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H5N1 avian influenza virus: human cases reported in southern China

Two cases of influenza due to the avian influenza A H5N1 virus were reported last week from Hong Kong (1). The cases occurred in a Hong Kong family who had recently visited the Fujian province of southern China. The daughter aged 8 years died following a respiratory illness; the cause of her death is unknown. The father and son also had respiratory illnesses; the father died and the son recovered. Both were infected with the H5N1 virus. The mother also had a respiratory illness, which is reported not to have been related to influenza infection. Investigations are continuing to determine where and how transmission of infection to the cases occurred. Genetic analysis of the virus carried out in Hong Kong has determined that the viruses are essentially avian rather than human in character (2). It is considered probable that transmission occurred directly from birds-to-humans and that human-to-human transmission of the virus would be inefficient and unlikely to lead to epidemic spread (3). Avian A (H5N1) viruses are known to circulate in wildfowl and domestic poultry populations and a number of outbreaks among bird populations (both domestic and wild) have already been reported this year (4).

The last known A (H5N1) infections of humans took place in Hong Kong in 1997, causing six fatalities (5). These infections were also thought to have occurred through bird-to-human transmission. Poultry flocks in Hong Kong were slaughtered and no further cases in humans were detected.

Since 1997 there have been periodic culls of poultry flocks in Hong Kong as a result of detection of avian influenza viruses. The Hong Kong authorities and the World Health Organization (WHO) are keeping the current situation in Hong Kong under close observation. The PHLS will continue to monitor the information arising from this incident and will maintain routine influenza activity surveillance in England and Wales.

Further information about this incident, and about avian influenza generally, can be obtained from the following web sites:

- PHLS: <http://www.phls.co.uk/topics_az/influenza/flufaq.htm>
- WHO: <<http://www.who.int/csr/disease/influenza/influenzanetwork/en/>>
- Hong Kong Government: <<http://www.info.gov.hk>>

1. World Health Organisation. WHO Communicable disease surveillance and response (CSR). Geneva: WHO, 20 February 2003. Available at <http://www.who.int/csr/don/2003_02_20/en/>
2. Tests show H5N1 virus genes are pure avian genes (press release). Hong Kong: Government of Hong Kong, 24 February 2003. Available at <<http://www.info.gov.hk/gia/general/200302/24/0224203.htm>>
3. China (Hong Kong): Influenza, H5N1 human case. Promed-ah-edr Influenza (03): 24 February 2003. In: *ProMed Mail* [online]. Boston US: International Society for Infectious Diseases, 24 February 2003 [cited 27 February 2003]. Available at <<http://www.promedmail.org>>
4. Crofts J. Avian influenza in Hong Kong. *Eurosurveillance Weekly* [serial online] 2003 [cited 27 February 2003] 7(3). Available at <<http://www.eurosurveillance.org/ew/2003/030116.asp>>
5. Claas EC, Osterhaus AD, van Beek R, De Jong JC, Rimmelzwaan GF, Senne DA, *et al.* Human influenza A H5N1 virus related to a highly pathogenic avian influenza virus. *Lancet* 1998; **351**: 472-7.

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National Institute for Clinical Excellence issues guidance on amantadine, oseltamivir, and zanamivir for the treatment of influenza

On 26 February 2003, the National Institute for Clinical Excellence (NICE) published guidance on the use of the antiviral drugs amantadine, oseltamivir, and zanamivir for the treatment of influenza. This recommended that amantadine should not be used for the treatment of influenza, while the neuraminidase inhibitors, oseltamivir and zanamivir, should only be used when influenza is known to be circulating in the community, and only then for 'at risk' groups. These are defined as those over 65 years of age, with chronic respiratory disease, cardiac disease or diabetes, and those who are immunocompromised. Both zanamivir and oseltamivir are recommended for the treatment of 'at risk' adults, and oseltamivir for 'at risk' children, who present with influenza-like illness (ILI) and who can start therapy within 48 hours of the onset of symptoms.

This guidance replaces earlier guidance on the use of zanamivir for treatment of influenza issued in November 2000. Further guidance on the use of antiviral drugs for prophylaxis is expected in June 2003.

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AIDSVAX trial disappointing

The recently released results of the first AIDS vaccine, AIDSVAX, to undergo phase III testing were disappointing (1). The overall efficacy of the vaccine was just 3.8%. The trial was conducted over three years and involved 5417 volunteers from Canada, Netherlands, Puerto Rico, and the United States. Volunteers from high-risk groups were given three vaccinations at three monthly intervals and a booster vaccination every six months. The volunteers were split into two groups, one received a placebo and the other group were given the vaccine. Twice the numbers of volunteers were vaccinated than those who received the placebo. For those people who became HIV infected, over the three years, 5.7% were vaccinated and 5.8% received the placebo. The trial participants were counselled in safer sex and were told not to rely on the vaccine to prevent HIV transmission.

The analysis was carried out on 5009 volunteers who received at least three vaccinations. While full scientific details are awaited, the information released, so far, show that there were significant differentials in the efficacy for non-white volunteers. There were fewer HIV infections in black and

other non-white ethnic groups. The numbers of those, for whom the vaccine was successful, although statistically significant, were small with less than 500 non-white volunteers. The reasons for the difference in the results for the different ethnic groups are unclear. At this stage it may be that this is simply a statistical artefact, but one possibility is that black people developed a stronger antibody response, leading to better protection against HIV.

The AIDSVAX vaccine is based on a genetically engineered protein found in HIV, the gp120 surface protein. The idea is that the vaccine would stimulate antibodies, which would neutralise the virus before it could infect host cells. This approach has been controversial because gp120 has a high mutation rate as well as being heavily 'glycosylated' (coated with sugars) which would be expected to prevent antibodies from binding to the protein (2).

1. Vaxgen Announces Initial Results of its Phase III AIDS Vaccine Trial (press release). Brisbane: VaxGen inc, 24 February 2003. Available at <<http://www.vaxgen.com/pressroom/index.html>>

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Antimicrobial resistance in 2000: England and Wales

The PHLS Communicable Disease Surveillance Centre (CDSC) has published *Antimicrobial resistance in 2000: England and Wales* (1), a report that, for the first time, brings together in one document antimicrobial resistance surveillance data from across the PHLS for a wide range of micro-organisms. It draws on the bacteraemia data that appear regularly in the *CDR Weekly* and also includes resistance data for a variety of infections (for instance, fungal, enteric, and sexually transmitted infections) from many sources including reference laboratory data and enhanced surveillance studies. The report gives an overview of the development and current state of antimicrobial resistance surveillance, identifies current issues and highlights some of the problems associated with interpretation of the data. The report will now be published annually, with the 2000 edition serving as a baseline.

Key findings

- For the three commonest causes of bacteraemia:
 - Forty-two percent (42%) of *Staphylococcus aureus* bacteraemias with susceptibility reports were caused by methicillin resistant strains (MRSA). No vancomycin resistance was confirmed.
 - Ampicillin/amoxycillin resistance in *Escherichia coli* bacteraemia reports remains at 55%, while gentamicin resistance was reported in 3%, and ciprofloxacin in 5%.
 - Penicillin resistance was reported in 7% of *Streptococcus pneumoniae* bacteraemia reports, and erythromycin resistance in 15%. Routine susceptibility testing may not, however, be detecting a significant proportion of penicillin, erythromycin and cefotaxime resistance.
- Resistance to anti-tuberculous drugs remained relatively stable in 2000, 6.4% of isolates being isoniazid resistant, 1.5% rifampicin resistant, and 1.1% resistant to at least isoniazid and rifampicin.
- Penicillin resistance in *Neisseria meningitidis* was still rare, but reduced susceptibility to penicillin is on the increase. Cephalosporin resistance was not reported.
- *Campylobacter* was the commonest reported enteric pathogen, with rising resistance to

ciprofloxacin (18% in *C. jejuni* and 26% in *C. coli*). Erythromycin resistance remained low.

- The commonest *Salmonella enteritica* serotypes are prone to multiple resistance, which was recorded in 67% of *S. Typhimurium* and 49% *S. Virchow* isolates.
- Nine percent (9%) of all isolates surveyed in the Gonococcal Resistance to Antimicrobials Surveillance Programme in 2000 were resistant to penicillin, 1.8% of isolates showed high-level resistance to ciprofloxacin, and a further 4.2% showed decreased susceptibility.
- Although *Candida albicans* remains the predominant yeast pathogen, there are increasing numbers of other yeast species that are less susceptible to fluconazole, such as *C. krusei* and *C. glabrata*.

Particular issues highlighted by the report include:

- The need to improve the consistency and completeness of laboratory reporting
- The lack of poor speciation for some organisms, such as the reporting of “coliforms” in certain infections, difficulties speciating *Acinetobacter* spp and differentiating *E. faecalis* and *E. faecium*
- Gaps in our knowledge about the susceptibility of organisms that are mainly identified through methods that do not require culture, such as *C. difficile*, *Chlamydia trachomatis*, and *Helicobacter pylori*
- The need to develop surveillance systems for organisms where there is not a formalised programme for susceptibility testing, such as HIV, hepatitis B and C, and invasive fungal infections
- The need for more information regionally and nationally (including clinical denominators) on less serious infections occurring in the community such as organisms causing urinary and respiratory tract infections
- The need for core sets of antibiotics to be used for susceptibility testing in all reporting laboratories
- The need for universal uptake of an agreed sensitivity test method

Controlling antimicrobial resistance has been assuming greater priority over the past few years, following publication of a number of key reports (2,3,4). A national strategy and action plan aiming to limit the development and further spread of resistance was published in 2000 and development of a new National Action Plan is currently underway. The key findings of this report support the highlighting of antimicrobial resistance as a key area requiring intensified action in the Chief Medical Officer’s strategy for combating infectious diseases (5). Surveillance is central to the control of antimicrobial resistance, signalling emerging problems that might warrant changed therapeutic approaches or new priorities for action, and indicating areas for further study.

The routine reports sent by microbiologists across England and Wales are the bedrock for this surveillance, and are greatly appreciated

The report *Antimicrobial resistance in 2000: England and Wales* is available on the PHLS website in pdf format at: http://www.phls.org.uk/topics_az/antimicrobial_resistance/amr.pdf and will also be circulated to medical microbiologists.

1. PHLS. *Antimicrobial resistance in 2000: England and Wales*. London: Public Health Laboratory Service, 2002. Available at <http://www.phls.org.uk/topics_az/antimicrobial_resistance/amr.pdf>.
 2. NHS Executive. Resistance to antibiotics and other antimicrobial agents. Health Service Circular HSC 1999/049. London: Department of Health, 1999.
 3. House of Lords Select Committee on Science and Technology. *Resistance to antibiotics and other antimicrobial agents*. 7th Report 1997-98, HL Paper 81. 17-3-1998. (Published by the Stationary Office).
 4. Government Response to the House of Lords Select Committee on Science and Technology Report: Resistance to Antibiotics and other Antimicrobial Agents. London: The Stationary Office, 1998.
 5. Department of Health. *Getting ahead of the curve: a strategy for combating infectious diseases (including aspects of health protection)*. London: Department of Health, 2002.
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Laboratory reports of *Haemophilus influenzae* by age group and serotype, England and Wales

Routine infant immunisation with conjugate Hib vaccine in the United Kingdom (UK) began in October 1992. Since then, the incidence of invasive Hib disease has fallen dramatically. Since 1998, however, an increase in the number of cases has been observed. This increase has affected all age groups, but is most marked in those aged between 1 and 4 years.

While the immunisation programme against Hib has been highly successful, further enhancement of immunity appears necessary. The Department of Health (DoH) is recommending an additional dose of Hib vaccine for all children aged between 6 months and 4 years* . The exact timing of this campaign will be determined by availability of Hib vaccine and modifications to the Child Health Computer systems for implementation.

[<http://www.doh.gov.uk/cmo/letters/cmo0301.htm>](http://www.doh.gov.uk/cmo/letters/cmo0301.htm)

[<http://www.phls.co.uk/publications/cdr/PDFfiles/2003/cdr0803.pdf >](http://www.phls.co.uk/publications/cdr/PDFfiles/2003/cdr0803.pdf)

Continued surveillance for cases of invasive *H. influenzae* disease is of great importance in monitoring the impact of the catch-up programme. Ongoing case ascertainment will occur through consultants in communicable disease control (CCDC) and microbiologists. Isolates of *H. influenzae* from cases of invasive disease should be submitted (on chocolate agar slopes) for confirmatory typing to Mary Slack, PHLS Haemophilus Reference Unit, Level 7, John Radcliffe Hospital, Oxford, OX3 9DU.

* Children aged between 6 months and 4 years on 1 April 2003 will be eligible for vaccination.

Table 1 Laboratory reports of *Haemophilus influenzae* by age group and serotype, England and Wales third quarter 2002 (2001)

	Age					Total
	<1 year	1-5 years	5-14 years	≥ 15 years	Not known	
b	4 (5)	23 (12)	3(4)	12 (5)	– (–)	42 (26)
nc	4 (5)	3 (4)	– (4)	25 (26)	1 (–)	33 (39)
a,e,f	– (–)	1 (2)	– (–)	2 (4)	– (–)	3 (6)
Not typed	– (2)	– (–)	2 (–)	25 (22)	1 (–)	28 (24)
Total	8 (12)	27 (18)	5 (8)	64 (57)	2 (–)	106 (95)

Table 2 Laboratory reports of *Haemophilus influenzae* by age group and serotype, England and Wales fourth quarter 2002 (2001)

	Age					Total
	<1 year	1-5 years	5-14 years	≥ 15 years	Not known	
b	8 (9)	54 (33)	14 (3)	39 (15)	– (–)	115 (60)
nc	6 (4)	8 (4)	1 (–)	40 (27)	–(–)	55 (35)
a,e,f	– (–)	1 (2)	– (–)	11 (8)	1(–)	13 (10)
Not typed	7 (5)	3 (5)	3 (–)	25 (31)	– (–)	38 (41)
Total	21 (18)	66 (44)	18 (3)	115 (81)	1(–)	221 (146)

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Enhanced surveillance of meningococcal disease: weeks 40-52/02

Regional enhanced surveillance of meningococcal disease (ESMD) began on 1 January 1998 in five regions of England and was extended to include all English regions, Wales, and Northern Ireland (from the 1 January 1999). The national enhanced surveillance system relies upon consultants in communicable disease control (CCDC) reporting confirmed and probable cases of meningococcal disease occurring in their district each week. Data are collated at the relevant regional PHLs Communicable Disease Surveillance Centres (CDSCs) and sent on to CDSC Colindale each month. These data are subsequently published quarterly in *CDR Weekly*. Additionally, CCDCs are asked to report details of any clusters of meningococcal disease occurring in educational establishments.

Fourth quarter of 2002: weeks 40-52/2002

In the fourth quarter of 2002, ESMD identified 634 cases of invasive meningococcal disease in the nine English regions, Wales, and Northern Ireland. This is an increase of 28% on the total of 457 in the previous quarter of 2002, but a decrease of 24% on the total of 835 in the equivalent quarter of 2001. North West reported the highest number of cases in this quarter (83), although the highest rate was in the North East (table 1).

Table 1 Meningococcal disease by region weeks 40-52/02

Region	B	C	Other	Infection not confirmed	Total	Rate per 100,000
North East	18	1	4	24	47	1.8
Yorkshire & Humberside	22	3	5	43	73	1.4
East Midlands	22	3	–	32	57	1.4
Eastern	17	–	3	20	40	0.7

London	16	5	–	43	64	0.9
South East	28	–	–	32	60	0.7
South West	28	2	4	40	74	1.5
West Midlands	24	1	2	38	65	1.2
North West	40	2	6	35	83	1.2
Wales	9	2	3	37	51	1.7
Northern Ireland	8	1	2	9	20	1.2
Total	232	20	29	353	634	

A clinical diagnosis of invasive meningococcal disease was reported for 573 cases in England and Wales compared to 329 cases of meningitis and septicaemia officially notified to CDSC during the same period. This implies that approximately 57% of clinically diagnosed meningococcal disease is formally notified. The overall case fatality rate in cases identified in ESMD with a clinical diagnosis (in England, Wales, and Northern Ireland) was 5.9/100 cases, whereas the case fatality rate for cases with septicaemia alone was 7/100 cases (table 2).

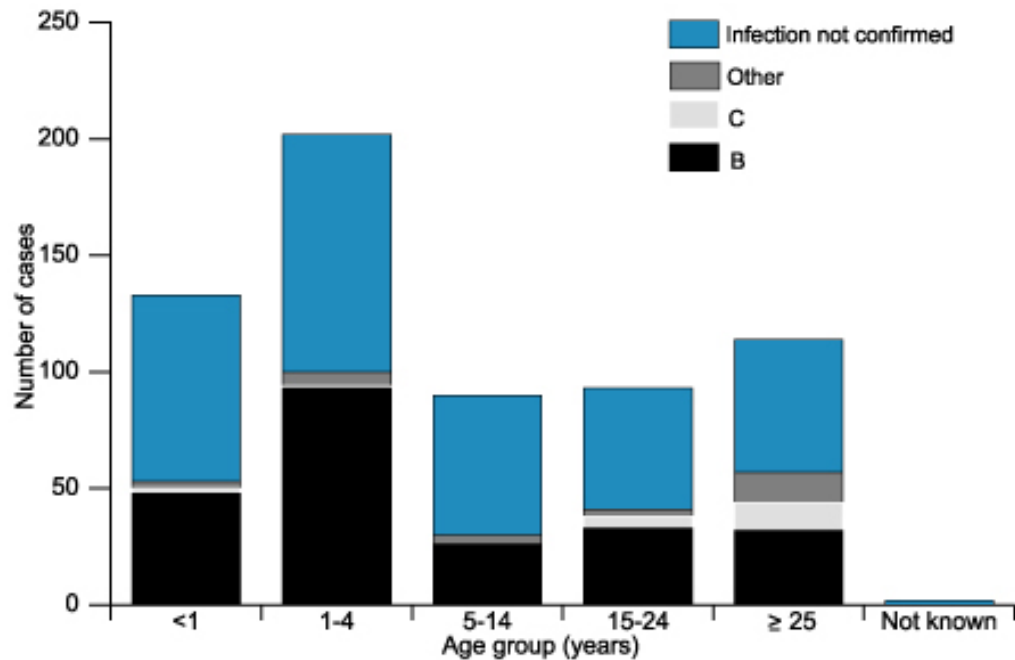
Table 2 Clinically diagnosed cases (deaths) of meningococcal disease: England, Wales, and Northern Ireland, weeks 40-52/02

Region	Meningitis	Septicaemia	Meningitis and Septicaemia	Not meningitis or septicaemia	Total
North East	10	24	9	1	44
Yorkshire & Humberside	21 (2)	39 (2)	5 (1)	5	70 (5)
East Midlands	16 (1)	26 (1)	13 (1)	2 (1)	57 (4)
Eastern	13	21 (2)	4	2	40 (2)
London	28 (2)	17 (1)	16 (1)	2	63 (4)
South East	21	30 (3)	9 (1)	–	60 (4)
South West	25 (1)	34 (2)	11 (2)	–	70 (5)
West Midlands	14	45 (2)	6	–	65 (2)
North West	29	31 (5)	9	–	69 (5)
Wales	2	32 (3)	1	–	35 (3)
Northern Ireland	4	13 (1)	–	2	19 (1)
Total	183 (6)	312 (22)	83 (6)	14 (1)	592 (35)

Two hundred and eighty-one of the 634 cases (44%) identified in ESMD were confirmed as *Neisseria meningitidis* infection, compared to 382 reports of laboratory confirmed meningococcal disease made to PHLS Meningococcal Reference Unit (MRU) in the same period.

Serogroup B *N.meningitidis* was detected in 83% (232/281) of confirmed cases identified in ESMD, serogroup C in 7% (20/281), and the remaining 10% included other serogroups and ungrouped cases. The number of other serogroups and ungrouped cases increased by 6% this quarter from weeks 27 to 39 in 2002, and was due to an increase in non-grouped, ungrouped, and Y. Over half (54%) of all confirmed cases were in children under 5 years of age, among whom serogroup B accounted for 92% of infections, serogroup C 2%, and other serogroups 6%. In children (under 14 years of age), three serogroup C infections occurred. Two of the infections were in children who were one month of age, and thus too young to be vaccinated. One case occurred in a two year old whose vaccination status is unknown (figure1).

Figure 1 Serogroups of *N. meningitidis* identified in cases in England, Wales, and Northern Ireland by age, weeks 40-52/02



There has continued to be an overall reduction in the observed number of cases of meningococcal disease compared to the equivalent period in the previous year: serogroup B fell by 18% (232 cases compared to 284 in 2001), serogroup C by 41% (20 cases compared to 34 in 2001), other serogroups by 38% (29 compared to 47 in 2001), and unconfirmed by 25% (353 compared to 470 in 2001). This trend may reflect a real reduction in meningococcal disease, since a decline is also observed in routine data: clinical notifications fell by 35% (329 compared to 507 in 2001), and laboratory reports by 26% (382 compared to 519 in 2001). The recent organisational changes in the NHS could have affected the completeness of reporting and may account for some of this decline. It is interesting to note that the majority of the decline in cases of serogroup C occurred in children rather than adults, implying the success of the MenC vaccine. Additionally, the large decline in other serogroups from the fourth quarter last year to the same quarter this year was due to a decrease in serogroup W135.

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Invasive meningococcal infections, England and Wales: laboratory reports, weeks 42-47/02

	Method of diagnosis			Total reports 42-47/02	Cumulative total† 2002
	CSF and blood		Other sites		
	culture	non-culture*	culture		
Group A	–	–	–	–	1
Group B	49	71	5	125	1215
Group C	10	7	–	17	154
Group W135	5	2	1	8	76
Group X	–	–	–	–	3

Group Y	1	1	-	2	23
Group Z	-	-	-	-	-
Group 29E	-	-	-	-	-
Ungroupable	1	-	-	1	2
Ungrouped	-	7	-	7	103
Total	66	88	6	160	1577

* latex antigen, microscopy, and polymerase chain reaction.

† combined CDSC and Meningococcal Reference Unit data

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Health Protection Agency inaugural conference

Health Protection Agency inaugural conference

In April 2003 the Health Protection Agency (HPA) comes into existence. It will incorporate the Public Health Laboratory Service, Centre for Applied Microbiological Research, National Focus for Chemical Incidents, and Consultants in Communicable Disease Control.

The inaugural conference of the HPA will be held at the University of Warwick from 15 to 17 September 2003.

Submissions for oral and poster presentations for multidisciplinary themed sessions are now invited from all staff in organisations joining the HPA, their collaborators, the NHS, and British universities.

The themes of the conference include:

- command and control of incidents and events
- environmental
- epidemiology
- emergency response
- information dissemination
- medical treatment and control strategies
- methodologies
- psychological aspects of major incidents
- quality management
- surveillance

Abstracts can be submitted online via the conference website, available at

<www.hpaconference.org.uk>, or as an attachment to the abstract manager, Margaret Clennett, email: (mclennett@phls.org.uk). The abstract submission form and Instructions to authors are on the conference website.

Further details, including the programme itself, registration fees and booking information will be available on the website later in 2003. Meanwhile, for more information contact Margaret Clennett, PHLS Central Library, 61 Colindale Avenue, London NW9 5HT tel: 0208 200 4400 ext 4617 email: mclennett@phls.org.uk