EPIDEMIOLOGICAL AND VIROLOGICAL ASSESSMENT OF INFLUENZA ACTIVITY IN EUROPE, DURING THE 2004-2005 WINTER

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The 2004-2005 influenza season in Europe started in late December 2004 and the first influenza activity occurred in the west and southwest (Spain, United Kingdom and Ireland). Influenza activity then moved gradually east across Europe during January and early February 2005, and from late February until late March, most movement was south to north. The intensity of clinical influenza activity in ten out of 23 countries was higher than during the 2003-2004 season, and lower or equal to the 2003-2004 season in the other 13 countries. The highest consultation rates were generally observed among children aged 0-14 years. However, the peak consultation rates due to influenza-like illness or acute respiratory infection were not especially high when compared with historical data. The predominant virus strain was influenza A (83% of total detections) of the H3 subtype (85% of H-subtyped A viruses), with fewer influenza B (17% of total detections) or A(H1) viruses (15 % of H-subtyped A viruses) detected. The vast majority of A(H3) viruses were similar to the reference strains A/Wellington/1/2004 (H3N2) and, subsequently, A/California/7/2004 (H3N2) that are closely related drift variants of the A/Fujian/411/2002 (H3N2) prototype vaccine strain. The B viruses co-circulated with A viruses during the whole influenza season in 11 out of 24 countries. Seven of these were located in the northeast of Europe and in these countries the proportion of B viruses was higher (range: 31-60%) than in the rest of Europe (range: 6-26%). In 13 out of 24 countries the B viruses circulated relatively late in the season. About 43% of all antigenically characterised B viruses were B/Hong Kong/330/2001-like (B/Victoria/2/87 lineage), a strain that is distinguishable from the vaccine influenza B strain, which was a B/Yamagata/16/88 lineage virus. Based on the viruses detected worldwide until February 2005, the World Health Organization modified the composition of the 2005-2006 influenza vaccine from the 2004-2005 season vaccine to include a new A(H3N2) component: an A/California/7/2004 (H3N2)-like virus.

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Introduction

Influenza has a considerable public health impact in Europe each winter. Seasonal epidemics are associated with higher general practice consultation rates [1], increased hospital admissions [2] and excess deaths [2, 3].

The European Influenza Surveillance Scheme (EISS) is a collaborative project of physicians (mainly in primary care), epidemiologists and virologists, and aims to contribute to a reduction in morbidity and mortality due to influenza in Europe by active clinical and virological surveillance of influenza [4-6]. The participating national reference laboratories have functioned within EISS as the Community Network of Reference Laboratories for Human Influenza in Europe (CNRL) since 2003 [7]. An important objective for the scheme has been the inclusion of all member states of the European Union (EU), as required by EU Decision 2119/98/EC on the establishment of dedicated surveillance networks for communicable diseases [8], and this was achieved at the end of the 2004-2005 season.

Including all members who participated in EISS during the 2004-2005 season (20 EU countries, Norway, Romania and Switzerland), the EISS project comprised 30 national influenza reference laboratories. The characteristics of the sentinel networks during the 2004-2005 season are summarised in Table 1. The median weekly population under clinical surveillance by the sentinel networks during the 2004-2005 season varied from 0.4% to 100% of the total population of a country, representing at least a median number of 17.8 million inhabitants of Europe [TABLE 1]. The sentinel surveillance is carried out by 12 902 general practitioners (GPs), paediatricians and other physicians, although during the 2004-2005 season the number of physicians reporting each week was often lower than this [TABLE 1]. In general, the age distribution of the population under surveillance is representative for the age distribution of the total population in a country, although in some countries the population under surveillance is skewed to the lower ages (partly due to a high proportion of paediatricians) and /or higher ages [TABLE 1]. Further data about representativeness of the population under surveillance in EISS can be found for most countries in Aguilera et al. [11].

A proportion of the sentinel physicians, in general representative for the surveillance network in a country, also collects nose and/or throat swabs for virological surveillance using a swabbing protocol that guarantees representative swabbing during the season [TABLE 1] [11]. Combining clinical and virological data in the same population allows the validation of clinical reports made by the sentinel physicians and provides virological data in a clearly defined population, the general population that visits a physician with an influenza-like illness (ILI) or acute respiratory infection (ARI) [12]. In addition to specimens obtained from physicians in the sentinel surveillance systems, the laboratories also collect and report results on specimens obtained from other sources (e.g. from hospitals or non-sentinel physicians). These data are called 'non-sentinel' in this paper and are collected to give a second measure of influenza activity and to analyse the representativeness of the virological data obtained from the sentinel physicians [12]. Based on the collection of virological data, the total population under surveillance of EISS was about 462 million inhabitants of Europe during the 2004-2005 season.

The identification of circulating viruses within the population and the recognition of virological changes are important tasks for EISS in order to fulfil its early warning function [7]. There is a particular need to detect and monitor the emergence or re-emergence of viruses with pandemic potential and viruses that have a 'mismatch' with the vaccine strain components, and to monitor their clinical impact.

This report presents an analysis and interpretation of influenza surveillance data collected by European countries that were active members of EISS during the 2004-2005 season.

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Table 1

Some characteristics of the national sentinel surveillance networks during the 2004-2005 season[1]

	No. of physicians in the sentinel networks			No. of physicians that reported ILI/ARI during the season		Population under surveillance during the season					Age distribution total population; %[2, 4]			% of sentinel physicians who took swabs[5]
						% of total population[2]		Age distribution; median %[3, 4]						
Country	GPs	Paedia-tricians	Other[6]	Median	Range	Median	Range	0-14	15-64	65+	0-14	15-64	65+	
Austria	42	14	–	38	18-47	0.7	0.3-0.9	37	51	12	16	68	16	n.k.
Belgium	71	–	–	39	29-44	0.4	0.3-0.5	18	66	17	17	66	17	61
Czech Republic	2230	1240	–	3115	3036-3181	47.3	46.2-48.3	18	64	18	15	71	14	n.k.
Denmark	150	–	–	125	98-143	3.4	2.7-4.0	19	66	15	19	66	15	100
England	360	–	–	294	152-319	1.1	0.5-1.2	18	67	15	19	65	16	17
France	378	74	–	376	282-415	0.6	0.6-0.7	23	61	16	19	65	16	n.k.
Germany	604	146	33	593	437-639	1.6	1.2-1.7	22	55	23	15	67	19	27
Ireland	68	–	–	61	52-68	2.5	2.2-2.7	n.k.	n.k.	n.k.	21	68	11	100
Italy	750	100	–	399	238-859	0.9	0.5-2.1	18	63	20	14	67	19	19
Latvia	113	–	–	n.k.	n.k.	8.7	n.a.	19	65	16	15	69	17	n.k.
Lithuania	321	327	396	n.k.	n.k.	39.7	39.7-40.0	n.k.	n.k.	n.k.	17	68	15	6 physicians[7]
Luxembourg	15	4	–	13	6-16	0.9	0.4-1.2	n.k.	n.k.	n.k.	19	67	14	n.k.
Malta	22	–	–	22	n.k.	n.k.	n.k.	n.k.	n.k.	n.k.	18	69	14	n.k.
Netherlands	67	–	–	41	37-44	0.6	0.4-0.9	18	69	14	19	68	14	49
Northern Ireland	93	–	–	75	60-88	7.0	5.7-7.8	20	66	14	22	65	13	67[8]
Norway	–	–	201	n.k.	n.k.	n.k.	n.k.	14	63	23	20	66	15	55 practices[7]
Poland	192	–	–	190	144-219	1.4	1.1-1.7	18	71	11	17	70	13	5
Portugal	170	–	–	40	20-68	0.6	0.3-1.0	16	66	19	16	67	17	24
Romania	240	102	–	225	206-240	2.2	1.7-2.2	28	58	15	16	70	15	n.k.
Scotland	90	–	–	n.k.	n.k.	8.1	6.1-8.4	n.k.	n.k.	n.k.	18	66	16	40 physicians[7]
Slovakia	2121	1202	–	n.k.	n.k.	100[9]	n.a	19	65	16	17	71	12	Not constant
Slovenia	14	12	12	36	19-44	3.5	1.5-4.1	34	59	7	14	70	15	100
Spain	391	102	–	n.k.	n.k.	1.3	0.6-1.4	18	63	18	15	69	17	100
Sweden	–	–	96	64	36-72	n.k.	n.k.	n.k.	n.k.	n.k.	18	65	17	n.k.
Switzerland	154	43	68	194	165-220	3.0	2.4-5.4	21	64	15	16	68	16	25
Wales	30	–	–	n.k.	n.k.	7.4	7.4-7.4	17	64	19	19	64	17	n.k.

1. Number of physicians reporting ILI/ARI and population under surveillance are based on weekly reports of these figures during the 2004-2005 season
ILI = Influenza-Like Illness; ARI = Acute Respiratory Infection; GPs = general practitioners; n.k. = not known; n.a. = not applicable
2. Total population figures and age distribution were derived from reference [9] for all countries except the United Kingdom. Data for all countries except Belgium and Italy were from 1 January 2005, for Belgium and Italy from 1 January 2004. For the United Kingdom administrations England, Northern Ireland, Scotland and Wales reference [10] was used; total population figures are from 2004 and the age distribution is from the Census 2001
3. Malta and Norway record encounters. The age distribution for Norway was calculated from age specific encounters. For Germany and Poland the age distribution was calculated from the proportion of the population under surveillance for which the age was known
4. Totals may not sum to 100 due to rounding
5. Aguilera et al. [11] and updated information
6. Germany and Switzerland: internists; Slovenia: "community practitioners" for 7 to 18 years-old; Lithuania: therapists; Norway and Sweden: practices
7. No or partial overlap with physicians/practices collecting clinical data
8. 67% of physicians agreed to take swabs, however, due to the mild season 38% of physicians actually took swabs during the 2004-2005 season
9. All GPs and paediatricians in Slovakia are obliged to report

Methods

Twenty six countries actively monitored influenza activity from week 40/2004 (27/9/2004- 3/10/2004) to week 20/2005 (16/5/2005 - 22/5/2005) during the 2004-2005 season [TABLE 1] (in this paper England, Northern Ireland, Scotland and Wales were considered as four separate countries as they each have their own surveillance system). This paper only presents data collected until week 16/2005 (18/4/2005 - 24/4/2005) as some networks stopped collecting clinical data at the end of the season and data was therefore incomplete for weeks 17-20/2005. In each of the countries, one or several networks of sentinel physicians reported consultation rates due to ILI and/or ARI on a weekly basis. Twenty one countries reported ILI consultations per 100 000 population; Malta, Norway and Sweden reported ILI per 100 consultations and the Czech Republic, France and Germany reported ARI consultations per 100 000 population.

Sentinel physicians also obtained nasal, pharyngeal, or nasopharyngeal specimens from a subset of patients and these were sent to the national reference laboratory or laboratories for virological analysis. The laboratories also collected and reported results on specimens obtained from other sources (e.g. from hospitals or non-sentinel physicians).

The virological data included results mostly from cell cultures followed by virus type and subtype identification and from rapid diagnostic enzyme-immunological or immunofluorescence tests identifying the virus type only. Many laboratories also routinely use reverse transcription polymerase chain reaction (RT-PCR) for detection, typing and subtyping [13]. About 75% (20/26) of the countries reported antigenic characterisation data and almost 50% (12/26) of the countries reported genetic characterisation data of the virus isolates during the 2004-2005 season.

During the influenza season, the weekly clinical and virological data were processed and analysed by the national centres and then entered into the EISS database the following week via the internet (www.eiss.org) [14]. The indicators of influenza activity were established on a weekly basis by the national coordinators: the intensity of clinical activity and the geographical spread of influenza (see Box), and the dominant type/subtype circulating in the population (definition not shown). The dominant type/subtype for the season as a whole was estimated per country using the algorithm shown in the box. During the 2004-2005 season eight countries entered a baseline (see Box).

Box. Definitions of indicators

Baseline

Level of clinical influenza activity calculated nationally representing the level of clinical activity in the period that the virus is not epidemic (summer and most of the winter) based on historical data (5-10 influenza seasons).

Intensity

The intensity of clinical activity compares the weekly clinical morbidity rate with historical data:

- Low – no influenza activity or influenza activity at baseline level
- Medium – usual levels of influenza activity
- High – higher than usual levels of influenza activity
- Very high – particularly severe levels of influenza activity (less than once every 10 years)

Geographic spread

The geographic spread is a WHO indicator that has the following levels:

- No activity – no evidence of influenza virus activity (clinical activity remains at baseline levels)
- Sporadic – isolated cases of laboratory confirmed influenza infection
- Local outbreak – increased influenza activity in local areas (e.g. a city) within a region, or outbreaks in two or more institutions (e.g. schools) within a region; laboratory confirmed
- Regional activity – influenza activity above baseline levels in one or more regions with a population comprising less than 50% of the country's total population; laboratory confirmed,
- Widespread – influenza activity above baseline levels in one or more regions with a population comprising 50% or more of the country's population, laboratory confirmed

Dominant virus

The assessment of the dominant virus for the season is based on:

- Sentinel and non-sentinel data (primary assessment sentinel data)
- A minimum number of 10 isolates
- If more than 10% of total A isolates are H-subtyped the H subtype is taken into consideration
- If more than 10% of total A isolates are N-subtyped the N subtype is also taken into consideration
- The limits for co-dominant virus types/subtypes are: 45%:55%

During the season a Weekly Electronic Bulletin was published each Friday on the EISS website, which allowed EISS members, public health authorities and the general public to view influenza activity in their own and neighbouring countries.

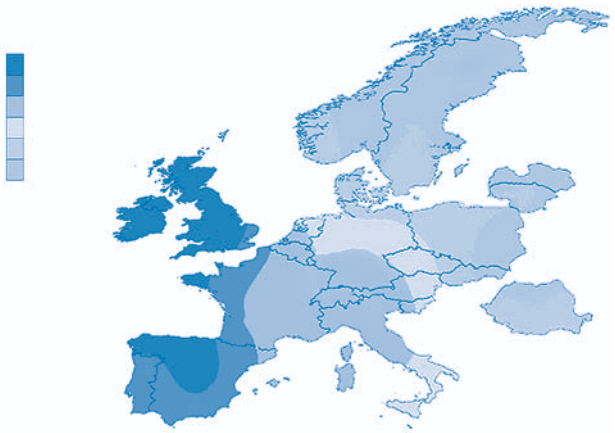
To analyse the timing of peak clinical influenza activity across Europe, a geographic information system (GIS) using centre coordinates of each country and the kriging method using the difference (in weeks) in timing of peak activity relative to the first country with peak activity [15], and plotting the longitude and latitude of the centre of each country against the week of peak activity, were applied. Kriging is an interpolation method of spatial prediction to estimate unknown point values by using known point values. The weights reflect the distances between locations for which a value is being predicted and the locations with measured values. It is considered the best linear unbiased estimator as it reflects the best minimum mean square error, and can minimise estimation error variance.

Results

The 2004-2005 influenza season in Europe began in December 2004 and clinical influenza activity first occurred in the southwest (United Kingdom, Spain and Ireland) and gradually moved east across Europe, starting in Italy/Portugal, France/Switzerland, Austria/Luxembourg, Slovenia/Czech Republic/the Netherlands/Belgium/Germany in subsequent weeks during January 2005 (see Figure 1 at http://www.eiss.org/documents/eurosurveillance_supplement_2004-2005_season.pdf). Thereafter, influenza activity moved in a more southerly-northerly direction starting in Poland/Lithuania/Sweden, Denmark/Norway and Romania/Slovakia/Latvia in subsequent weeks from February until March. A similar movement was seen when the timing of peak clinical influenza activity across Europe was analysed. By regression analysis of plots of the longitude and latitude of the centre of each country against the week of peak influenza activity, both the west-east ($R2 = 0.6796$; $p<0.001$) and south-north ($R2 = 0.2496$; $p=0.018$) movement were statistically significant. The timing is nicely visualised in figure 1.

Figure 1

Timing of peak clinical influenza activity across Europe during the 2004-2005 season



Note: The isobars on the contour maps represent interpolated time of peak activity distributed spatially at 2 week intervals. Countries included in this spatial analysis were Austria, Belgium, Czech Republic, Denmark, France, Germany, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Switzerland, Sweden, and the United Kingdom. Reproduced from [15] with permission from Reiko Saito

The peak intensity of clinical influenza activity ranged from low in Scotland and Wales to high in ten countries, and 15 of 25 countries reported widespread influenza activity during the 2004-2005 season [TABLE 2] (see also Figure 1 at http://www.eiss.org/documents/eurosurveillance_supplement_2004-2005_season.pdf). The peak levels of ILI/ARI consultation rates in Europe were reached between week 50/2004 and 12/2005 [TABLE 2], covering a period of 13 weeks between the first and last peak. The week of peak ILI/ARI consultation rates coincided roughly with the week of peak sentinel influenza virus detections [TABLE 2]. A detailed breakdown of the sentinel clinical and virological data by week and country is available from the EISS website (see Figure 2 at http://www.eiss.org/documents/eurosurveillance_supplement_2004-2005_season.pdf).

In countries reporting age specific data (N=20), the highest consultation rates during the influenza peak were observed among children in the age groups 0-4 years and 5-14 years in 12 countries [TABLE 2]. In four of these countries the consultation rate was slightly higher in the 5-14 age group than in the 0-4 age group

Table 2

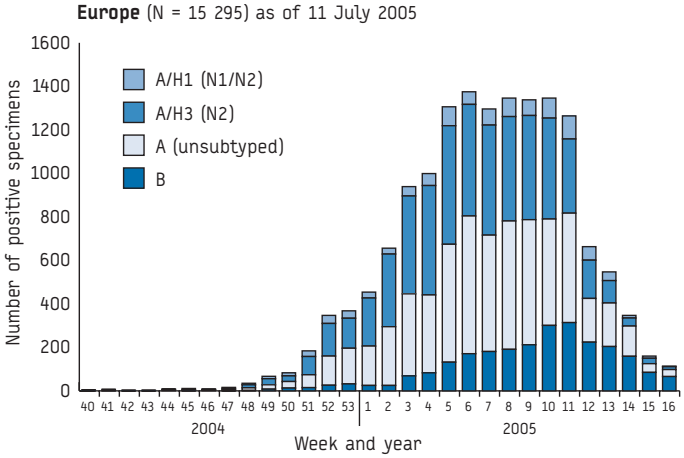
Overview of influenza activity during the 2004-2005 season[1]

Country (N=26)	Week(s) of peak clinical activity	Most affected age groups[2]	Intensity (peak level)	Week(s) of peak virus detections[3]	Dominant virus type/subtype	Geographical spread (peak level)
Influenza-like illness:						
England	No peak	None	Medium	5	A(H3N2)	Regional
Scotland	No peak	n.a.	Low	5 + 10	A(H3)	Sporadic
Wales	No peak	None	Low	7	A	Sporadic
NorthernIreland	50 + 1	0-4	Medium	n.a.	A(H3)	Sporadic
Ireland	1	n.a.	Medium	53	A(H3N2)	Local
Spain	2-3	5-14, 0-4	High	2	A(H3)	Widespread
Portugal	5	5-14, 65+	High	4	A(H3)	Widespread
Belgium	6-8	5-14, 0-4	Medium	9	A(H3N2)	Widespread
Italy	6	0-4, 5-14	High	5	A(H3N2)	Widespread
Switzerland	6	0-4, 5-14	Medium	5	A(H3)	Widespread
Austria	7	0-4	High	9	A(H3N2)	Widespread
Luxembourg	7	n.a.	High	7	A(H3N2)	Widespread
Netherlands	7	0-4, 65+	High	7	A(H3)	Widespread
Slovenia	7	0-4, 5-14	Medium	8	A(H3N2) + B	Widespread
Malta	8-9	n.a.	n.a.	n.a.	n.a.	n.a.
Poland	8-11	0-4, 5-14	High	10	A(H3) + B	Regional
Denmark	11	0-4, 5-14	High	8	A(H3N2)	Widespread
Latvia	11-12	0-4, 5-14	Medium	9.	A(H3)	Regional
Lithuania	11	n.a.	High	n.a.	n.a.	Regional
Romania	11	15-64, 5-14	Medium	11	A(H3N2)	Regional
Slovakia	11	5-14, 0-4	Medium	10	A(H3) + B	Local
Sweden	11	n.a.	Medium	9	A	Widespread
Norway	12	5-14, 15-64	Medium	7	A(H3N2)	Widespread
Acute respiratory infections:						
France	6	0-4, 5-14	Medium	5	A(H3N2)	Widespread
Germany	7-9	0-4, 5-14	High	10	A(H3)	Widespread
Czech Republic	8	0-4, 5-14	Medium	9	A	Widespread

1. Sentinel data, except for dominant virus type/subtype for which sentinel and non-sentinel data were taken into account. For definitions of indicators see the Box
n.a. = not applicable as no data was available or insufficient data was available. No peak = activity was not above baseline or was flat during the whole season
2. If two age groups are shown the sequence is: most affected, second most affected
3. Estimated primarily taking into account the percentage of influenza virus positive specimens and secondarily the absolute number of isolates when the percentage of positive specimens was ambiguous

Figure 2

Total number of sentinel and non-sentinel specimens positive for influenza viruses by week for Europe as a whole during the 2004-2005 season



and in the other eight countries the consultation rate was slightly higher in the 0-4 age group than in the 5-14 age group [TABLE 2]. In Austria and Northern Ireland the consultation rate was clearly highest in the 0-4 age group. Although in the Netherlands, Norway, Portugal and Romania the consultation rate was also high in the younger age groups, in the Netherlands and Portugal the consultation rate was highest among people aged 65+ years in one week and in Norway and Romania the consultation rate was also high in the 15-64 years age group [TABLE 2].

For Europe as a whole, the largest number of positive specimens was detected between week 5/2005 and 11/2005 [FIGURE 2]. A total of 15 295 sentinel and non-sentinel specimens were positive for influenza virus: 12 745 (83%) were influenza A and 2550 (17 %) were influenza B. Of all haemagglutinin-subtyped viruses (N=6648), 5651 (85%) were H3 and 997 (15%) were H1. All 2102 neuraminidase-subtyped A(H3) viruses were of the N2 subtype and of the 467 neuraminidase-subtyped A(H1) viruses 465 (99%) were N1 and only about 1% (2 viruses) N2. The predominant virus circulating in the individual countries was mostly influenza A(H3) [TABLE 2]. The B viruses co-circulated the whole season with A viruses in 11 out of 24 countries [TABLE 3]. Seven of these countries were located in the northeast of Europe and the proportion of B viruses in this region was higher (range: 31%-60%) than in the rest of Europe (range: 6%-26%) [TABLE 3]. In 13 out of 24 countries, the B viruses circulated relatively late in the season [TABLE 3]. The distribution of B viruses over sentinel and non-sentinel sources was variable [TABLE 3]. A detailed breakdown by country of the virological data collected in the sentinel and non-sentinel systems is available from the EISS website (see Figure 2,

Table 3

Characteristics of influenza B viruses circulation during the 2004-2005 season[1]

Country (N=26)	Influenza B virus detections			Characterised influenza B viruses[2]			Circulation of influenza A and B viruses[3]
	% of sentinel and non-sentinel viruses	% of sentinel viruses	% of non-sentinel viruses	% of total detected B viruses	% of characterised B viruses		
					Victoria lineage	Yamagata lineage	
Influenza-like illness:							
England	14	14	14	63	18	82	Successive
Scotland	14	17	14	1	0	100	Co-circulation
Wales	21	47	19	n.a.	n.a.	n.a.	Successive
Northern Ireland	13	21	11	n.a.	n.a.	n.a.	Successive
Ireland	20	26	4	3	0	100	Successive
Spain	15	13	24	0	n.a.	n.a.	Successive
Portugal	17	14	19	15	0	100	Successive
Belgium	11	8	15	3	0	100	Successive
Italy	26	27	16	11	64	36	Successive
Switzerland	n.a.	13	n.a.	90	49	51	Co-circulation
Austria	38	39	n.a.	31	15	85	Co-circulation
Luxembourg	6	6	n.a.	80	75	25	Co-circulation
Netherlands	20	37	17	n.a.	n.a.	n.a.	Successive
Slovenia	60	67	38	3	0	100	Co-circulation
Malta	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Poland	41	48	8	77	83	17	Co-circulation
Denmark	11	12	11	11	0	100	Successive
Latvia	42	53	42	4	33	67	Co-circulation
Lithuania	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Romania	33	34	25	97	75	25	Co-circulation
Slovakia	31	27	50	85	0	100	Co-circulation
Sweden	n.a.	n.a.	10	3	0	100	Successive
Norway	26	23	27	9	8	92	Co-circulation
Acute respiratory infections:							
France	9	9	9	27	15	85	Successive
Germany	20[4]	13	24[4]	90[4]	74	26	Successive
Czech Republic	32	32	n.a.	39	0	100	Co-circulation

1. n.a. = not applicable as no data is available or insufficient data is available

2. Antigenic and/or genetic. Reference strains used during the 2004-2005 season were for the B/Victoria/2/87 lineage B/Hong Kong/330/2001 and for the B/Yamagata/16/88 lineage B/Jiangsu/10/2003

3. Sentinel and non-sentinel combined. Successive: the influenza A virus decrease overlapped with the influenza B virus increase. Co-circulation: influenza A and B viruses circulating together during the whole season

4. Personal communication, Dr B Schweiger, Germany. Non-sentinel virus detections were not reported to EISS, but non-sentinel characterisations were

Tables 1 and 2 at http://www.eiss.org/documents/eurosurveillance_supplement_2004-2005_season.pdf).

Twenty one of the 26 countries reported antigenic and/or genetic characterisation of the haemagglutinin for a total of 4 253 virus isolates. Of the 3964 antigenically characterised isolates 179 were also genetically characterised. An additional 289 isolates were characterised genetically only. In total (N=4253), the haemagglutinin of 1604 (38%) viruses was reported as A/Wellington/1/2004 (H3N2)-like, of 1012 (24%) as A/California/7/2004 (H3N2)-like, 92 (2%) as A/Fujian/411/2002 (H3N2)-like, two (0.05%) as A/Panama/2007/99 (H3N2)-like, 774 (18%) as A/New Caledonia/20/99 (H1N1)-like, 437 (10%) as B/Jiangsu/10/2003-like (B/Yamagata/16/88 lineage) and 332 (8%) as B/Hong Kong/330/2001-like (B/Victoria/2/87 lineage). In countries reporting influenza B characterisations, influenza B/Hong Kong/330/2001-like viruses were always reported in combination with B/Jiangsu/10/2003-like viruses [TABLE 3]. Circulation of only B/Jiangsu/10/2003-like viruses was reported by Belgium, the Czech Republic, Denmark, Ireland, Portugal, Scotland, Slovakia, Slovenia and Sweden [TABLE 3]. B/Hong Kong/330/2001-like viruses were most prevalent (>50% of characterised B viruses) in Germany, Italy, Luxembourg, Poland and Romania [TABLE 3].

About 60% of the 3964 antigenically characterised viruses had an H3 similar to one of the two A(H3N2) drift variants A/Wellington/1/2004 (H3N2) (1 582; 40%) and A/California/7/2004 (H3N2) (770; 19%), which are distinguishable from, but closely related to, the A/Fujian/411/2002 (H3N2)-like 2004-2005 vaccine virus A/Wyoming/3/2003. Ninety-two viruses (2%) had an H3 antigenically similar to A/Fujian/411/2002 (H3N2). Two viruses had an H3 antigenically similar to the former vaccine strain A/Panama/2007/99 (H3N2). The H1 of 759 (19%) viruses was antigenically similar to the 2004-2005 vaccine strain A/New Caledonia/20/99 (H1N1). Among the 759 antigenically characterised B viruses, 433 (57%) were B/Jiangsu/10/2003-like and 326 (43%) were B/Hong Kong/330/2001-like.

Discussion

The 2004-2005 influenza season in Europe began in December 2004, which was late in comparison to the previous season, which began in October/November 2003 [6]. Peak clinical influenza activity was, for all countries with the exception of Italy and Germany, more than five weeks later than in the 2003-2004 season. The 2004-2005 season was dominated by the spread of a drift variant relative to the A/Fujian/411/2002 (H3N2)-like virus that circulated in the 2003-2004 season, represented by the reference strains A/Wellington/1/2004

(H3N2) and, subsequently, A/California/7/2004 (H3N2). In addition, almost half of all characterised B viruses were B/Hong Kong/330/2001-like (B/Victoria/2/87 lineage), viruses antigenically distinguishable from the vaccine B virus (B/Yamagata/16/88 lineage). The peak clinical influenza activity was higher than during the 2003-2004 season [6] in ten out of 23 countries, of which Italy, Luxembourg, Poland, Slovenia and Spain reported a peak consultation rate that was more than twice as high as during the previous season. However, ILI/ARI consultation rates during the 2004-2005 season were not especially high compared with data from previous seasons [16,17].

The general progress of influenza activity across Europe during the 2004-2005 season differed from most previous seasons in that there was a west-east movement at the beginning of the season changing into a south-north movement later on in the season. Analysis of five previous seasons (1999-2000 to 2003-2004) indicated that there was a west-east movement of influenza activity in three seasons (2001-2002, 2002-2003 and 2003-2004), but that in the 2001-2002 season there was also a south-north movement similar to that found for the 2004-2005 season [18]. These analyses were done by plotting the longitude and latitude of the centre of each country against the week of peak incidence. Recently, Saito et al [15] applied the method of kriging to influenza data and as presented in this paper [FIGURE 1] this method has the advantage of visual presentation of the timing of peak clinical influenza activity on the map of Europe. The European map generated [FIGURE 1] indicates different timing in individual countries, which may be an artefact, as only the coordinates of the centre of a country were included. However, practice-based data from Germany indicated a similar south-north/east pattern as that observed in the EISS European analysis [19]. EISS is currently working on the extension of the method applied on the German data to include more European countries. In addition, further research is needed to determine what drives the direction of the movement or timing, such as type, subtype and antigenic characteristics of the founder virus, humidity, temperature, UV radiation and air traffic.

Although the age groups most affected were 0-4 years and 5-14 years, it should be noted that the estimated consultation rates for the different age groups are influenced by several factors such as consultation behaviour, estimation procedure, case definition, vaccination coverage and obligatory doctors visit for absence from work or school, which may differ between countries.

The continuous drift of the A(H3N2) viruses has led to the selection of the new reference viruses A/Wellington/1/2004 (H3N2) and A/California/7/2004 (H3N2), and both were reported to EISS during the 2004-2005 season. However, reference reagents for the antigenic characterisation of A/California/7/2004 (H3N2)-like viruses became available only halfway through the season, and retrospective analysis of a number of isolates from early in the season showed that a majority of these also resembled A/California/7/2004-like rather than A/Wellington/1/2004 (H3N2)-like. It is therefore possible that many of the viruses from the beginning of the season, which were recorded as A/Wellington/1/2004 (H3N2)-like at the time, actually belonged to the A/California/7/2004 (H3N2) drift variant. A recent analysis using antigenic cartography with data from the Netherlands and from the World Health Organisation (WHO) reference strains clearly showed the antigenic drift; when compared with large jumps of the A(H3N2) virus in the past, however, the recent drift was small and did not have a large clinical impact [20].

The influenza B virus detection results clearly demonstrated that there are differences between specimens collected from sentinel patients and non-sentinel patients. In only eight out of 19 countries was the proportion of B virus detections similar in sentinel and non-sentinel specimens. In eight other countries, most B virus detections were done in sentinel specimens, and in three countries, most detections were done in non-sentinel specimens [TABLE 3]. As influenza B virus infections are mostly mild and patients with these infections generally do not visit and are not admitted to hospitals, differences in the professions of doctors included in the sentinel and non-sentinel systems may explain these differences [21]. Another explanation might be the differences in age distribution of the population under surveillance in the sentinel systems [TABLE 1] and the differences in age distribution of the patients from whom a swab is taken. There are sentinel systems where a high proportion of specimens come from children, while others have a more balanced age distribution [21]. More systematic research into the structures of the various surveillance systems is needed to support these explanations.

Influenza B viruses currently circulating are antigenically and genetically divided into two distinct lineages represented by B/Yamagata/16/88 and B/Victoria/2/87 viruses, which have evolved to such an extent that antibodies raised to viruses of one lineage offer reduced cross-reactive protection against viruses of the other lineage [22,23]. The trivalent influenza vaccine, however, contains only one B virus component. Between 1990 and 2001, B/Yamagata/16/88 lineage viruses circulated worldwide and B/Victoria/2/87 lineage viruses circulated only in Asia. Since 2001, however, B/Victoria/2/87 lineage viruses have predominated in many countries, including in Europe, and the vaccine strain was changed accordingly. As B/Yamagata/16/88 lineage viruses predominated in the 2003-2004 season, a B/Yamagata/16/88 lineage virus was included in the northern hemisphere vaccine for the 2004-2005 season. In the 2004-2005 season there were more influenza B virus detections in Europe than in the 2003-2004 season: 15% compared with 0.9% [6]. In addition, 43% of the viruses belonged to the B/Victoria/2/87 lineage that was not included in the vaccine, and in five countries, the proportion of B/Victoria/2/87 lineage viruses among total B virus detections was higher than 50% (range 64-83%) [TABLE 3]. Notably, the 2005 season in New Zealand was dominated by circulation of influenza B viruses (almost 90% of total influenza viruses) and most of these belonged to the B/Victoria/2/87 lineage (almost 80% of the total number of characterised B viruses), which was also not included in the vaccine for the 2005 southern hemisphere season [24,25]. However, despite that, the clinical impact was less severe than that from the predominant circulation of A/Fujian/411/2002 (H3N2)-like viruses in the 2004 season in New Zealand [25,26]. In Australia, in contrast, mainly influenza A(H3) viruses (74% of all isolates) circulated during the 2005 season [24]. In the United States, about a quarter of all influenza viruses isolated during the 2004-2005 season were of the B type and, of the antigenically characterised B viruses, about 75% belonged to the B/Yamagata/16/88 lineage (strain in the vaccine) and 25% to the B/Victoria/2/87 lineage [27]. Since by February 2005 most B viruses isolated in the world were of the B/Yamagata/16/88 lineage type, the vaccine for the 2005-2006 northern hemisphere season again contains a B/Shanghai/361/2002-like virus (B/Yamagata/16/88 lineage) similar to the 2003-2004 season [22,28]. Since by September 2005 most B viruses belonged to the B/Victoria/2/87 lineage, the B/Victoria/2/87 lineage virus B/Malaysia/2506/2004 will be included in the vaccine for the 2006 southern hemisphere season [23]. Preliminary results show that B/Victoria/2/87 lineage viruses are predominating during the 2005-2006 season in Europe [29].

The WHO announced the composition of the influenza vaccine for the 2005-2006 northern hemisphere season in February 2005 [22]. Based on the analysis of influenza viruses from all over the world up until February 2005, the A/Fujian/411/2002 (H3N2)-like vaccine strain in the influenza vaccine of 2004-2005 has been exchanged for a more recent virus: an A/California/7/2004 (H3N2)-like virus. In Europe, the vaccine composition recommended by the European Agency for the Evaluation of Medicinal Products, which is based on the WHO recommendations, has been used during the vaccine campaigns for the 2005-2006 season in Europe [28].

During the 2004-2005 season the A(H5N1) influenza virus causing epizootics in Asia and transmission to humans with fatalities [30] was not detected in poultry or humans in Europe. However, A(H5N1) infected birds smuggled into Belgium [31] and the by accidental worldwide distribution of an A(H2N2) virus in a quality control panel [32] in autumn 2004, highlighted the threat of introduction of a potential pandemic virus in Europe. Rapid inventories on the

level of laboratory preparedness carried out by the EISS coordination centre in January 2005 revealed that 26 of 32 national reference laboratories for human influenza and 22 of 25 European countries were prepared for detection of the A(H5N1) virus. However, only 12 of the laboratories were able to detect or identify specifically the A(H2) virus. The establishment of the CNRL and virology task groups strengthened the preparedness level of EISS as a whole by providing organised support through distribution of up to date RT-PCR detection protocols, recent sequence information, A(H5) controls for RT-PCR detection and the establishment of a reagent and sequence database [7]. These preparations proved useful when the A(H5N1) virus was recently introduced in many countries in Europe, probably by migrating birds, causing infections of wild birds and poultry [33], and since January 2006, human infection in Turkey [34].

The virological, epidemiological and clinical experts within EISS have been carefully monitoring the spread of virus strains in Europe during the 2005-2006 season. Assessment of the influenza activity is made in collaboration with the WHO Collaborating Centre in London and the European Centre for Disease Control and Prevention and is reported on the EISS website on a weekly basis.

Contributors

The members of EISS contributed by weekly submission of influenza surveillance data to EISS during the 2004-2005 season. CS Brown, TJ Meerhoff, A Meijer and WJ Paget carried out weekly analysis of the data and published the Weekly Electronic Bulletins during the 2004-2005 season. TJ Meerhoff extracted the clinical and virological data from the EISS databases for the paper and drafted the graphs for the supplement. A Meijer carried out the overall analysis of the data and prepared the body of the manuscript. TJ Meerhoff, LE Meuwissen and WJ Paget assisted in the analysis of the epidemiological data. CS Brown assisted in the analysis of the virological data. J van der Velden, as chair person of EISS, contributed by supporting the daily operation of EISS during the 2004-2005 season.

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Article Supplement available at:

http://www.eiss.org/documents/eurosurveillance_supplement_2004-2005_season.pdf for i) movies showing the spread of influenza across Europe, ii) graphs of the weekly consultation rates and virus detections by country, and iii) tables with a detailed breakdown by country of the virological data from sentinel and non-sentinel sources.

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