
Global Update

Influenza A(H5N1)

Influenza viruses are divided into types A, B and C, plus subtypes of A. Types A and B circulate in human populations and mutate constantly, resulting in the need for a modified vaccine every year. At times a new influenza virus appears to which nobody is immune because no one has previously been exposed to it. This is called an antigenic shift and it occurs at irregular intervals. Some antigenic shifts result in local epidemics or global pandemics.

Influenza was first described by Hippocrates in 412 BC and the first well-described pandemic of influenza-like disease occurred in 1580. Since that time 31 such possible influenza pandemics have been documented, with three occurring in this century: in 1918, 1957 and 1968. There is evidence that the viruses which caused these epidemics originated from animal (1918 = swine, 1957 and 1968 = avian strains). In 1976, a new influenza virus from pigs caused human infections and severe illness. A vaccine against swine influenza was developed and administered in some countries, although no pandemic in fact occurred.

The most devastating of the 20th century influenza pandemics was that known as the Spanish Flu which killed more than 20 million people around the globe between 1918 and 1920. The virus responsible for this pandemic is now known as influenza A(H1N1).

In May 1997, influenza A(H5N1) virus

was isolated from a child who died with Reye's Syndrome in Hong Kong. Prior to this, the H5N1 virus was known to infect only various species of birds, including chickens and ducks. It was first discovered in terns in South Africa in 1961 and can be deadly to chickens: in spring 1997, thousands of chickens died in Hong Kong after contracting it.

After the first human case occurred in May 1997, intensive surveillance revealed 15 additional cases by the end of 1997, all of them in Hong Kong, Special Administrative Region of China. Although the exact means of transmission of H5N1 to humans have not yet been identified, there is no clear-cut evidence of any human-to-human transmission. Infection with the virus is believed to come through contact with infected birds.

Symptoms: In humans, the spectrum of illness caused by influenza virus infection in general can range from asymptomatic to fatal. Initial symptoms include fever, cough and chills, and most influenza infections cause only self-limited illness that does not require hospitalization. While the elderly and young age groups tend to have more severe illness from influenza in general, symptoms after infection with the H5N1 strain are severe in other age groups as well.

Up to the end of 1997, there were four deaths among people infected by the H5N1 virus: the first case, the two year-old who died of complications from Reye's Syndrome, a 54 year-old-man, a 13-year-old girl and a 60-year-old* woman. However,

the severity of infections identified so far may not be representative of the spectrum of illness caused by H5N1 infection in humans, as milder cases may not have come to hospitals for treatment.

Monitoring and surveillance: Intensified influenza surveillance was initiated during August in Hong Kong and Guangdong Province, China following the identification of the first case of human H5N1 infection. Most surveillance activities were focused in hospitals, with some increased surveillance in outpatient facilities and, beginning on December 8, influenza surveillance was further intensified to include all outpatient facilities in Hong Kong. Surveillance of the production and transport of pigs and fowl for market has also been stepped up in regions of China neighbouring Hong Kong.

Based on present knowledge, there appears to be no risk of transmission of the H5N1 virus to humans from raw, chilled or frozen poultry foods. While H5N1 is unlikely to be transmitted through consumption of foods, the application of the WHO Ten Golden Rules for Safe Food Preparation is recommended to provide adequate protection from all poultry-borne diseases. In particular, attention should be given to the thorough cooking of foods, avoiding contact between raw and cooked foods, and diligent hand washing during food preparation.

Next steps in investigating the virus: The investigation is now focussing on determining specific characteristics of viruses isolated from the confirmed cases of human influenza H5N1 and on determining how these persons became infected, whether other persons in Hong Kong and Southern China are being infected with the influenza H5N1 virus and whether there is evidence of human-to-human transmission

of H5N1 viruses. At the same time, studies of birds and other animals are being conducted to identify the natural reservoir of the virus and the extent of its spread in the animal population. Chickens are not thought to be an efficient reservoir because the infection causes fatal disease in this species.

Vaccine development: At present, WHO does not recommend the production of a specific H5N1 vaccine. However, WHO's Collaborating Centres on influenza are working with various H5 strains to prepare high growth reassortants which could be used for vaccine production, in case of need. This work is complicated by the fact that the original virus isolates from Hong Kong also kill fertilized eggs which are used for vaccine production. The preparation of a vaccine would take several months after the selection of a suitable virus strain.

To minimize any potential risk to laboratory staff or others who may come into contact with the virus, work with the live pathogenic H5N1 virus is restricted to laboratory containment BSL-3 and strains for research in such laboratories will only be made available after approval of the local safety committee, national veterinary and public health authorities and WHO, Geneva.

In the meantime, the WHO Collaborating Center for Influenza at the Centers for Disease Prevention and Control (CDC) in Atlanta, USA has prepared a kit of reagents for diagnosis of H5N1 which has been despatched to the 110 National Influenza Centers in 82 countries which make up the WHO network for influenza surveillance.

Isolates from the first and second H5N1 cases are sensitive to amantadine and rimantadine in laboratory experiments,

and WHO is recommending prophylaxis using either of these drugs for hospital staff and other people in close contact with in-

fluenza patients. There is no reason to impose travel restrictions or quarantine in Hong Kong or elsewhere.

Foodborne Disease Possibly 350 Times More Frequent Than Reported

Recent surveys indicate that foodborne diseases may be 300-350 times more frequent than the reported cases tend to indicate. It is believed that hundreds of millions of people worldwide suffer from diseases caused by contaminated food. Developing countries suffer the most from a wide range of diseases including cholera, campylobacteriosis, *Escherichia coli* infections, salmonellosis, shigellosis, brucellosis, and hepatitis A. The annual incidence of some 1.5 billion episodes of diarrhea in children under five years of age, resulting in over three million deaths is an indication of the scale of the problem, since a significant proportion of the diarrheal disease cases are of foodborne origin.

Paradoxically, in spite of safe water supplies, sound standards of hygiene and application of technologies such as pasteurization, a number of industrialized countries have experienced an increase in the incidence of foodborne diseases in recent years. Surveys indicate that no less than 5-10% of the population are involved annually. On top of that, the emergence of *Listeria monocytogenes*, *Escherichia coli* 0157 and multi-antibiotic resistant *Salmonella typhimurium* are justifiably perceived as new significant threats to public health. Witness

the much-publicised outbreaks of *Escherichia coli* 0157 as far apart as Japan and Scotland last year.

In addition to the human suffering caused by foodborne diseases in terms of death and ill-health, substantial economic costs are involved, affecting individuals and families, industries, health care systems and entire communities. At the national level, epidemics of foodborne diseases affect both tourism and trade. When cholera broke out in Peru in 1991, over US\$ 700 million were lost in fish and fishery products exports. In the three months following the start of the epidemic, US\$ 70 million were lost due to closure of food service establishments and a decrease in tourism. The global value of international trade in agricultural products and commodities was estimated at US\$ 381 billion in 1993.

The WHO report quotes American statistics. "Each year, seven foodborne pathogens (*Campylobacter jejuni*, *Clostridium perfringens*, *E. coli* 0157:H7, *Listeria monocytogenes*, *Salmonella*, *Staphylococcus aureus*, and *Toxoplasma gondii*) cause an estimated 3.3 -12.3 million cases in the United States and up to 3900 deaths. Their costs in human illness were estimated at US\$ 6.5-34.9 billion annually".

Europe

In France, the number of outbreaks rose from 594 in 1990 to 732 in 1992. Where the agent was identified, *Salmonella* was re-

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sponsible for 83-87% of outbreaks. Egg and meat products were associated with various outbreaks caused by a number of different *Salmonella* strains. In Germany, about 1,000 cases of salmonellosis were linked to the consumption of paprika and paprika-powdered potato chips which makes it the largest documented outbreak from contaminated spices. Powdered infant formula was responsible for 48 known cases of salmonellosis in infants under seven months from 14 regions in Spain in 1994. The implicated strain was a lactose-fermenting *Salmonella virchow*. In Scotland, there was a large meatborne *Escherichia coli* 0157 outbreak with 396 cases and 11 deaths at the end of last year. The persons involved had eaten cold cooked meats from a butcher or had eaten cooked steak in gravy at a church lunch supplied by the same **butcher**.

Africa

Little in the way of foodborne surveillance is done in Africa. As a result, the data are extremely scarce. Occasionally, acute illness directly associated with a food is documented as, for instance, in Tanzania, where the first major botulism outbreak claiming at least 18 deaths occurred in 1991. The outbreak was caused by consumption of locally-made fish meal. An outbreak of *Escherichia coli* 0157 in Egypt in 1994 was traced to hamburgers and dairy products. As a follow-up, a survey of 175 foods obtained from slaughter-houses, supermarkets and farmers' homes was conducted for *Escherichia coli* 0157. The bacterium was detected in 6% of unpasteurized milk, 60% of fresh retail beef, 4% of boneless chicken, and 4% of lamb meat samples.

Because of civil wars and national conflicts, refugees and misplaced populations are an increasing concern. Last year, 500,000 refugees returned from east Zaire

to Rwanda. The epidemiological sentinel stations registered about 14,000 consultations and 47 deaths. Diarrheal disease accounted for two-thirds of all consultations. How much of this diarrheal disease is due to unsafe water and food is not known, but they are suspected to be major vehicles of transmitting this type of disease.

Asia

Except for a few countries such as Japan, relatively little in the way of surveillance of foodborne disease is carried out in Asia. In recent years in Japan, *Salmonella* has become much more frequent which is explained, at least partially, by changes in the national diet - eggs and egg products are now more popular than even before. There were a number of outbreaks in Japan last year caused by *Escherichia coli* 0157:H7 resulting in 9578 cases and 11 deaths. No responsible foods have yet been identified, except in a few isolated cases.

A comparative study of food borne outbreaks in the Republic of Korea and Japan between 1971 and 1990 revealed considerable differences in the morbidity and mortality as well as in agents involved. Most incidents occurred in the workplace and the home in the Republic of Korea, whereas they were more frequent in restaurants and hotels in Japan. Seafood was often implicated in both countries, but food of animal origin was much more frequently associated with outbreaks in the Republic of Korea.

Oceania

In Australia, some trends in notifications of food borne diseases are apparent for 1991-1995. Laboratory isolates for *Campylobacter* and *Salmonella* are increasing, those for *Shigella* and *Yersinia* are decreasing and those for *Listeria monocytogenes* vary slightly from year to year.

New Zealand updated its notifiable diseases in 1996 to include botulism, campylobacteriosis, cryptosporidiosis, giardiasis, listeriosis, toxic shellfish poisoning, VTEC, and yersiniosis. A recent summary for the years 1980 to 1995 indicates that the agents responsible for illness are similar to those in other industrialized countries with *Salmonella* being the predominant cause of morbidity and mortality.

North America

In both the United States and Canada, Salmonellosis cases seem to have reached a plateau of about 40,000 and 9,000 each year, respectively, despite the fact that *Salmonella enteritidis* has become a major egg-borne pathogen in the United States in the last 15 years. Illnesses from *Escherichia coli* 0157 are being documented in outbreaks from both countries, not only from ground beef but also from vegetables, milk and apple juice. In 1994, 593 cases of *Salmonella enteritidis* were identified in Minnesota, USA, after a nationally-distributed brand of ice cream was eaten. Pasteurized ice cream mix had been transported in a tanker previously used for to carry non-pasteurized liquid egg. The United States commitment to epidemiological surveillance was reinforced by the presidential proposal for the 1998 budget to allocate US\$43 million for a programme to detect foodborne outbreaks before they become widespread. This will help to reduce morbidity and mortality due to foodborne dis-

eases, estimated at 6.5-33 million people and 9000 deaths annually.

Central and South America

All Central, South American and Caribbean countries have some form of notifiable disease system. Diarrheal diseases are one of the main causes of death in young children. The causes are not generally known but amebic dysentery, trichinosis, giardiasis, shigellosis, brucellosis, *Escherichia coli*, and hepatitis infections are all documented from Latin America and the Caribbean. Cholera, initially identified in Peru in 1991 with a total of 600000 cases, rapidly spread to other countries, and in 1994 caused 112611 cases and 1229 deaths. The total number of cases and deaths from 1991 to 1994 was 1061188 and 9989, respectively. The source of infection was probably contaminated food and water. The disease was spread partly through probably contaminated food and water. The disease was spread partly through consumption of street-vended foods and beverages containing ice. Undercooked or raw seafood may also have been implicated. Shellfish may be contaminated not only with local sewage, but waste water pumped from ships in harbour.

Most Latin American countries now recognize that foodborne disease is important enough to justify some kind of surveillance scheme and are trying to develop better ways of determining numbers of cases and their causes.