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News

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 [HPA to collaborate in development of botulinum vaccine with Emergent BioSolutions](#)

HPA to collaborate in development of botulinum vaccine with Emergent BioSolutions

The Health Protection Agency (HPA) is beginning a two-year collaboration with Emergent BioSolutions in the United States (US) to develop vaccines to prevent botulism. Research and development of these vaccines will be performed at the Agency's Centre for Emergency Preparedness and Response at Porton Down in Wiltshire. Emergent BioSolutions and the HPA will be sharing technology and expertise to develop both toxoid and recombinant botulinum vaccines. There is currently no licensed vaccine to prevent botulism.

The initial objectives will be the development of both multivalent botulinum toxoid vaccines and multivalent recombinant botulinum vaccines. The botulinum toxoid vaccine under development, which targets a number of serotypes, is derived from a pentavalent botulinum toxoid vaccine previously produced by Emergent. That vaccine has been used in more than 11,000 people for more than 30 years under investigation of new drug applications (INDs) held by the Centers for Disease Control and Prevention (CDC) in Atlanta, and the US Department of Defense. The toxoid vaccine is manufactured from native botulinum toxin using methods similar to those used for the production of other licensed toxoid vaccines.

The recombinant botulinum vaccine development program targets specific serotypes. This development program will use recombinant technology to express the non-toxic light chain portion of the toxin molecule for use as the vaccine antigen. The light chain recombinant vaccine may possess significant advantages over vaccines based upon the heavy chain portion of the toxin. Initial data has shown advantages in stability, immunogenicity, and the potential for multivalent formulations.

Botulism is a disease caused by the toxins of *Clostridium botulinum* bacteria (1). These toxins are the most potent known. Botulism is generally characterized by a progressive descending motor paralysis, which affects the shoulders, upper arms, lower arms, respiratory muscles, and legs. If left untreated, death may be caused by paralysis of the respiratory muscles. Other symptoms seen with botulism include double vision, blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, and generalized muscle weakness.

Natural outbreaks of botulism are generally due to ingestion of preformed toxin in spoiled foodstuffs (foodborne) (2), contamination of wounds by the *Clostridium botulinum* bacteria, including unsterile injecting practices by injecting drug users (wound botulism) (3), or in the case of infants, by ingestion of the organism, (infant botulism) (4).

Botulinum toxin is of potential use as a weapon because of its extreme potency and lethality, as well as the need for prolonged intensive care among affected people (5). Terrorists have already attempted to use botulinum toxin as a weapon.

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5. Arnon SS, Schechter R, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, et al. Botulinum toxin as a biological weapon: medical and public health management. *JAMA* 2001;285:1059-70. Available at <<http://jama.ama-assn.org/cgi/content/full/285/8/1059#ACK>>.

Influenza and other respiratory viruses surveillance in the United Kingdom: October 2003 to May 2004



Summary

Influenza activity remained low in the United Kingdom (UK) during the 2003/2004 season and began early. Clinical indices peaked during late November 2003, but remained at the lower end of the range of 'normal seasonal activity' in England, and at baseline levels in Scotland and Wales. The virological season was dominated by the emergence of the antigenic drift variant influenza A/H3N2/Fujian-like strain. This was the predominant circulating strain in the UK, with only sporadic influenza A (H1N1) and influenza B detections made during the season.

Rates of clinical illness were highest among children aged under 4 years. In England and Scotland there were 17 influenza associated deaths among children aged 18 years and under who were found to be infected with the influenza A (H3N2)-Fujian-like strain. The International 2003/2004 season was marked by the re-emergence of avian influenza A (H5N1) in poultry and humans in south east Asia.

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Influenza and other respiratory viruses surveillance in the United Kingdom: October 2003 to May 2004

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Summary

Influenza activity began early and remained low in the United Kingdom (UK) during the 2003/2004 season. Clinical indices peaked during late November 2003, but remained at the lower end of the range of 'normal seasonal activity' in England, and at baseline levels in Scotland and Wales. The virological season was dominated by the emergence of the antigenic drift variant influenza A/H3N2/Fujian-like strain. This was the predominant circulating strain in the UK, with only sporadic influenza A (H1N1) and influenza B detections made during the season.

Rates of clinical illness were highest among children aged under 4 years. In England and Scotland there were 17 influenza associated deaths among children aged 18 years and under who were found to be infected with the influenza A (H3N2)-Fujian-like strain. The International 2003/2004 season was marked by the re-emergence of avian influenza A (H5N1) in poultry and humans in south east Asia.

Keywords: *influenza, epidemiology, outbreak, surveillance*

Introduction

The Health Protection Agency (HPA) monitors the activity of influenza and other respiratory viruses in the United Kingdom (UK) throughout the year. Particular importance is placed on the period between October (week 40) and May (week 20) during which time influenza rates normally reach their highest levels in the UK. The HPA collects information from a variety of different sources to provide vital information on circulating virus strains. In this way, novel influenza viruses, which may have epidemic potential, are detected as early as possible. Influenza surveillance undertaken by the HPA also contributes towards the

composition of influenza vaccine for the following year. Other data are used to assess the health impact (morbidity and mortality) of influenza and other respiratory diseases, and provide timely information to healthcare professionals, the media, and the public.

Methods

HPA influenza surveillance relies on the timely collection of clinical and virological data across the UK. Information sources have been described previously (1). A brief summary is provided in table 1.

Results

Clinical

England – Royal College of General Practitioners (RCGP). The peak of influenza activity in England during 2003/04 occurred earlier, and at a higher level than observed in 2001/2002 and 2002/2003, and earlier than any season since 1993/1994. Nevertheless, general practitioner (GP) consultations for influenza-like illness in the RCGP sentinel surveillance scheme peaked at a rate of 62 per 100,000 population in week 46/03, which is barely above baseline. Rates remained at the lower end of the range for normal seasonal activity (50-200/100,000) for four weeks, before declining to baseline levels after week 49/03 (less than 50/100,000).

The highest GP consultation rates occurred in children aged 4 years and under (157/100,000 week 49/03). Consultation rates in all other age groups remained substantially lower (figure 1).

Consultation rates by RCGP region showed a similar pattern for northern, central, and southern regions. Rates were highest and activity was earlier in the central region (79/100,000 in week 46/03) than in northern or southern regions where rates peaked at 66/100,000 in week 47/03 and 58/100,000 in week 49/03 respectively.

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Table 1 Data sources for influenza surveillance in the UK

Data type	Organisation	Description
Clinical	<ul style="list-style-type: none"> Royal college of general practitioners (RCGP) Weekly Returns Service, (England and Wales). 	Weekly morbidity data derived from 73 sentinel GP practices. Each new consultation is recorded and defined by using diagnostic guidelines. (Rates per 100,000 population for influenza and flu-like illness).
	<ul style="list-style-type: none"> HPA Communicable Disease Surveillance Centre (CDSC) Northern Ireland. (Northern Ireland). 	Weekly morbidity data derived from sentinel GP practices for influenza and flu-like illness, and call rates for all causes to out-of-hours GP co-operatives.
	<ul style="list-style-type: none"> HPA Communicable Disease Surveillance Centre (CDSC) Wales. (Wales). 	Weekly morbidity data derived from sentinel GP practices for influenza (Rates per 100,000 population for influenza)
	<ul style="list-style-type: none"> Health Protection Scotland (SCIEH) (Scotland). 	Weekly morbidity data derived from sentinel GP practices for each consultation for influenza-like illness. (Rates per 100,000 population for influenza).
	<ul style="list-style-type: none"> NHS Direct. (England and Wales). 	Weekly total call, cold/flu and fever call rate derived from a 24-hour nurse advice and health information service.
	<ul style="list-style-type: none"> Medical Officers of Schools Association (MOSA) (England and Wales). 	Weekly rates per 1000 boarding school children for influenza and flu-like illness.
	<ul style="list-style-type: none"> Influenza Vaccine uptake monitoring. Influenza/Respiratory virus section, HPA Centre for Infections (CFI), Colindale. (England). 	Monthly data collected from October to December derived from general practices through flu immunisation coordinators in primary care trusts (PCTs) before forwarding to CFI for data at the regional and national level).
Virology	<ul style="list-style-type: none"> Respiratory Virus Unit (RVU), HPA Centre for Infections (CFI), Colindale. (UK). 	Analysis of influenza strains: subtyping, antigenic and genetic characterisation of viruses referred from UK laboratories (HPA and NHS).
	<ul style="list-style-type: none"> RCGP/CFI Virological surveillance Scheme. (England). 	Community-based sampling by GPs participating in the RCGP spotter practice scheme.
	<ul style="list-style-type: none"> CFI virological surveillance of influenza scheme (England and Wales) 	Community-based sampling by 45 sentinel GPs.
	<ul style="list-style-type: none"> HPA/NHS laboratory reports. (England and Wales). 	Positive respiratory virus specimens routinely reported to CFI from NHS and HPA laboratories.
Mortality	<ul style="list-style-type: none"> Office for National Statistics (ONS). (England and Wales). 	Weekly registration of deaths by age and cause.
Outbreak		Information on outbreaks of influenza and other respiratory illness reported to the HPA Influenza/Respiratory Virus Team, Centre for Infections, Colindale.

RCGP consultation rates for acute bronchitis peaked in week 02/04 at 227/100,000. The peak rate for those aged under 4 years occurred in week 51 (682/100,000). This was lower than for 2002/03 (727/100,000 in week 48/03). The peak rate among those aged 65 years and over occurred in week 02/04 (592/100,000), compared to 442/100,000 in week 01/03, 2002/2003. Consultation rates for acute bronchitis remained low in all other

age groups during 2003/04.

Wales – The Communicable Disease Surveillance Centre (CDSC Wales). Consultation rates in the sentinel GP scheme co-ordinated by the Communicable Disease Surveillance Centre (CDSC) Wales remained within the range for baseline activity (<25/100,000) for the duration of the 2003/2004 season. The peak rate

Figure 1 RCGP weekly consultation rates for influenza-like illness by age, England: 2003-2004.

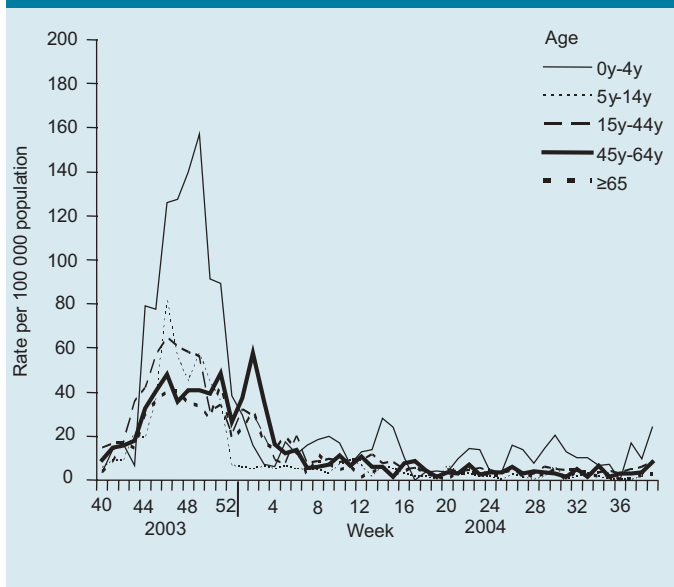
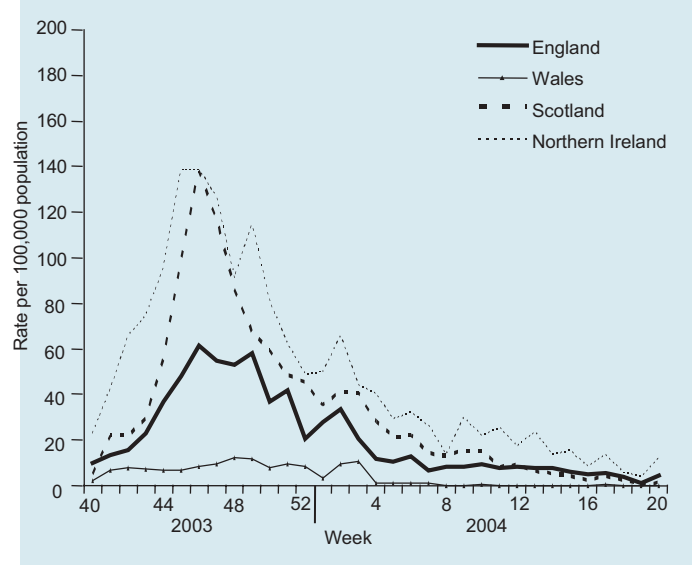


Figure 2 General Practitioners consultation rates for influenza or influenza-like illness: England, Wales, Scotland and Northern Ireland.



occurred in week 48/03 (week ending 26/11/2003) at 12/100,000 population (figure 2).

Scotland - Health Protection Scotland. A peak consultation rate for influenza-like-illness of 138/100,000 was reported in week 48/03 from its sentinel GP scheme. Activity remained within the range specified for normal seasonal activity (50-600/100,000), but declined back to below baseline levels after week 50/03 (figure 2).

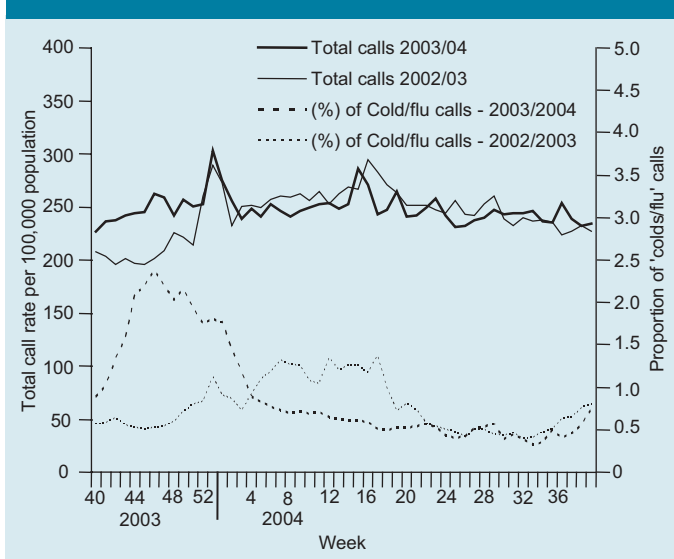
Northern Ireland - The Communicable Disease Surveillance Centre (CDSC Northern Ireland). This was the fourth year of the enhanced surveillance scheme in Northern Ireland, which provides

information regarding influenza and influenza-like illness from 23 spotter practices across the country. Baseline levels have not yet been established for this scheme. The combined rate for influenza and influenza-like illness occurred early in the season during week 45/03 (week ending 07/11/2003) at 138/100,000. This rate was substantially higher than observed during 2002/03 (74/100,000). The peak rates for flu-like illness by age group occurred in week 45/03 and week 47/03 in those aged under 4 years.

NHS Direct total call activity

Two peaks occurred in the NHS Direct total call rate during the 03/04 season; one in week 52/03 (303/100,000) and the second in week 15/04 (286/100,000). The rise in the proportion of cold/flu calls occurred between weeks 44/03 to 50/03 reaching a peak in week 46/03 (2.4%). Within the different age groups, the highest proportion of cold/flu calls was recorded for those aged between 5 and 14 years (3.9% in week 46/03) (figure 3).

Figure 3 NHS Direct total call rate and proportion of 'cold/flu' calls: 2003 -2004 and 2002 - 2003.

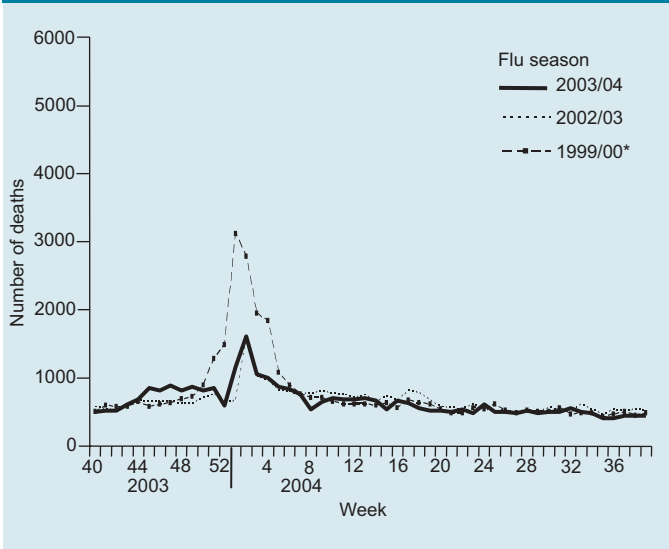


Outbreaks

The HPA's Centre for Infections (CFI) received twenty-five outbreak reports during the 2003/2004 season. Of these, five were from residential homes for the elderly and twenty from schools, thirteen of whom participate in the Medical Officers of Schools Association (MOSA) sentinel scheme. The majority of outbreaks occurred in late October to December. Two school outbreaks occurred late in the influenza season, in May and June 2004 respectively.

Attack rates varied considerably, ranging from 13.9% to 68%, the latter associated with an outbreak in a residential home for the elderly. In fifteen of the outbreaks, specimens were collected for virological investigation. Influenza A (H3) was identified as the causative agent in nine outbreaks, and influenza A (H1N1) was detected in samples from school children

Figure 4 Weekly deaths due to all causes, in England and Wales, registered with the Office for National Statistics (ONS), 2003/2004 and recent years.



*The 99/00 data has been adjusted using a comparability ratio in order for this to be compared with data from Jan 2001 onwards when there was a change in the ICD coding.

in the final two outbreaks of the 2003/2004 season.

Mortality

The total number of weekly deaths due to all causes, in England and Wales, registered with the Office for National Statistics (ONS) peaked at 16,282 in week 02/04 (figure 4). This figure was lower than the 2002/2003 season (18,303 in week 02/03). The cumulative total of deaths registered during the season (348,811 between week 40/03 and 20/04) did not differ greatly from the 2002/2003 figure for the same period of 357,279.

The combined number of deaths attributed to acute bronchitis, pneumonia, and influenza between weeks 40/03 and 20/04 (24,650) was also similar to the 2002/2003 figure of 24,226. Influenza was recorded as

Table 2 Estimated excess mortality due to influenza in England and Wales*

Influenza Season	Number of excess deaths
88/89	–
89/90	22,719
90/91	3284
91/92	2661
92/93	–
93/94	9486
94/95	139
95/96	10,359
96/97	17,648
97/98	–
98/99	13,493
99/00	17,359
00/01	–
01/02	4626
02/03	4015
03/04	2012

*Every year the model is revised to incorporate the current season's data. The fitted model then not only creates a figure for the most recent season, but also readjusts the previous years' figures.

Table 3 Virological typing of positive specimens received by ERNVL/RVU* during the 2003/04 influenza season (week 40/03 – week 20/04), PCR or virus isolation

Source	Influenza type/subtype						B	Total	RSV*
	A/H1	A/H1N1	A/H1N2	A/H3	A/H3N2	(A) total			
Hospital	2	1	–	584	442	1029	5	1034	6
Community	–	–	–	303	75	378	–	378	44
Total	2	1	–	887	517	1407	5	1412	50

*ERNVL = Enteric, Respiratory, and Neurological Virus Laboratory. RVU = the Centre for Infections Influenza/Respiratory Virus Team.

the primary cause of death in 65 cases during the 2003/2004 season. This surpassed the influenza deaths recorded for the past four years, but still remained substantially lower than the 540 influenza deaths registered in the last influenza epidemic of 1999/2000.

A total of 24 suspected influenza associated deaths in England and Scotland were reported to the HPA's Centre for Infections (CFI), and Health Protection Scotland on an *ad hoc* basis during this season. These deaths were in individuals aged 18 years or under and 17 were later identified as being due to the influenza A (H3N2) Fujian-like strain.

The annual estimate of excess mortality due to influenza (using data from ONS) was calculated using a time series model (2). The total estimated number of excess deaths attributable to influenza between week 40/03 and week 29/04 for the 2003/2004 season was 2012. This is lower than the revised figure of 4015 for 2002/2003 (Table 2).

Virological

Respiratory Virus Unit (RVU), HPA Centre for Infections (CFI). Between weeks 40/03 and 20/04, the CFI's Enteric, Respiratory, and Neurological Virus Laboratory (ERNVL) received 998 samples from community sources, of which 378 (38%) were positive for influenza. The majority of these (303 (80%)) were identified as influenza A (H3) viruses. In addition, 1034 positive influenza specimens were detected from hospitals and the majority were typed as influenza A (H3) (table 3). Community derived detections were predominantly from those aged between 15 and 44 years, while the hospital detections were mainly from children aged under 4 years.

Of the 344 isolations characterised between week 40/03 and week 20/04, 340 were characterised as A/Fujian/411/2002 (H3N2)-like, two as Panama/2007/99 (H3N2)-like and two influenza B viruses as B/Shanghai/361/2002-like. Although Fujian-like strains were antigenically drifted from Panama/2007/99 (*ie*, the H3N2 vaccine component for 2003/2004 northern hemisphere) some cross protective immunity was still

provided by the vaccine.

Laboratory reports. Laboratory reports with a week of specimen between week 40/03 and week 20/04 yielded:

- 1517 confirmed influenza A infections (peak of 181 detections in week 47/03); of these 825 were detected by serological test methods and 692 by direct immunofluorescence (DIF) and PCR. Isolates were referred to RVU/CFI for further characterisation.
- 42 confirmed influenza B infections (with no definable peak); of these 29 were detected by serological test methods and 13 by DIF and PCR reported from HPA and NHS laboratories in England and Wales.
- 5165 confirmed respiratory syncytial virus (RSV) infections (peak of 626 detections in week 01/04); of these 705 were detected by serological test methods and 4460 by DIF and PCR.

Parainfluenza activity followed a similar pattern to that of previous years. Parainfluenza serotypes 1 and 2 peaked in the winter months and reports of serotype 3 dominated from week 07/04 onwards. The majority of these serotype 3 reports were from those in the under 4 years age group. It is, therefore, possible that the moderate levels of acute bronchitis reported in this age group from May 2004 onwards could be partially attributable to parainfluenza serotype 3, as both RSV and influenza activity had declined.

Community Surveillance schemes (RCGP/CFI virological surveillance scheme). Between weeks 40/03 and 20/04, 659 samples from the RCGP community based surveillance scheme were tested for influenza. Of these, 250 (38%) were positive for influenza and 29 (4%) positive for RSV. Of the specimens positive for influenza 62 (25%) were influenza A (H3N untyped) and 199 (75%) A(H3N2). No positive specimens of influenza B or influenza A (H1) subtypes were detected.

CFI/CDSC virological surveillance scheme. Sixteen laboratories participated in the scheme during 2003/04. Forty-one GPs submitted 559 specimens. Influenza A was detected in 124 (22%) of these specimens, and 30 (5%) other viruses including RSV were detected. The age group with the highest positivity rate for influenza was the 5 to 14 years age group at 50%, with those aged under 4 years (24%), 15 to 64 years (38%), and for those aged over 65 years (13%).

Virological data from Northern Ireland. Between weeks 40/03 and 20/04, a total of 77 influenza A (H3) detections were made from non sentinel specimens with a further 39 from sentinel GP practices. No influenza B infections were detected this season. Of the 77 confirmed influenza infections, approximately one-third of the patients were co-infected with other respiratory viruses (3).

Virological data from Scotland. There were 78 influenza positive specimens referred to the CFI's

Influenza/Respiratory Virus Unit (RVU), from hospital sources in Scotland between week 40/03 and 20/04. Influenza A (H3N2) was identified in 31 (40%) specimens and influenza A (H3) was detected in 47 (60%) samples. Health Protection Scotland reported a significant increase in community and hospital detections of influenza compared to the previous winter with 53% of the total positive samples obtained from children aged under 4 years (4).

Influenza activity elsewhere. Influenza activity across Europe was marked by an initial surge of influenza activity in western Europe beginning in Ireland, UK, Spain, and Portugal, followed by Norway, France, and Belgium. A second wave, concentrated in the central and eastern European countries followed. All European influenza activity was dominated by the new drift variant A/Fujian/411/2002 (H3N2) and tended to show the highest clinical incidence in the youngest age groups (those aged under 14 years). No unusually high levels of mortality or severe morbidity were detected. Other influenza viruses that were detected sporadically this season included: influenza B (B/HongKong/330/2001-like and B/Sichuan/379/99-like), A (H1N1), and A (H1N2).

The United States (US) reported an early rise in influenza activity this season with the percentage clinical consultations for influenza-like illness crossing the national baseline at week 45/03 as opposed to week 3 in 2002/2003. The clinical indicators also reached higher levels this season than those of last season or in the most recent A (H3N2) season of moderate severity of 1999/2000.

Vaccine uptake monitoring on behalf of the Department of Health

The uptake target set by the Department of Health for all patients aged 65 years and over was 70% for the 2003/2004 season. Of the 303 Primary Care Trusts (PCTs) in England, 303 (100%) took part and 239 (79%) achieved uptake rates of 70% or more, a greater coverage than the 68.6% achieved for the 2002/2003 season. Of the 8,157,671 people aged 65 years and over who were registered with a GP practice in England, 5,788, 754 (71%) received the influenza vaccine.

Vaccine match. In the UK, the majority of circulating strains isolated in 2003/04 showed a partial match with the corresponding influenza vaccine component. The influenza A Fujian/411/2002(H3N2)-like subtype that predominated in the UK was not included in the vaccine for the 2003/04 season, but a degree of cross protection was offered by the influenza A (H3N2) strain that was included (A/Panama/2007/99).

SARS surveillance and associated flu detection

The emergence of Severe Acute Respiratory Syndrome (SARS) during the 2002/2003 influenza season facilitated the early detection of influenza A(H3N2) viruses in 2003/2004. Of those potential SARS cases analysed in the UK from weeks 49/02 to 20/03, 53 (31%) were positive for influenza viruses decreasing to nine (11%) in weeks 21/03 to 39/03 when influenza activity

is traditionally low in the UK (5).

Discussion

Influenza activity during the 2003/2004 season was characterised by an unusually early rise in both GP consultation rates and virological influenza detections. This is the first season since 1995/96 that clinical reports of influenza exceeded baseline levels during late October and early November. This rise was associated with the widespread emergence of a drifted virus influenza A (H3N2)/Fujian/411/2002-like, that was detected in very low numbers during the 2002/03 winter (1) and which had caused widespread outbreaks in the southern hemisphere during the summer of 2003 (May to August). It dominated the flu season in the UK and Europe throughout 2003/04, with only sporadic cases of influenza B and influenza A (H1N1) being reported.

Despite the early start to the influenza season in the UK, clinical indicators did not rise far above baseline levels in those countries that apply thresholds. In England and Scotland, GP consultation rates remained at the lower end of the range for normal seasonal activity, and in Wales activity remained within baseline levels. Rates of influenza-like illness were highest among the younger age groups; particularly in children aged under 4 years. During the last four years, influenza activity has remained at low levels and, therefore, the rise in consultation rates for those aged under 4 years was not entirely unexpected. These children would have had little previous exposure to influenza, in comparison with other age groups, and therefore have shown greater susceptibility to the newly emergent antigenic variant.

Reports of laboratory confirmed RSV followed the usual seasonal pattern during 2003/2004, characterised by a gradual increase in RSV detections from mid-October, reaching a peak in early January. The RSV peak was marginally higher this season compared with 2002/2003, but it was not significantly larger than levels recorded in previous seasons. Total reports of RSV detected through NHS and HPA laboratories (direct immunofluorescence and PCR only) indicate a small rise in RSV cases detected during 2002/2003 (4965 reports) in comparison with last season (4505 reports).

Childhood deaths attributable to Influenza

During the 2003/2004 influenza season a number of deaths in children associated with acute respiratory illness were reported from the US, Canada, and the UK (6). A total of 24 suspected influenza associated deaths were reported among those aged 18 years or under during the 2003/04 season in both England and Scotland. Of these, 17 were associated with infection with influenza A (H3N2) Fujian-like strain. A recent investigation into these deaths failed to reveal any pre-existing medical conditions which would have placed these children in a high risk category, and thus did not indicate a failure in delivery of existing vaccination policy. Nevertheless, the study recommended that the current vaccination policy – to vaccinate children aged 6 months and over only if they have an underlying medical condition which puts them at increased risk

of a serious complication of influenza virus infection – should be reviewed (6).

The mortality data received from ONS (England and Wales) for both adults and children, did not seem to indicate a significant increase in influenza related deaths during the 2003/2004 season, and there is currently no evidence to suggest that the number of registered influenza deaths for 2003/2004, in comparison with epidemic years, is in any way remarkable.

In the light of the public concern over the child deaths, two US studies looked into the effectiveness of the 2003/04 influenza vaccine against the currently circulating strain. During years in which the inactivated influenza vaccine is well matched against the circulating strain, effectiveness against illness among healthy adults aged 65 years and under is estimated between 70% and 90%. The studies concluded that during the 2003/2004 season, the vaccine offered between 38% and 52% effectiveness in adults and children against laboratory confirmed influenza.

Despite this reduction in effectiveness both studies concluded that, although not optimally matched with the circulating strain, there were still considerable health benefits to receiving the vaccine (7).

This conclusion supports the latest recommendations from a subgroup of the Joint Committee on Vaccinations and Immunisation (JCVI), which has endorsed the current immunisation policy, but recommended that improved vaccine uptake be pursued in young children with conditions that put them at high risk of complications from influenza infection.

Thresholds

The Chief Medical Officer for England has approved changes to the thresholds used to describe levels of influenza activity for the 2004/2005 season in England and Wales (RCGP scheme). Thresholds, and a standard set of definitions, are used to provide a clear and consistent message to the general public and media about the level of influenza virus circulation, and provide an indication to GPs when sufficient virus is circulating in the community to warrant the use of antiviral drugs (table 4).

In light of data analysis undertaken by the HPA, the previous thresholds were considered to be no longer appropriate for the levels of influenza activity recently observed in England given a secular decline in GP consultation rates for influenza like illness (ILI) over recent years (8).

Using the new criteria, levels of activity in three years (1996/97, 1998/99, and 1999/2000) would have been classified as 'epidemic'. Further examination of the epidemics in 1996/1997, 1998/1999, 1999/2000 revealed that they were of a similar impact to the 1989/1990 epidemic in terms of both the morbidity they caused and the laboratory isolates generated. This was additional justification for lowering the threshold (8).

Influenza vaccination uptake. During 2004/2005, the CFI on behalf of the Department of Health, will begin monitoring vaccine uptake rates among those aged

under 65 years at high risk. This will be carried out in addition to the monitoring of vaccine uptake in those aged 65 years and over and for health care workers, both of which have been carried out for the last three years. For the first time, reporting will be through the web-based Vaccine Tracking Programme, sponsored by the DH.

Vaccine recommendations. The World Health Organization (WHO) announced the vaccine composition for the 2004/2005 (northern hemisphere winter) in February 2004. It was recommended that the vaccine contain the following:

- An A/New Caledonia/20/99(H1N1)-like virus
- An A/Fujian/411/2002(H3N2)-like virus*
- A B/Shanghai/361/2002-like virus†

Avian influenza (H5N1) in poultry and humans in south east Asia

The 2003/04 influenza season was characterised by the outbreak of avian influenza A (H5N1) in humans and poultry stocks in south east Asia. Outbreaks of avian influenza are of particular concern due to their devastating effect on the poultry industry and the wider global health implications of a possible emergence of a human influenza strain with pandemic potential (9).

The Republic of Korea was the first to issue reports of highly pathogenic avian influenza (HPAI), later identified as influenza A (H5N1), among commercial poultry stocks in early December 2003. By the end of the year more than 1.3 million chickens and ducks had been killed by avian influenza or culled in order to prevent further spread of the infection.

In January 2004, Viet Nam informed WHO about an outbreak of unexplained severe respiratory illness in humans, later identified as influenza A (H5N1). It also reported widespread outbreaks of HPAI in backyard poultry flocks. By the end of January, Thailand had also reported laboratory confirmed cases of H5N1 from infected humans and poultry. This news was rapidly followed by further widespread poultry outbreaks in Cambodia, China, Indonesia, Japan, and Laos (10). Over 100 million birds were culled as a control measure and although initially reported as successful by many countries, ongoing outbreaks continue to be reported in Cambodia, China, Malaysia, Thailand, and Viet Nam, suggesting that the virus is widely prevalent and may have become endemic in domestic fowl. By the end of May 2004, 34 human cases had been confirmed as influenza A (H5N1) infections, 23 (68%) of whom have died.

On the 27 September 2004, the United Nations Food and Agriculture Organisation (FAO) and the World Organisation for Animal Health (OIE) issued a statement describing the avian influenza epidemic as a 'crisis of global importance' (11). The two

*The currently used vaccine virus is A/Wyoming/3/2003. A Kumamoto/102/2002 is also available as a vaccine virus.

† Candidate vaccine viruses include B/Shanghai/361/2002 and B/Jilin/20/2003, which is a B/Shanghai/361/2002-like virus.

Table 4 Past and future thresholds used by the Centre for Infections to describe influenza activity

	Consultation rate per 100,000 population for influenza and influenza-like illness.	
	Old threshold	Revised threshold
Baseline activity	<50	<30
Normal seasonal activity	50-200	30-200
Higher than average seasonal activity	>200-400	Discarded
Epidemic activity	>400	>200

organisations warned that it is unlikely that the virus will be eradicated in the near future, and that major investment is required to strengthen veterinary services, in particular surveillance, early warning, detection, reporting, and response.

The ongoing poultry outbreaks pose a significant threat to human health, as the virus has jumped directly from infected poultry to humans on a number of occasions. It is of continuing concern that the virus may reassort its genes with those of a human influenza virus and acquire the ability to move readily from human-to-human and trigger a pandemic.

Previous outbreaks of influenza A (H5N1). The current ongoing outbreak is not the first time that avian influenza A (H5N1) has crossed the species barrier from poultry to humans without an intermediate host. The first human outbreak of H5N1 occurred in Hong Kong in 1997. Six out of 18 human cases of H5N1 infection died, and 1.5 million chickens were slaughtered to successfully control the outbreak (12). Although initially successful, Hong Kong health authorities were forced to employ these control methods again in 2001 and early 2002 to prevent further H5N1 poultry outbreaks spreading to humans.

The last recorded human cases of H5N1 occurred in February 2003 among Hong Kong residents who had travelled in mainland China. Two samples were obtained during this outbreak and confirmed as H5N1, with one death positively attributed to avian influenza (13). Further research stimulated by the Hong Kong avian influenza outbreak in 1997 has also indicated that the H5N1 strain is capable of infecting humans directly without the intermediate step of infecting a mammalian host, as previously thought necessary (14).

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