure Number of HTLV reports by year of diagnosis: 1988 to 2006



This update presents surveillance findings for new HTLV diagnoses made in England and Wales between 2002 and 2006.

During 2006 there were 97 new HTLV diagnoses made in England and Wales . Of these individuals 32 (33%) were male and 64 (67%) female (sex was unreported in one individual and is awaiting follow up). Median age at diagnosis for men was 51 years and for women was 58 years. Where available (76) 64 reports were from individuals infected with HTLV-1, 5 with HTLV-2 and seven were coinfectd.

A clinician report, collecting detailed information, was received for 43 (44%) individuals diagnosed during 2006. Where probable route of infection was reported (31/43) seven were infected heterosexually, four through mother to infant transmission, 19 through either route, and one through blood transfusion. Probable country of infection was reported for 15 individuals, of whom seven were infected in the Caribbean and five were infected in the UK .

Where reported (39/43) seven individuals were tested as blood donors, 24 because they were symptomatic, one had a positive partner, two had a positive blood relative and four were tested for other reasons. Clinical presentation at diagnosis was reported for 38 (88%) individuals with clinician reports, of whom seven were asymptomatic, seven had ATLL, nine had HAM/TSP and twelve had non-HTLV symptoms. Of all 97 individuals diagnosed in 2006, five are known to have died.

References

1. Kaplan JE, Khabbaz RF. The epidemiology of human T-lymphotropic virus types I and II. *Rev Med Virol* 1993; **3** : 137-48.
2. Hall WW, Ishak R, Zhu SW, Novoa P, Eiraku N, Takahashi H *et al* . Human T lymphotropic virus II (HTLV-II): epidemiology, molecular properties and clinical features of infection. *J AIDS* 1996; **13** (suppl 1):S204-214.

3. Payne LJC, Tosswill JHC, Taylor GP, Zuckerman M, Simms I. In the shadow of HIV – HTLV infection in England and Wales 1987-2001. *Commun Dis Public Health* 2004; **7**(3): 200-206

HIV Drug resistance in the United Kingdom: data to end of 2005

This report is an update on the prevalence of HIV drug resistance in the United Kingdom (UK) in both individuals who have had no previous exposure to antiretroviral therapy (drug-naïve) and those who have received treatment at some point in the past (drug-experienced) [1]. The systematic collation of HIV resistance data from HIV infected drug-naïve individuals is crucial to understanding the epidemiology of transmitted drug resistance, whilst data from those already receiving antiretroviral drugs provides indirect evidence of the contribution drug resistance makes to virological failure. All findings are based upon genotypic reports received by the UK HIV Drug Resistance Database founded in 2001, which aims to collect all tests conducted as part of routine clinical care across the UK [2].

Resistance conferring mutations are classified according to the class of antiretroviral agent to which they confer a reduced sensitivity, in accordance with the International AIDS Society, United States guidelines [3] as well as additional mutations agreed by virologists within the UK Collaborative Group on HIV Drug Resistance. The three classes include: nucleoside/nucleotide reverse transcriptase inhibitors (NRTI); non-nucleoside reverse transcriptase inhibitors (nNRTI); and protease inhibitors (PI). This classification is likely to be an oversimplification given the complex relationship between single and multiple mutations on drug susceptibility and clinical outcome. With the exception of most nNRTI mutations, a single drug resistant mutation does not result in resistance to all drugs within a particular class [3], therefore these data may overestimate the extent of resistance.

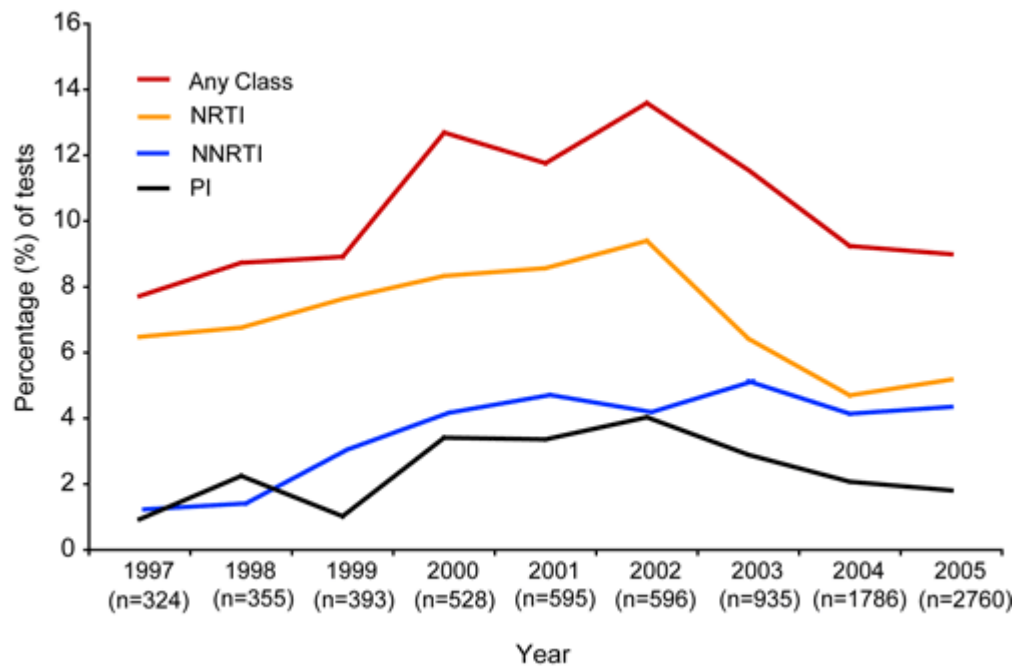
Results

This analysis included 8272 resistance tests on drug-naïve and 11608 resistance tests on drug-experienced patients reported until the end of 2005. Linkage to clinical data to ascertain and verify treatment status is, however, incomplete for 2005. Estimates of the prevalence of drug-naïve resistance are based on the single earliest test per patient, while estimates in drug-experienced patients are based on the single latest test per patient, per calendar year. The data presented here excludes those infected vertically as well as children under the age of 16 years as their resistance characteristics are likely to be distinct.

Drug Naïve

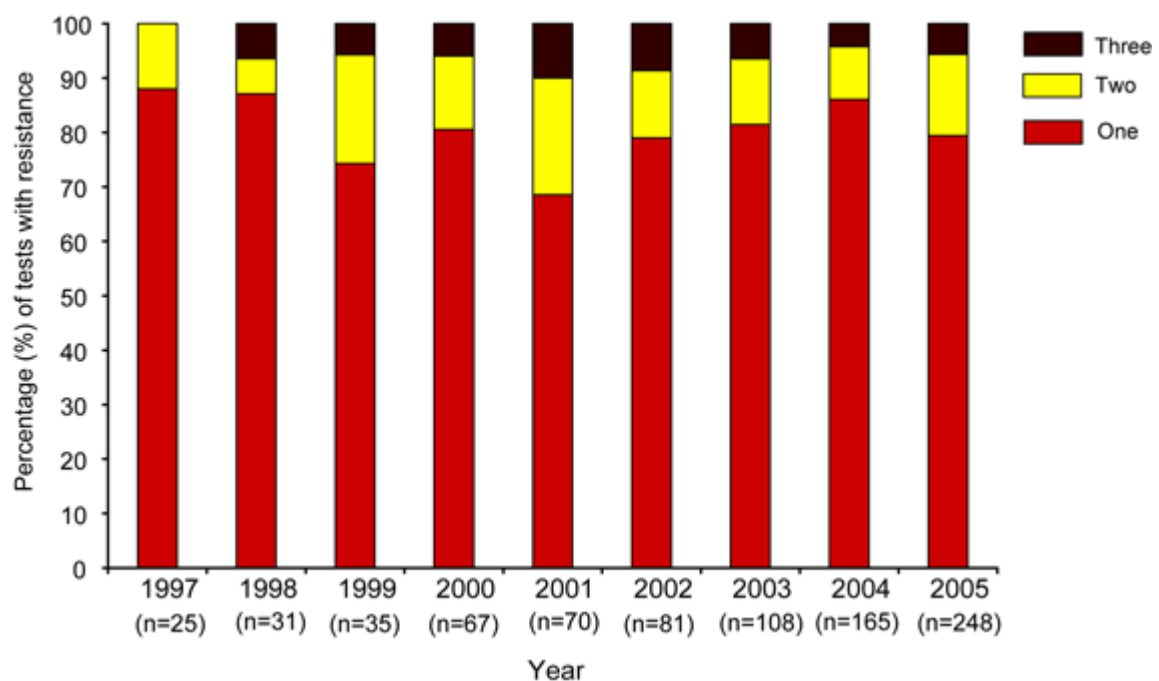
The numbers of test carried out for drug-naïve individuals has increased dramatically over recent years, from 528 in 2000, to 2760 in 2005. The increase in the overall number of tests has been closely accompanied by an overall fall in the proportion of tests harbouring any resistance mutations from a peak of 13.6% in 2002 to 9.0% in 2005 (figure 1). The fall in baseline resistance has mainly been driven by a specific decline in NRTI resistance, decreasing from a high of 9.4% in 2002 to 4.7% in 2004, but increasing slightly to 5.2% in 2005. The prevalence of PI resistance has continued to fall, but at a lower rate from 4.0% in 2002 to 1.8% in 2005, while nNRTI resistance has been largely stable since 2003.

Figure 1 Proportion and characteristics of HIV drug resistance in drug-naïve patients by calendar year



The degree to which an individual's therapy is compromised can be expressed in terms of the number of antiretroviral classes to which their virus has shown resistance. The proportion of tests harbouring mutations to any class of drug has been steady over time at around 10%. Of those 830 samples that have harboured drug resistant mutations (1997 to 2005), the majority (668, 80.5%) showed resistance to only one single class, with 112 (13.5%) and 50 (6.0%) samples showing resistance to two and three classes respectively. The relative proportions of those harbouring mutations to one, two, and three classes over time are shown in figure 2.

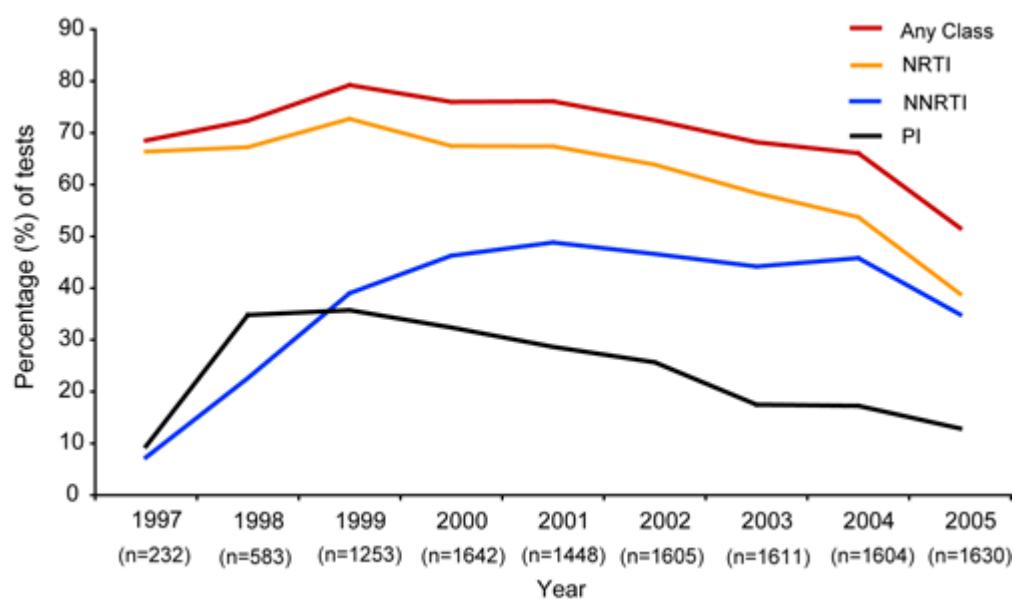
Figure 2 Proportion of HIV drug resistance in drug-naïve patients by calendar year, as a proportion of those that exhibited resistance: number of antiretroviral classes compromised



Drug Experienced

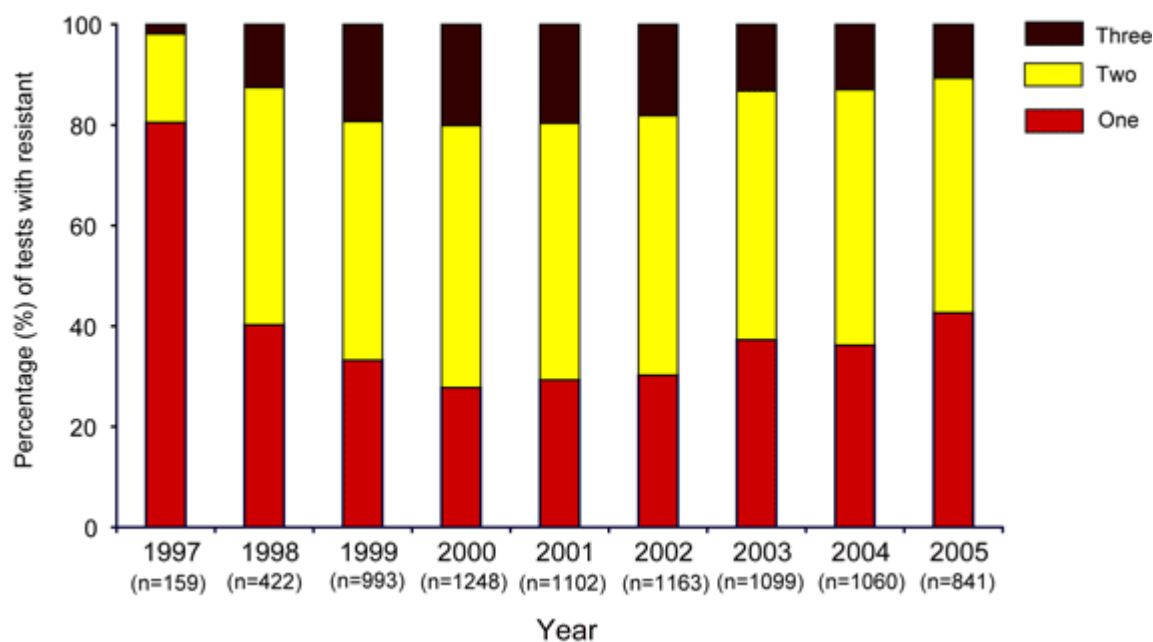
The number of resistance tests reported each year in drug-experienced individuals has remained at around 1600 per year since 2000. The overall prevalence of drug resistance to any class of drug has had a steadier, if less pronounced, decrease over time compared to those drug-naïve individuals. In 1999, 79.3% of those who experience virological rebound had resistance to at least one class of drug, which by 2005 had fallen to 51.6% (figure 3). As with drug-naïve individuals, this is largely due to a sustained decrease in NRTI resistance. Between 2004 and 2005, however, there has been a steep decline in resistance to all three classes falling from 53.7% to 38.9% in NRTIs, 45.8% to 34.9% in nNRTIs and 17.3 to 12.9% in PIs.

Figure 3 Proportion and characteristics of HIV drug resistance in drug-experienced patients by calendar year



Resistance to multiple antiretroviral classes has also decreased over time. In 2000, resistance to all three classes of anti-retroviral therapy (ART) commonly used as part of highly active anti-retroviral therapy (HAART) reached a maximum of 20.1% of those with resistance to all 3 classes, and steadily decreased to just 10.7% by 2005 (figure 4). Resistance to two classes has also decreased from a high of 52.1% of those with resistance in 2000, to 46.7% in 2005. Resistance to a single class has therefore accounted for an increasing proportion of drug resistance in experienced patients, rising from 27.8% in 2000, to 42.7% in 2005. The resistance levels presented here are, however, reflective of those patients who have experienced virological failure and have received a resistance test; they do not represent all those on therapy, many of whom are achieving viral suppression with no presumed resistance. In addition these data also reflects changes in the availability and the targeting of resistance testing.

Figure 4 Proportion of HIV drug resistance in drug-experienced patients by calendar year, as a proportion of those that exhibited resistance: number of antiretroviral classes compromised



Discussion

The number of resistance tests performed on drug-naïve individuals each year has rapidly increased from 528 tests in 2000 to 2760 in 2005, due in part to the change in the BHIVA guidelines, recommending a baseline resistance test for all newly diagnosed individuals [4]. This increase has been accompanied by a dramatic and sustained fall in the proportion of samples harbouring resistance mutations. Prior to the revised BHIVA guidelines, HIV resistance testing was generally focused on specific risk groups or centres where testing was routine, generating potential bias within the dataset. Therefore the data presented here for more recent years are likely to better reflect the national pattern of HIV drug resistance. Also accounting for the reduction in resistance in drug naïve patients is the fact that heterosexual transmission now accounts for the largest proportion of newly diagnosed infections in the UK [5]. In 2005 there were 3194 heterosexually acquired infections out of a total 7645 newly diagnosed infections [5]. Almost 3000 of these new infections were probably acquired in Africa where antiretroviral exposure is much more limited, and the presence of pre-existing resistance is therefore lower than for those infected in the UK. Analyses are planned to examine trends in transmitted drug resistance within each key exposure category within the UK.

Resistance mutations are common in those who experience ART failure, however much of this resistance arises from a subgroup of people who initially started nucleoside mono- or dual- therapy between 1987 and 1996. In 2004, over a third of tests performed showed no evidence of resistance; by 2005 this proportion had reached almost a half, suggesting that there are other increasingly important causes of virological failure. However, of those treatment-experienced individuals who experienced virological failure in 2005 and harboured a resistant mutation, 10.7% were resistant to all three classes of antiretroviral agents. Surveillance of HIV drug resistance is required not only to monitor time trends in transmitted resistance, but also to assess the likely requirement for new classes of antiretroviral agents in highly drug experienced patients.

The data indicate that the proportion of individuals, both drug-naïve and drug-experienced, with evidence of drug resistance (among those tested) is decreasing. Furthermore, when resistance is detected it is frequently to a single drug class only. However, the levels of transmitted drug resistance remain significantly high; highlighting the importance of targeted

health promotion campaigns at both HIV uninfected and infected individuals, reinforcing safe sex messages.

* In reverse transcriptase, any mutation at G190 or T215. In protease, V32I and I47V/A in combination, or seven or more minor lopinavir mutations, count as a single major protease mutation.

References

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Standard Method updates

The development of National Standard Methods and Algorithms is undertaken under the auspices of the Health Protection Agency (HPA) in conjunction with the NHS and the National Public Health Service for Wales (NPHSW), and with professional societies including the Association of Medical Microbiologists, Association of Clinical Microbiologists, Institute of Biomedical Science, Clinical Virology Network, and the Scottish Microbiology Association. Over 200 methods are available from the HPA Standards Unit website which covers bacteriology, virology/serology, food, water, and environmental microbiology.

National standard methods are educational and encourage participating laboratories to retain an enquiring attitude. In addition, they are designed to help ensure that laboratories provide a good clinical and public health microbiology service. Evidence of using standard operating procedures is an essential requirement of accreditation schemes. For more information, please contact the HPA Standards unit, email: <standards@hpa.org.uk>.

Monthly content update - August 2007

QSOP 33 European Directive on *in vitro* diagnostic medical devices (98/79/EC) (re-issue)

<http://www.hpa-standardmethods.org.uk/documents/qsop/pdf/qsop33.pdf>

BSOP 29 Investigation of specimens for MRSA (re-issue)

<http://www.hpa-standardmethods.org.uk/documents/bsop/pdf/bsop29.pdf>

VSOP 2 Gastroenteritis: Sporadic Cases (re-issue)

<http://www.hpa-standardmethods.org.uk/documents/vsop/pdf/vsop2.pdf>

VSOP 17 Isolation of Herpes Simplex virus associated with Herpes Genitalis (re-issue)

<http://www.hpa-standardmethods.org.uk/documents/vsop/pdf/vsop17.pdf>

VSOP 22 Immunofluorescence and isolation of viruses from respiratory samples (new issue)

<http://www.hpa-standardmethods.org.uk/documents/vsop/pdf/vsop22.pdf>