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Aventis Pasteur recalls VAQTA hepatitis A vaccines

The United Kingdom (UK) Medicines Control Agency (MCA, < <http://www.mca.gov.uk/>>) in co-ordination with all other member states of the European Union (EU) issued a Class II Drug alert on Monday 3 December, announcing the recall of the VAQTA hepatitis A vaccines marketed in Europe by Aventis Pasteur MSD and manufactured by Merck in the United States. The recall applies to both adult and paediatric preparations (launched in 1997 and 1998 respectively) and to all batches of vaccine currently within their expiry date. Previous batches that have now expired (including those marketed under their generic name 'Hepatitis A vaccine, purified, inactivated, for adults') may also have been affected. Those holding stocks of vaccine are requested to quarantine affected batches. Aventis Pasteur MSD will contact customers shortly to arrange return of unused doses. For medical queries contact Aventis Pasteur MSD's vaccine information service on the special freephone number 0800 587 2390. (NB: This number should only be used for medical enquiries regarding VAQTA).

The antigen content in some pre-filled syringes was found in Germany to be below the established minimum specification on re-testing of a sample of vaccine doses. It is therefore possible that some patients who have received any of the formulations of VAQTA described above may be inadequately protected against infection with hepatitis A virus and/or have reduced duration of protective immunity. The problem with vaccine potency appears to be sporadic, possibly related to the filling process, which means that it is not possible to predict which vaccine recipients might be inadequately protected. Individuals who have received VAQTA products can be reassured that the vaccine is not being recalled for reasons of safety.

No substantial threat to public health is anticipated as most hepatitis A vaccinations are given for short term low-risk exposures during travel abroad. Hepatitis A virus transmission has been effectively reduced in most member states of the EU by the high levels of hygiene and sanitation, and vaccination has made a very small contribution to its epidemiology in most countries (1).

No true vaccine failures have been reported to the UK MCA or regulatory authorities in other countries. PHLS surveillance data include very limited information on vaccination status, but three cases of hepatitis A virus infection have been reported in previously vaccinated individuals in England and Wales, one in 1997 and two in 1998. No outbreaks have been reported to CDSC that could be traced to failure of vaccine. All possible vaccine failures should be reported to the MCA.

Individuals who have received VAQTA in the past and require ongoing protection can be re-vaccinated

with an alternative brand of vaccine or tested for serological evidence of immunity. The response from public health authorities to the VAQTA recall has varied in different countries. Ireland and the UK are advocating re-vaccination of recipients of VAQTA who are at ongoing risk while Germany has proposed serological testing prior to re-vaccination if indicated.

The UK Department of Health has made recommendations (2) which apply only to those at continuing risk of hepatitis A who have been immunised with VAQTA products:

- Those who have previously been immunised with these products should start their immunisation schedule again with another hepatitis A vaccine product.
- Those who have been immunised with one of these products in anticipation of travelling to areas with higher incidence of hepatitis A in the near future, for example for a 'winter sun' holiday, should be re-immunised immediately, with another product. Hepatitis A vaccine is effective prevention even if given immediately before departure (3).
- Those who have received both a VAQTA product and another hepatitis A vaccine product as part of their immunisation should, for continuing protection, receive a further dose of another hepatitis A vaccine product. A period of at least six months should have elapsed between the two doses of the alternative vaccines (4).

Implementing these recommendations may be particularly difficult in certain hard to reach high-risk groups who are at ongoing risk, such as injecting drug users (1).

On the basis of the information that has been made available, most recipients of VAQTA are likely to have adequate antibody levels. Small studies of adverse reactions to three doses of the same vaccine, but with a lower antigen content than adult VAQTA, did not find increased reactogenicity on the third dose (5,6). Up to 40% of subjects receiving a different vaccine following priming with VAQTA, however, experienced a local reaction (7). Adverse events that occur following re-vaccination should be reported in the usual way to the MCA.

1. Crowcroft NS, Walsh B, Davison K, Gungabissoon U. Guidance for control of hepatitis A virus infection. *Commun Dis Public Health* 2001; **4**(3): 213-27.

2. Department of Health. *Hepatitis A vaccine (CEM/CMO/2001/16)*. London: Department of Health, 4 December 2001. Available from <www.doh.gov.uk/cmo/cmo01_16.htm>.

3. CDSC. Human normal immunoglobulin (HNIG): lack of availability for travellers. *Commun Dis Rep CDR Wkly* 2000; **10** (34): 301.

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5. Jilg W, Bittner R, Schätzl H, Raßhofer R, Schmidt M, Deinhardt F. The immune response to different doses of inactivated hepatitis A vaccine. *J Hepatol* 1993; **18** (supplement 2): S38-40.

6. Carlsson R-M, Claesson BA, Iwarson SA. Dose response study of an inactivated hepatitis virus vaccine. *J Hepatol* 1993; **18** (supplement 2): S41-5.

7. Clarke P, Kitchen N, Souverbie F. A randomised comparison of two inactivated hepatitis A vaccines, Avaxim and Vaqta, given as a booster to subjects primed with Avaxim. *Vaccine* 2001; **19**: 4429-33.

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First influenza isolate in United Kingdom this season

The first isolate of influenza A (H3N2) this winter has been obtained from a nose and throat swab from a 5 year old child in the south of England. The onset of infection was during week 46 (week ending 18 November). The isolate has been antigenically characterised by the Enteric, Respiratory, and Neurological Virus Laboratory (ERNVL), Colindale, as influenza A (H3N2) Panama-like, which is one of the strains included in the current season's influenza vaccine.

Influenza A (H3N2) has also been detected in two hospital-derived specimens from the south of England using PCR. These have yet to be characterised further by ERNVL.

Indicators of acute respiratory virus activity, including influenza, continue to remain at low levels, both within the United Kingdom (UK), and across Europe. In England, general practitioner consultation rates of acute bronchitis are continuing to increase but remain within the range expected for the time of year. Laboratory reports of respiratory syncytial virus (RSV) and *Mycoplasma pneumoniae* made to CDSC remain low, but are expected to increase over the next few weeks.

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Outbreak of parainfluenza

Manchester PHL has reported an outbreak of respiratory virus infection associated with a primary school in the north of England. Twenty-five children aged 8 to 10 years showed upper and lower respiratory tract symptoms, four of whom were positive for parainfluenza virus 2, parainfluenza virus 3, RSV, or *Bordetella pertussis*.

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Summary report of UK influenza surveillance, 2000/01

A report summarising influenza and other acute respiratory virus activity during 2000/01 is being published this week as a supplement to the *CDR Weekly*. It details the key features of clinical and virological activity within the UK, with accompanying graphs and interpretation.



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Consultation on NHS screening standards for infectious diseases in pregnancy

Comments are now being invited on newly developed draft screening standards for infectious diseases in pregnancy. The offer of screening for rubella antibody, syphilis, HIV and hepatitis B is an integral part of antenatal care in England. In accordance with its remit to advise on standards and monitoring arrangements for antenatal screening programmes, the Antenatal Subgroup of the UK National Screening Committee has considered screening standards for infectious diseases in pregnancy. Both generic standards and specific standards for each of the four diseases have been developed in consultation with the Public Health Laboratory Service and relevant expert groups: the Expert Advisory Group on AIDS, Advisory Group on Hepatitis, and the Joint Committee on Vaccination and Immunisation.

Comments are invited, especially from all professionals involved in antenatal screening, including doctors, midwives, and laboratory staff, and lay groups concerned with antenatal care. The draft standards are available at <www.nsc.nhs.uk/hottopic/hottopic_ind.htm>

All comments should be sent to Helen Janecek, Project Manager, UK National Screening Committee – Antenatal Subgroup, Royal College of Obstetricians and Gynaecologists, 27 Sussex Place, Regent's Park, London NW1 4RG, email: hjanecek@rcog.org.uk by 31 January 2002.

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Prolyliminopeptidase-negative isolates of *Neisseria gonorrhoeae*

The detection of preformed enzymes is used to identify *Neisseria* spp. cultured from clinical specimens

in a number of commercial systems, most commonly the API NH, Gonochek II and Neisseria PET kits. *Neisseria gonorrhoeae* is identified in these kits by the coloured reaction product of the prolyliminopeptidase enzyme (1). In a previous study in the United Kingdom only two of 398 *N. gonorrhoeae* isolates gave negative results in the prolyliminopeptidase enzyme test (2).

During the last five weeks the Gonococcus Reference Unit (GRU) of the PHLS Genitourinary Infections Reference Laboratory has received 17 isolates from laboratories requesting confirmation of identity because of negative prolyliminopeptidase test results in the API NH kit (16 isolates) or the Gonochek II kit (one isolate). All 17 isolates were confirmed by the GRU as *N. gonorrhoeae* using the sugar utilisation test in CTA medium (Becton Dickinson, Oxford, UK) and the Phadebact Monoclonal GC Test (Launch Diagnostics, Longfield, UK).

These isolates were cultured from specimens taken between 11 October and the 13 November throughout England (six in London, four in Manchester, two in Brighton and one each in Birmingham, Gloucester, Stevenage, Stockport and Swindon). Fifteen patients were male and two were of unstated gender. Ten isolates were from the urethra, four were from the rectum, and three from the throat. All isolates belonged the WII/III serogroup. Twelve strains have so far been characterised with regard to auxotype, 11 of which were prototrophic, and was provisionally classified as arginine-requiring. Restriction fragment length polymorphism analysis of PCR-amplified *opa* gene fragments (3) has revealed only minor differences among the nine isolates tested so far.

These results suggest the widespread dissemination of highly related prolyliminopeptidase-negative strains of *N. gonorrhoeae* around England. Laboratories obtaining inconclusive or dubious identifications with kits that use a prolyliminopeptidase test should use an additional, non-biochemical, identification system such as the Phadebact Monoclonal GC test to confirm the identity of *N. gonorrhoeae* isolates.

1. D'Amato RF, Eriquez LA, Tomfohrde KM, Singerman E. Rapid identification of *Neisseria gonorrhoeae* and *Neisseria meningitidis* by using enzymatic profiles. *J Clin Microbiol* 1978; **7**: 77-81.

2. Dealler SF, Gough KR, Campbell L, Turner A, Hawkey PM. Identification of *Neisseria gonorrhoeae* using the Neisstrip rapid enzyme detection test. *J Clin Pathol* 1991; **44**: 376-9.

3. Palmer HM, Leeming JP, Turner A. Investigation of an outbreak of ciprofloxacin-resistant *Neisseria gonorrhoeae* using a simplified *opa*-typing method. *Epidemiol Infect* 2001; **126**: 219-24.

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	Number of reports received					Total reports
	44/01	45/01	46/01	47/01	48/01	44-48/01
Adenovirus (excluding EM faeces)	8	23	3	18	15	67
Coronavirus	–	–	–	–	–	–
Influenza A	–	3	3	19	6	31
Influenza B	–	1	4	22	5	32
Parainfluenza	8	18	13	31	15	85
RS virus	30	94	143	475	187	929
Rhinovirus	–	1	2	6	–	9
<i>Chlamydia sp</i>	8	5	1	5	5	23
<i>Coxiella burnetti</i>	2	1	–	1	2	6
<i>Legionella sp</i>	3	6	3	4	8	24
<i>Mycoplasma pneumoniae</i>	12	19	2	31	18	82

Adenovirus (excluding types 40, 41, group F, EM faeces): 67 cases were reported. Thirty-four patients had eye infections.

Coronavirus: no cases were reported

Influenza A: 31 cases were reported. Northern and Yorkshire region reported 12 cases, Trent one, North West nine, South east four, South West one. Twenty-six per cent of cases were aged less than 15 years.

Influenza B: 32 cases were reported. M 67y had recent foreign travel. Northern and Yorkshire fifteen, North West nine, Eastern one, South East three, South West two, Wales two. Twenty-five per cent of cases were aged less than 15 years.

Parainfluenza (type 1,11; type 2,25; type 3,30; type 4,1; untyped 18): 85 cases were reported. 1 patient had pneumonia. 3 patients had bronchiolitis. M 8mths had immune deficiency; M 10mths who had hospital acquired infection; two males 5y, F 5y and F 7y were infected in an outbreak. Northern and Yorkshire eleven, Trent twelve, West Midlands six, North West 32, Eastern four, London one, South East 14, South West four, Wales one. Fifty-nine per cent of cases were aged less than 1 year.

Respiratory syncytial virus: 929 cases were reported. 139 patients had bronchiolitis. M age n/k had severe combined immune deficiency syndrome (SCIDS); F 8y was infected in an outbreak; F 75y had recent foreign travel. Northern and Yorkshire 150 cases, Trent 49, West Midlands 68, North West 506, Eastern 71, London 14, South East 31, South West 27, Wales 13. Seventy-three per cent of cases were aged less than 1 year.

Rhinovirus: 9 cases were reported. Northern & Yorkshire two, Trent one, West Midlands three, South East three. Forty-four per cent of cases were aged less than 1 year.

Respiratory chlamydia (*C. psittaci*, 2 ; *C. pneumoniae*, 5; *Chlamydia spp*, 4): 24 cases were reported. Three patients had pneumonia.

Coxiella burnetii: six cases were reported. Northern & Yorkshire one, West Midlands one, Eastern one, South West two, Wales one.

Legionella: 24 cases were reported with pneumonia. Twenty-two were male aged 31 to 86 years and two were female aged 44 and 54 years. Three males, aged 60, 65 and 66 years, died. Eight cases were associated with travel: Spain (2), England (1), Turkey (1), France (1), Italy (1), Sri Lanka (1) and one case travelled to both Seychelles and Mauritius. Sixteen cases, one female aged 44 years and fifteen males aged between 31 and 66 years, had community acquired infection, including three of four males, aged 31, 37 and 52 years, associated with a cluster in North West London. One case, a 60 year old male, had a hospital acquired infection.

Mycoplasma pneumoniae: 82 cases were reported. 15 patients had pneumonia. M 5y had cervical lymphadenopathy; F 4y had joint swelling and urticaria; F 68y had neutropaenia; F 74y with Guillain-Barre syndrome. Northern & Yorkshire (10 cases), Trent (2 cases), West Midlands (3 cases), North West (13 cases), Eastern (16 cases), London (2 cases), South East (11 cases), South West (18 cases), Wales (7 cases). 40% of cases were aged less than 15 years.

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Common animal associated infections, England and Wales: laboratory reports, weeks 44-48/01

Organism	Total reports for weeks 44-48/01		Cumulative totals for weeks 01-48	
	2001*	2000	2001*	2000
<i>Borrelia burgdorferi</i> **#	63	18	234	297
<i>Leptospira hardjo</i> **##	–	1	4	8
<i>Leptospira icterohaemorrhagiae</i> **##	1	–	5	22
<i>Leptospira other</i> **##	5	3	23	13
<i>Pasteurella haemolytica</i>	3	–	6	3
<i>Pasteurella multocida</i>	19	25	261	217
<i>Pasteurella pneumotropica</i>	6	1	9	3
<i>Pasteurella spp</i>	7	9	67	56
<i>Toxocara canis</i>	–	–	–	3
<i>Toxocara cati</i>	–	–	–	–
<i>Toxocara spp</i>	–	1	3	4
<i>Toxoplasma gondii</i>	6	2	30	34
<i>Toxoplasma spp</i>	6	4	53	50

* provisional data; ** by specimen date; # Lyme Disease Reference Laboratory and CDSC;

Leptospira Reference Laboratory and CDSC

Common imported infections, England and Wales: laboratory reports, weeks 44-48/01

Organism	Total reports for weeks 44-48/01		Cumulative totals for weeks 01-48	
	2001*	2000	2001*	2000
Arbovirus	–	–	–	1
Dengue virus	1	–	1	4
<i>Ascaris</i> spp	21	11	120	110
Hookworm (unspecified)	8	6	56	64
<i>Ancylostoma duodenale</i>	–	–	–	–
<i>Necator americanus</i>	–	–	–	–
<i>Leptospira</i> spp	1	1	11	16
<i>Hymenolepis diminuta</i>	–	–	1	1
<i>Hymenolepis nana</i>	–	4	42	23
<i>Hymenolepis</i> spp	–	–	1	–
<i>Schistosoma haematobium</i>	5	1	50	56
<i>Schistosoma intercalatum</i>	–	–	–	–
<i>Schistosoma mansoni</i>	5	1	20	12
<i>Schistosoma</i> spp	3	4	33	35
<i>Strongyloides stercoralis</i>	2	2	27	15
<i>Strongyloides</i> spp	–	–	2	4

* provisional data

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'Public health doctors should not lead public health' – a debate

A meeting of the Section of Epidemiology and Public Health of the Royal Society of Medicine is to be held from 18.00 to 19.30 pm on Thursday 13 December. There will be a debate entitled '*Public health doctors should not lead public health*'. The motion will be proposed by Professor Klim McPheerson, MRC Health Services Research Collaboration, University of Bristol. The motion will be opposed by Quentin Sandifer, Director of Public Health, Iechyd Morgannwg Health Authority, seconded by Ros Sanwell-Smith, president of the Section of Epidemiology and Public Health. Registration with mince pies and mulled wine is at 17.30. The meeting will be held at The Royal Society of Medicine, 1 Wimpole Street, London W1G 0AE. For further information and registration contact Jennifer Mullins, The Royal Society of Medicine, 1 Wimpole Street, London W1G 0AE; tel: 020 7290 3918; fax: 020 7290 2989, email: epidemiology@rsm.ac.uk or book online at www.rsm.ac.uk/epidemiology by 7 December 2001.

Flights of hazard

A one-day conference organised by the Royal Society of Medicine about health risks of international travel will be held on Monday 21 January 2002. The programme will consist of four sessions, the first detailing what can be done before you travel, including where information can be obtained, medical fitness to fly, immunisation and prophylaxis issues. Mental health on board the aircraft, the cabin environment, medical kits on board, and medico legal issues will be covered in the second session. The two afternoon sessions will look at sleep and jetlag, transportation of the critically ill patient, the healthy and sick returning traveller, and the topical issue of deep vein thrombosis. The meeting will be held at The Royal Society of Medicine, 1 Wimpole Street, London W1G 0AE. Pre-registration is necessary. For further information and registration contact Natalie Barter, Academic Conference Department, The Royal Society of Medicine, 1 Wimpole Street, London W1G 0AE; fax: 020 7290 2977; email: natalie.barter@rsm.ac.uk

CDR Supplement

CDR Supplement

Influenza surveillance in the United Kingdom: October 2000 to May 2001

NL Goddard, CA Joseph, M Zambon, M Nunn, D Fleming, JM Watson



Influenza surveillance in the United Kingdom: October 2000 to May 2001

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Summary

The 2000/01 influenza season was characterised by low levels of activity associated with influenza A (H1N1) and influenza B throughout the United Kingdom. Respiratory syncytial virus and acute bronchitis also remained at low levels. Consultation rates with general practitioners for influenza-like illness remained within the range of 'normal seasonal activity', with older children and young adults predominantly affected. A large number of outbreaks were reported. Over the New Year period there were low attack rates for respiratory infections, especially in the elderly, and only limited disruption to health services.

Keywords: *influenza, epidemiology, outbreak*

Introduction

Surveillance of influenza and other acute respiratory virus activity provides a timely assessment of the nature and extent of circulating viruses. Data are communicated to health professionals to inform decisions when there are high levels of virus in circulation. Circulating strains of influenza are monitored and compared with previous strains and the current vaccine. These observations are used to contribute to the decision about the vaccine composition for the following year. At the end of the season, the impact of influenza on morbidity and mortality is assessed and compared with previous years.

Methods

Details of data used in influenza surveillance in England and Wales have been described in detail previously^{1, 2, 3} and are summarised in table 1. Thresholds – used to describe different levels of influenza activity based on consultation rates with general practitioners in different sentinel schemes in England, Wales, and Scotland – have also been previously described⁴.

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Results

Clinical

Royal College of General Practitioners (RCGP) Weekly Returns Service

In the Royal College of General Practitioners (RCGP) sentinel surveillance scheme, weekly general practitioner (GP) consultations for influenza and 'influenza-like illness' (ILI) remained below baseline (less than 50 new episodes per 100 000 population) until week 5/01 and peaked at 81/100 000 in week 6/01. This rate remained at the lower end of the range for 'normal seasonal activity' of 50-200/100 000 population. Rates declined rapidly and returned to baseline levels in week 10/01 (figure 1)

Consultation rates were highest in the RCGP central region (100/100 000) while the lowest peak was in the RCGP northern region (63/100 000). The highest consultation rates were in children aged 5 to 14 years (112 /100 000 in week 6) followed by people aged 15 to 44 years (91/100 000 in week 5) (figure 2).

GP consultation rates for acute bronchitis peaked in 01/01 with a rate of 213/100 000 population. This rate was substantially lower than the peak seen during the 1999/00 season (380/100 000). Consultation rates were highest among children aged 0 to 4 years (773/100 000 in week 50), followed by people aged 65 years or over (430/100 000 in 01/01). Again, these rates were well below the peak rate seen in 1999/00 (1061/100 000 in people aged 65 years or over). GP consultation rates for 'total respiratory disease' also remained lower than seen during the 1999/2000 season with a peak rate of 939/100 000, compared with 1118/100 000 in 99/00.

PHLS Communicable Disease Surveillance Centre (CDSC) Wales

Consultation rates in the sentinel GP scheme co-ordinated by CDSC Wales remained within the range for 'baseline activity' of less than 25/100 000 population for the entire 2000/01 season. Rates peaked at 18/ 100 000 in week 10/01 (figure 3).

Scotland

In the sentinel GP scheme co-ordinated by the Scottish Centre for Infection and Environmental Health (SCIEH),

Table 1 Data sources for influenza surveillance in Britain			
Clinical	Virological	Deaths	Other
Royal College of General Practitioners (RCGP) Weekly Returns Service ² <i>Weekly rates per 100 000 population for influenza and flu-like illness</i>	Enteric, Respiratory and Neurological Laboratory (ERNVL) Influenza Section (UK WHO National Centre) ⁴ <i>Analysis of influenza strains: subtyping, antigenic and genetic characterisation of virus</i>	Office for National Statistics <i>Weekly deaths by age and cause</i>	Reports of outbreaks of influenza <i>Follow up of outbreaks in nursing homes, schools etc</i>
PHLS Communicable Disease Surveillance Centre (CDSC) Wales ³ <i>Weekly rates per 100 000 population for influenza</i>	RCGP/ERNVL Virological Surveillance Scheme ^{5,6} <i>Community based sampling for influenza</i>		Reports from other European countries, US, WHO, etc
Scottish Centre for Infection and Environmental Health (SCIEH) <i>Weekly rates per 100 000 population for influenza-like illness</i>	PHLS Virological Surveillance of Influenza Scheme <i>Community based sampling for influenza</i>		
Medical Officers of Schools Association (MOSA) <i>Weekly rates per 1000 boarding school children for influenza and flu-like illness</i>	PHLS/NHS laboratory reports <i>Laboratory reports of influenza A or B</i>		

GP consultation rates for influenza and ILI remained below the threshold for baseline activity (less than 50 episodes / 100 000 population) until week 52/00, and peaked at 62 /100 000 in 02/01. This rate remained at the lower end of the range for 'normal seasonal activity' of 50-600 /100 000 population. Rates fluctuated before returning to baseline levels in week 08/01.

Outbreaks

During the 2000/01 influenza season 30 outbreaks of ILI were reported to CDSC. Twenty of the outbreaks occurred in schools that participate in the Medical Officers of Schools Association (MOSA) reporting scheme, six occurred in non-MOSA schools, two in nursing homes, and one each in a hospital and a naval training base. The duration of the

outbreaks ranged from one to six weeks, with the number of individuals affected in each outbreak ranging from less than ten to approximately 300. Specimens were taken from individuals in ten of the outbreaks, and influenza virus was isolated from all but two of the outbreaks. Two outbreaks (one in November and one in December 2000) were associated with influenza A, and five outbreaks (three in January and two in February 2001) were associated with influenza B.

Mortality

The weekly total number of deaths due to all causes remained low throughout the 2000/01 influenza season, peaking at 12 345 in week 01/01. This figure is substantially lower than the peak of 20 772 seen during the 1999/00 influenza season (figure 4). Thirty-six deaths were directly attributed to

Figure 1 Weekly consultation rates for influenza and influenza like illness: RCGP Weekly Returns Service, 1988-2001

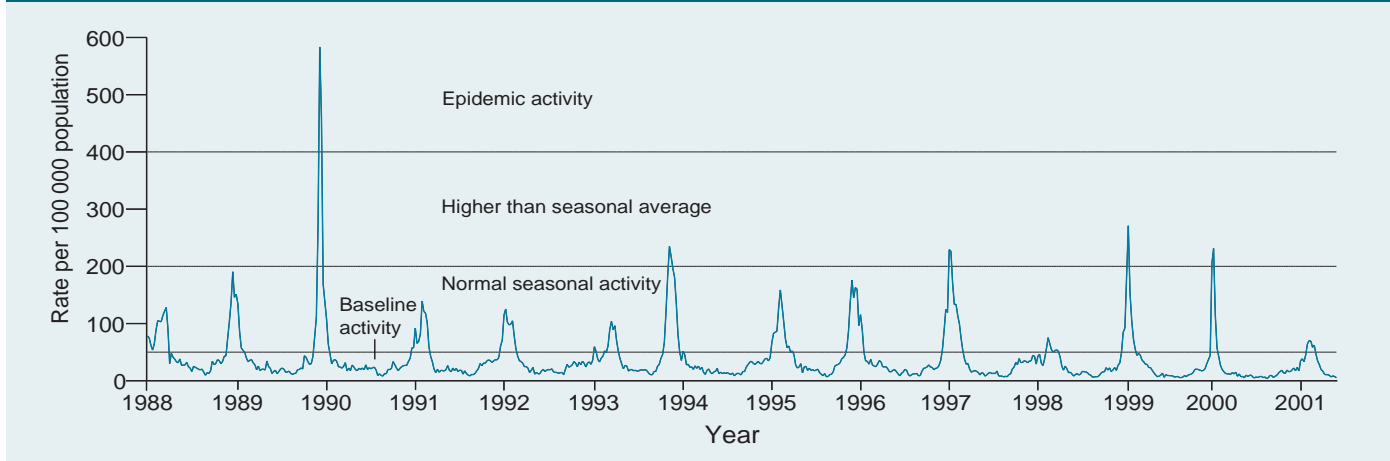


Figure 2 RCGP consultation rate for influenza and influenza-like illness by age, 2000-01

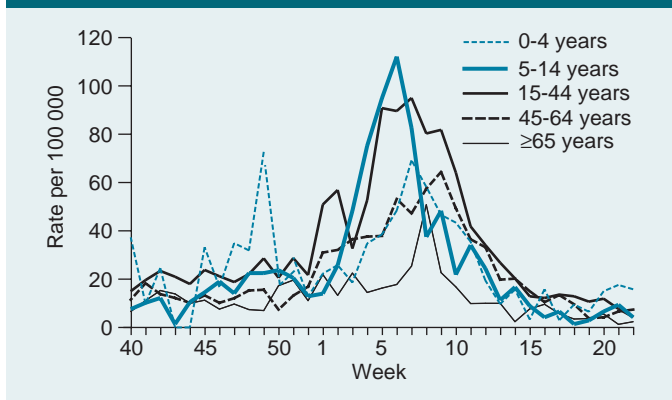
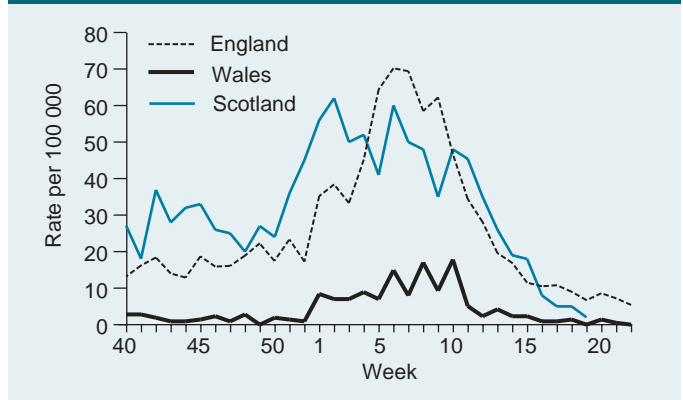


Figure 3 GP Consultation rates for influenza and influenza-like illness for England, Wales, and Scotland, 2000-01



influenza between week 40/00 and week 16/01. This figure is provisional and may be revised later, although it remains considerably lower than the 503 deaths attributed to influenza during 1999/00. The total estimated number of excess deaths attributed to influenza between weeks 40/00 and 33/01, using a time series method based on the method of Serfling⁵, was 0 (unpublished PHLS data) (table 2).

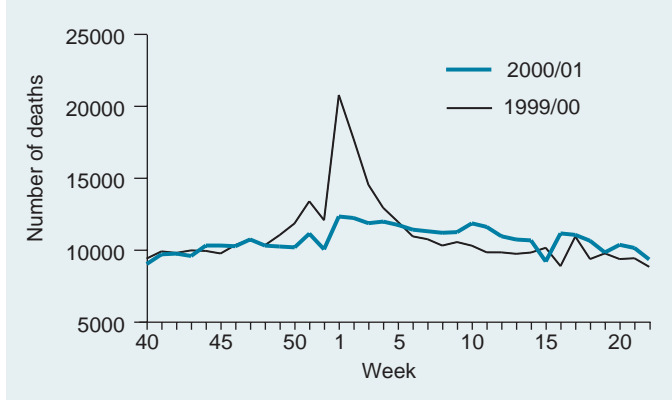
At the beginning of 2001 the Office for National Statistics (ONS) implemented the ICD-10 coding system for cause of death. An exercise is being undertaken by ONS to assess the impact of the new classification, especially in relation to trends in mortality by disease.

NHS Direct total call rate activity

During the winter of 2000/01, there were two distinct peaks in the NHS Direct total call rate for England and Wales. The first peak occurred over Christmas (week 52/00) when the total call rate was 205/100 000 population. A second peak in the total call rate (weeks 05/01 and 06/01: 192/100 000) coincided with the peak in influenza activity indices from other sources (RCGP and PHLS).

As well as total call data, counts of callers with 'colds/flu' (use of 'colds/flu' algorithm by NHS Direct nurse) were collected from six NHS Direct sites (population coverage=16 million). These preliminary data show a similar pattern to total calls.

Figure 4 Deaths due to all causes notified to ONS by week of notification



Virological

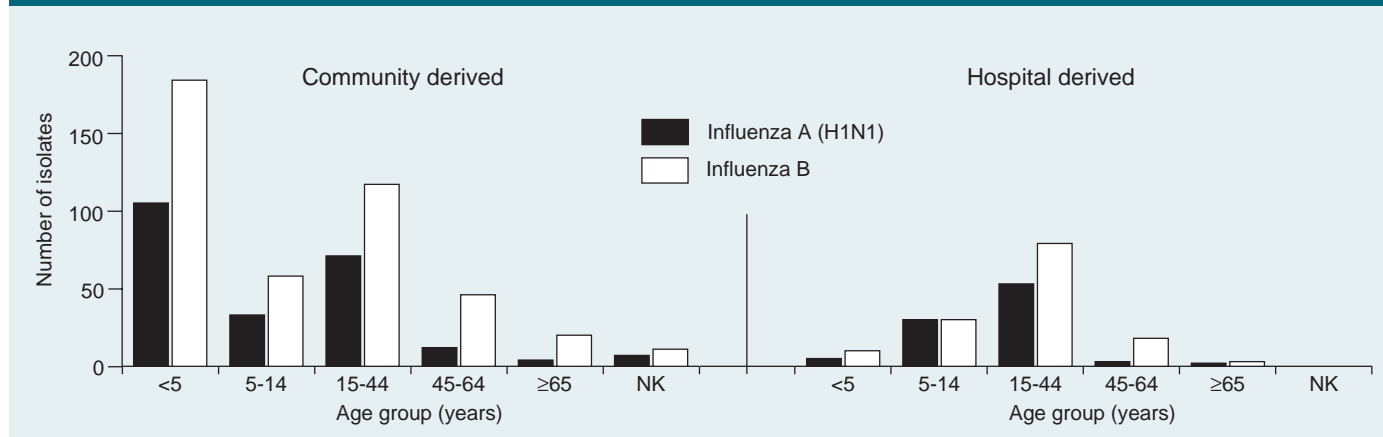
PHLS Enteric, Respiratory, and Neurological Virus Laboratory (ERNVL) Influenza Section

Between 2 October 2000 and 29 April 2001 the PHLS Enteric, Respiratory, and Neurological Virus Laboratory (ERNVL) confirmed 883 influenza isolates from samples from both community and hospital sources. Three hundred and twenty-three (37%) were influenza A (H1N1) and 560 (63%) were influenza B. The majority of influenza A (H1N1) isolates were antigenically similar to the current vaccine strain, A/New Caledonia/20/99, although three isolates were more closely related to an older H1N1 strain, A/Bayern/7/95. The influenza B isolates were closely related to B/Yamanashi/166/98, the current influenza B vaccine strain. Community-derived isolates were predominantly from patients from the 5 to 14 year and 15 to 44 year age groups. Hospital derived isolates, however, were mainly from children less than 5 years and patients aged from 15 to 44 years (figure 5). No influenza A (H3N2) viruses were isolated during the 2000/01 season.

Table 2 Excess mortality due to influenza in England and Wales

Year	Number of excess deaths
1988/89	150
1989/90	25786
1990/91	6552
1991/92	4807
1992/93	1051
1993/94	9480
1994/95	–
1995/96	13579
1996/97	28987
1997/98	790
1998/99	17873
1999/00	19543
2000/01	–
Total	128598

Figure 5 Age distribution of community- and hospital-derived influenza isolates, 2000/01



RCGP/ERNVL influenza and RSV detection by PCR from RCGP community-based surveillance

Between 2 October 2000 and 29 April 2001, 729 samples from community-based surveillance were tested by polymerase chain reaction (PCR). Two hundred and fifty-two samples (35%) tested positive for influenza (86 influenza A (H1N1) and 166 influenza B). Forty-three (5.9%) tested positive for respiratory syncytial virus (RSV) (figure 6). The highest positivity rate for influenza detection was in samples derived from children aged from 5 to 14 years (58.1%), and the highest rate for RSV detection was in samples derived from children aged from 0 to 4 years (21.3% positive).

PHLS virological surveillance of influenza⁶

Eighteen laboratories contributed to the scheme during 2000/01. Overall, 120 out of 490 (24%) specimens tested positive for influenza (35 influenza A and 85 influenza B) by DIF and/or culture. Five specimens tested positive for RSV and 14 specimens were positive for other respiratory viruses.

Antigenic characterisation of influenza isolates received by ERNVL in 2000/01

All of the influenza isolates were antigenically similar to either A (H1N1)-A/New Caledonia/20/99-like or B/Sichuan/

379/99-like viruses included in the vaccine composition for 2000/01.

Laboratory reports

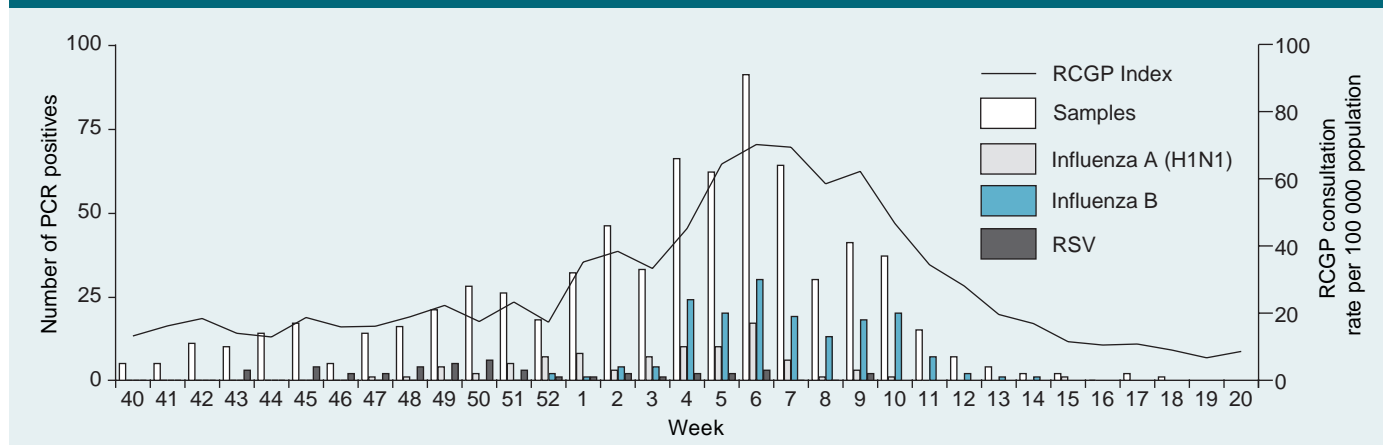
Clinical specimens that yield positive results for influenza or respiratory syncytial virus (RSV) either by single elevated serological titre, antigen detection, seroconversion, or culture at PHLS, NHS and some private laboratories are reported through a voluntary scheme to CDSC each week. Laboratory reports by week of specimen showed that 562 confirmed influenza A infections were identified between weeks 40/00 and 13/01, with the peak in week 04/01 (59 confirmed infections). Eight hundred and two influenza B infections were reported during the weeks 40/99 and 13/00, with the peak in week 09/01 (120 infections).

Between weeks 40/00 and 13/01, 8796 laboratory reports of RSV were made to CDSC, with the peak in week 50/00 (996 reports). Of these, 7074 (80%) were specimens taken from infants aged from 0 to 4 years.

Influenza activity elsewhere

The predominant influenza strain circulating in Europe during 2000/01 was influenza A (H1N1). Activity associated with influenza A (H1N1) was reported until the end of February, after which time influenza B became the

Figure 6 Influenza and RSV detections (by PCR) from RCGP community surveillance, 2000-01 (by week of sample date)



predominant circulating strain in most European countries. Germany, Italy, and Spain remained the exception where isolates of influenza A (H1N1) continued to be reported towards the end of the season.

Reports of influenza C were received from France during week 09/01 (the first since 1961), and sporadic reports of influenza A (H3N2) were made from Spain during week 10/01. Generally, levels of influenza activity remained limited throughout the season. Higher levels were reported in Denmark, France, and Germany over the Christmas and New Year period, but reporting was interrupted by the holiday period. Widespread activity occurred in Sweden from weeks 8 to 13/01. Influenza activity declined and reached low levels across most other parts of Europe at the beginning of March 2001.

Detailed country reports can be obtained from the World Health Organization website at <oms2.b3e.jussieu.fr/flunet/>.

Antigenic characterisation of recent influenza virus isolates worldwide

The majority of isolates characterised worldwide in the 2000/01 season were H1N1 viruses, which co-circulated with influenza B in some countries. The choice of the influenza A (H1N1) vaccine strain for the 2001/02 season, A/New Caledonia/20/99(H1N1)-like virus, the same as in 2000/01, reflects the fact that few antigenic drift variants were isolated. The recommendation of the influenza A (H3N2) vaccine strain, A/Moscow/10/99(H3N2)-like virus, also remains unchanged. Influenza B viruses circulating throughout the world in 2000/01 were characterised as B/Sichuan/379/99-like, with some limited circulation of B/Yamanashi/166/98-like viruses in south east Asia. The choice of B/Sichuan/379/99 as a vaccine strain reflects the requirement to update vaccine components from time to time, even in the absence of significant antigenic drift

Match between vaccine and circulating strains

The match between influenza vaccine components and circulating strains in 2000/01 was good (see above) and the vaccine is likely to have provided substantial protection.

Discussion

Influenza activity in Britain during the 2000/01 season was very low, with levels similar to those seen during 1997/98. The main feature of the season was the co-circulation of influenza A (H1N1) and influenza B with approximately equal numbers of both viruses isolated in samples submitted from the community. Influenza A first appeared in November and influenza B began to circulate in late December and predominated as the circulating strain from the end of January until the end of March. Incidence rates of ILI did not rise appreciably until the turn of the year and remained above baseline activity (50 new episodes per 100 000) between weeks 4 and 12.

During the period when influenza B predominated, clinical rates were highest among older children and adults (aged 5 to 14 years, and 15 to 44 years). The majority of individuals in these age groups will not have received influenza vaccination as they are not in the high-risk groups. Influenza B characteristically produces attack rates that are higher among children compared to adults^{7,8},

and lower levels of excess morbidity and mortality associated with influenza infection due to decreased numbers of influenza associated complications in the elderly.

Consultation rates for acute bronchitis peaked during week 01/01, with rates highest in children aged from 0 to 4 years and adults aged 65 years or over. Laboratory diagnoses of RSV infections also peaked at the same time and are likely to have contributed to levels of acute bronchitis and ILI in young children and the elderly. Despite this, rates of acute bronchitis were generally low throughout the season. *Mycoplasma pneumoniae* infections also remained at low levels during 2000/01. Increased levels are expected during 2001/02 in line with the four-yearly epidemic cycle of this infection.

Many outbreaks of influenza were reported throughout the season. Some schools reported approximately 50% of pupils affected with influenza-like illness and upper respiratory tract infection, although it is not possible to calculate attack rates for these outbreaks due to incomplete case ascertainment. Many of the outbreaks were investigated virologically, highlighting the importance of the MOSA scheme as an early warning system underpinned by characterisation of influenza isolates from community-derived cases.

Influenza activity across Europe coincided with that seen in the UK, with levels reported as 'sporadic' or 'low' in the majority of the fourteen countries contributing to the European Influenza Surveillance Scheme (EISS) throughout the 2000/01 season. In contrast to the situation seen in the UK, influenza A (H1N1) remained the predominant circulating strain across most of Europe until March, when influenza B began to co-circulate.

Surveillance methodology

Many of the sources of data used for influenza surveillance are well established. Surveillance data traditionally focused on clinical consultations with GPs and virological confirmation through laboratory reports. In the last two years, however, additional sources of data such as NHS Direct and molecular technologies have been introduced to enhance the surveillance data collected.

Problems in interpretation of NHS Direct data have been encountered due to expansion of the service between October and December 2000, excess calls over Christmas (when other health services are closed), and the continuing rise in the baseline total call rate. Call rates to NHS Direct ranging between 100 and 200/100 000 week are much less than contact rates in general practice which average 8000/100 000 per week.

The timeliness of NHS Direct data, and its ability to mirror other surveillance systems, may offer the opportunity for further surveillance of influenza during the winter of 2001/02.

Enhanced surveillance of influenza began in Northern Ireland during the 2000/01 season, coordinated by the Communicable Disease Surveillance Centre (Northern Ireland)⁹. Sixteen GP practices provided weekly information on the number of consultations for influenza and ILI, while a subset took nose and throat swabs for enhanced virological monitoring. As this is the first year of this scheme baseline values cannot be determined, and there is no previous data available for comparison.

ERNVL tested community derived specimens from RCGP sentinel surveillance practices for influenza and RSV using PCR molecular methods for the first time in 2000/01, and increased the yield of positive results. An overall influenza positivity rate of 38.6% was obtained using PCR, compared with 14% using isolation alone, demonstrating the increased sensitivity of this methodology. The use of isolation as a detection method, however, remains essential for identifying circulating and new strains through virus typing. This is not possible using PCR.

The PHLS virological surveillance of influenza scheme will be enhanced during 2001/02 as part of the continuing development of the surveillance methodology. The case definition for inclusion in the study has been widened to include acute bronchitis, and the number of swabs collected from patients presenting to GP practices will be increased. Denominator data will also be collected from a subset of the participating practices.

A study of acute respiratory admissions made through accident and emergency departments is due to be piloted during the 2001/02 season. This study aims to address the current gap in surveillance data on hospital admissions.

Additionally, data from the PHLS will be used in the continuing pilot study *Forecasting the Nation's Health* being undertaken by the Health Forecast Unit of the Met Office.

National influenza vaccination campaign

Following a change in UK policy for influenza immunisation for autumn 2000, immunisation was recommended for all people aged 65 years and over in addition to those at high risk in younger age groups. The Department of Health set a target of 60% uptake in all health authorities, and for the first time vaccine uptake was monitored during the season. Figures from all 99 health authorities in England to the end of December 2000 showed that the national uptake rate among those aged 65 years and over was 65%.

Timely monitoring of vaccination uptake among patients aged 65 years or over will be undertaken by the PHLS Communicable Disease Surveillance Centre on behalf of the Department of Health for the 2001/02 season.

Vaccine recommendations

The recommended components for the 2001/02 vaccine for the northern hemisphere are¹⁰:

A/Moscow/10/99(H3N2)-like virus*

A/New/Caledonia/20/99(H1N1)-like virus

B/Sichuan/379/99-like virus**

* A/Panama/2007/99 is an A/Moscow/10/99(H3N2)-like virus

** The most widely used vaccine strain is B/Sichuan/379/99

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