

## Avian flu virus could evolve into dangerous human pathogen, experts fear

An unprecedented epidemic of avian influenza has affected huge populations of domestic and migratory birds across Asia triggering fears the virus could mutate into a dangerous human pathogen.

The bird flu strain, known as A (H5N1), has been reported in eight countries: Cambodia, China, Indonesia, Japan, Lao People's Democratic Republic, Republic of Korea, Thailand and Viet Nam among bird populations since mid-December 2003. As of 23 February 2004, there has been a total of 32 laboratory-confirmed human cases in the region of which 22 have died.

The United Nations Food and Agriculture Organization, World Organization for Animal Health and WHO proposed a control programme in January to help countries eradicate the disease calling for a mass cull of birds infected or exposed to the virus and called on international donors to help countries compensate farmers for the loss, described as a disaster for agricultural production.

"The real issue now is to avoid the emergence of a pandemic, and that means to eliminate the animal reservoir. And that should be done in a safe way so that persons are not going to be exposed to the virus without being protected," said Klaus Stohr, WHO project leader of the Influenza Surveillance and Scientific Groups for the H5N1 Influenza Outbreak.

Experts say this winter's epidemic could have serious implications because some H5N1 strains have proved to be infectious and capable of causing severe disease in humans. Unlike SARS, scientists have not yet found evidence of human-to-human transmission of H5N1. A field investigation in Viet Nam of a family cluster including two confirmed cases and an unexplained death due to acute respiratory illness found no conclusive evidence of human-to-human transmission but it has not yet been ruled out.

Apart from the immediate risk of transmission to humans who are in close



REUTERS/Sukree Sukplang

Buddhist monks prepare for the cremation of the first human to die from bird flu in Thailand. The six-year-old boy died in Kanchanaburi Province, 150 km west of Bangkok on 1 February 2004.

contact with infected birds, the widespread presence of the virus across Asia increases the chances of co-infection with human and avian viruses and, potentially worse, could trigger the exchange of genes within viruses from other species creating a new, more lethal human virus.

"This is a serious global threat to human health," said WHO Secretary-General, Dr Lee Jong-wook.

"We have faced several emerging infectious diseases in the past. This time, we face something we can possibly control before it reaches global proportions if we work cooperatively and share needed resources," said Lee.

Whilst diagnostic tests and expensive anti-viral medicines are available,

there is not yet a vaccine for the virus. About a dozen pharmaceutical companies are working hard to develop one but success may be several years away.

Human cases of the virus have at present only been found in Viet Nam and Thailand. Viet Nam has suffered the most widespread avian flu outbreak among birds this winter as well as the highest number of human cases — 15 of 23 people infected with the H5N1 virus have died.

In Thailand, a two-year-old boy from Suphanburi Province and a 27-year-old woman from Uttaridit Province recovered from bird flu earlier in February, but the other seven cases including a 13-year-old boy have died.

Most human cases were in direct contact with sick or dead birds, although no one involved in culling birds appears to have caught avian flu, WHO said. Avian flu is believed to have first jumped species from bird to man in 1997, when an outbreak of the disease caused by the A (H5N1) virus among birds triggered 18 human cases in Hong Kong Special Administrative Region of which 6 died.

WHO is conducting investigations into reports of H5N1 infection of domestic cats from a single household in Thailand. Fourteen out of the 15 cats have died, two of which have been reported infected with H5N1 by the Faculty of Veterinary Sciences at Thailand's Kasetsart University. According to WHO, confirmation of the virus in cats is not likely to enhance the present risks to human health.

First symptoms are fever, sore throat and cough, but the disease can lead also to hepatitis and even damage to the heart or kidneys.

For the latest information on avian flu, visit: <http://www.who.int/csr/don/en/> ■

Fiona Fleck, *Geneva*

## WHO refutes malaria malpractice allegations

WHO's Roll Back Malaria department has refuted allegations by an international group of 13 malaria researchers accusing WHO and the Global Fund to Fight, AIDS, Tuberculosis and Malaria (GFATM) of failing to promote available and effective malaria treatment in favour of ineffective but less-expensive drugs.

In a commentary published in the UK-based medical journal, the *Lancet* (2004;363:237–40), the critics led by Amir Attaran from London's Royal Institute of International Affairs, accuse the two agencies of blocking the introduction of highly effective artemisinin-based combination therapy (ACT) whilst continuing to approve grants for the conventional chloroquine and sulfadoxine-pyrimethamine in countries where these treatments are failing.

"For WHO and GFATM to provide chloroquine and sulfadoxine-pyrimethamine treatments ... at least wastes precious international aid money and at most, kills patients who have malaria ... at least tens of thousands of children die every year as a direct result," say

the authors who compare the agencies with a "doctor who knowingly furnished treatments that failed perhaps 80% of the time, while withholding the alternatives as "too expensive".

In a letter published in the *Lancet* (2004;363:397), Fatoumata Nafo-Traoré, Director of WHO's Roll Back Malaria Department, counters the accusations pointing out that "WHO has been making many of the same arguments for the past 3 years and fully supports the use of ACT."

Chloroquine and sulfadoxine-pyrimethamine have become increasingly ineffective due to the development of resistance in the deadly species of malaria, *Plasmodium falciparum*. Surveillance and clinical trial data in East Africa, for example, show that up to 64% of patients given chloroquine and 45% given sulfadoxine-pyrimethamine will fail treatment, and those figures are climbing, say the critics, Attaran et al.

They point out that artemisins, on the other hand, which form the basis of ACT treatments, have been used in Chinese traditional medicine for 2000 years, with no observed resistance. "In studies done on nearly every continent, ACT successfully treats 90% or more of patients," say Attaran et al.

The problem is cost: ACT is around ten times more expensive forcing most African countries to stick with conventional but increasingly useless malaria treatments. At the centre of the criticisms voiced in the *Lancet* is the continued approval by GFATM and WHO of funding for chloroquine and sulfadoxine-pyrimethamine for those countries which should be switching to ACT. "When those same countries seek financial aid from [GFATM] to purchase ACT, they are forcefully pressured out of it by governments such as the USA, whose aid officials say that ACT is too expensive ... and WHO signs its approval," say Attaran et al.

According to WHO, one reason for poor countries' continuing applications to GFATM for the cheaper but less-effective anti-malaria drugs has been their uncertainty about GFATM — which has only been in existence for two years — as a source of long-term support. In other words, countries did not wish to switch to a more expensive drug only to see this income cut off a few years later. "Governments need to trust that sustainable funding from the Global Fund [GFATM] and other sources

will be available before they can make the commitment — of up to US\$ 2 per head per year — of switching to ACTs," said Nafo-Traoré.

Both agencies have also emphasized their roles as advisers or funders, insisting that antimalarial drug policy decisions must be led by national governments. However, as Nafo-Traoré points out, since 2001 "WHO has been actively promoting the use of ACT in countries before resistance to currently used monotherapies reaches an unacceptable level." Since 2001, South Africa (KwaZulu Natal), Zambia, Zanzibar and Burundi have switched to ACTs as first-line treatment. By 2004 WHO expects at least 16 African countries to have adopted ACTs as first-line treatment. According to WHO, this timeframe is exceptionally short for such a far-reaching policy change. In addition, the threshold for the unacceptable level of therapeutic failures has been lowered from 25% to 15% and "countries will be strongly encouraged to modify their treatment policies accordingly," says Nafo-Traoré.

Rather than refusing requests for suboptimal drugs which are based on current national policy, says Nafo-Traoré, GFATM has generally stipulated a policy review within a short period of time as a condition of funding. "As a result, WHO is able to work more effectively with decision-makers in countries to accelerate rational and feasible policy change."

Malaria causes more than one million deaths worldwide every year, 90% of which occur in Africa, costing the continent more than US\$ 12 billion every year. ■

## West Africa prepares for the final battle against polio

Ten West African countries will begin a massive, synchronized polio immunization campaign on 23 February 2004 aimed at vaccinating 63 million children in the region in just a few days. The campaign comes just one month after Health Ministers gathered for an emergency meeting at WHO in Geneva calling for commitment to end polio transmission in 2004.

Political, religious and traditional leaders from Benin, Burkina Faso, Cameroon (due to begin vaccination on 20 February), Central African Republic, Chad (due to join the campaign in

March), Ghana, Niger, Nigeria, Côte d'Ivoire and Togo will come together to launch the campaign and tens of thousands of vaccinators will go house-to-house over three days to administer the vaccine directly to every child.

"After eight years of incredible collaboration and investment, Africa is standing on the verge of a well-deserved triumph in public health," said Dr Ebrahim Samba, WHO Regional Director for the African Region.

However, hopes of a quick end to polio in Africa have been overshadowed by the recent polio outbreak in Nigeria. Until mid-2003, Nigeria was part of Africa's polio success story, with only a few northern states remaining polio-endemic and the country's capital, Lagos — Africa's most densely populated city — polio-free for over two years. However, suspension of immunization campaigns in the northern state of Kano fuelled by unfounded rumours about the safety of polio vaccine led to an outbreak of the virus which then spread to the neighbouring polio-free countries of Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Ghana and Togo.

"The disease is now threatening to make a comeback, and the whole continent is on the brink of re-infection unless these campaigns stop the further spread of the virus," said Samba.

"Before this new wave of cases, Africa had made the most rapid progress of any continent to secure a polio-free future for its children," said Rima Salah, UNICEF's Regional Director for West and Central Africa. "It would be an unspeakable tragedy to allow the virus to slip back now. National and community leaders must take a stand to stop the spread of the disease and ensure a victory over polio for the entire continent."

The campaign to "Kick Polio Out of Africa," launched by Nelson Mandela and other African leaders, has cut the number of children with paralysis caused by polio down from 205 cases per day in 1996 to just 388 a year in 2003.

Since its launch in 1988, the Global Polio Eradication Initiative, spearheaded by WHO, Rotary International, the US Centers for Disease Control and Prevention and UNICEF has seen the number of polio-endemic countries drop from 125 to just six — Afghanistan, Egypt, India, Niger, Nigeria and Pakistan.

Despite the resurgence of polio in West Africa which has put millions of

children at risk, partners in the Global Polio Eradication Initiative remain hopeful that if the upcoming campaigns reach every child, polio transmission in Africa can still be stopped in 2004.

"Africa has proved it can stop polio — now its time to finish the job," said Samba. ■

## WHO issues guidelines for herbal medicines

WHO has released guidelines for ensuring the safety, efficacy and environmental sustainability of the US\$ 60 billion a year herbal medicines market amidst an increasing number of reports indicating adverse health reactions caused by the misuse of medicinal plants.

The *WHO guidelines on good agricultural and collection practices for medicinal plants*, issued on 10 February 2004, are intended for national regulatory bodies and offer advice on cultivation and collection methods, site selection, climate and soil considerations and the correct identification of seeds and plants. They also offer guidance on post-harvest operations such as labelling and legal components including national and regional laws on quality standards, patent status and benefits sharing.

Representing an annual global market of US\$ 60 billion every year, herbal medicines account for around 20% of the overall drug market.

According to WHO, up to 80% of the population in Africa depends on traditional medicine for primary health care and in China, herbal medicines account for 30–50% of total medicinal consumption. In Europe, North America and other industrialized regions over 50% of the population have used complementary or alternative medicine at least once.

"It is not a binding guideline for any country, but it is a model or a sort of checklist which they can use to make their own national regulations," said Hans Hogerzeil, acting Director of WHO's Essential Drugs and Medicines department.

Although, 70 countries have a national regulation on herbal medicines, the legislative control of medicinal plants lacks structure due to differing definitions of medicinal herbs and products and diverse approaches to their licensing, dispensing, manufacturing and trading.

Hogerzeil described an enormous unregulated industry in which huge

amounts of leaves and traditional medicines are being shipped from various exporting countries such as China, India and Pakistan to many other countries. "Somebody has to regulate that, at least their safety," he said.

According to WHO, reports of patients experiencing negative health consequences caused by the use of herbal medicines are on the rise. These cases are usually linked to the poor quality of herbal medicines, the incorrect identification of plant species or inadequate labelling.

For example, ephedra or Ma Huang, traditionally used in China to treat respiratory congestion, was marketed in the states as a dietary aid. Overdosage led to at least a dozen deaths, heart attacks and strokes prompting the US Food and Drug Administration to issue a consumer alert in December 2003 on the safety of products containing ephedra.

The guidelines also address growing concerns over the potential threat to biodiversity posed by the booming herbal medicines market. Over-harvesting may lead to the extinction of endangered species and the destruction of national habitats and resources, warned WHO. ■

## Oral diseases increasing in developing countries

Oral diseases such as tooth decay, gum disease and oral and pharyngeal cancers are still a problem in the developed world and have also become a threat to oral health in developing countries, says a new report released on 24 February 2004 by WHO's Global Oral Health Programme.

According to the report ([http://www.who.int/oral\\_health/publications/report03/en/](http://www.who.int/oral_health/publications/report03/en/)), an estimated five billion people worldwide have experienced tooth decay. While it appears to be less severe in most African countries, the report states that tooth decay is expected to increase in many developing countries in Africa as a result of the growing consumption of sugars and inadequate exposure to fluorides. ■