

SPECIAL REPORT

Pandemic flu: from the front lines

As the novel H1N1 pandemic flu virus infects people worldwide, researchers in some of the affected countries describe in their own words the scientific and public-health challenges they face.

MEXICO

POPULATION 110 MILLION

Data suggest that Mexico has seen two waves of infection — the first, which peaked in late April, affected the Mexico City area, and the second, broader wave spanned June through August in southern states, including Chiapas, Yucatan and Quintana Roo. To prepare for a potentially larger wave this winter, Mexico is raising public awareness, standardizing timely diagnosis and treatment and reinforcing equipment and management protocols in intensive-care units throughout the country.

To improve surveillance, Mexico has accelerated the upgrading of its public-health laboratory network. The national reference laboratory and 28 states will soon have real-time PCR for running diagnostic tests. This builds on a restructuring of Mexico's national surveillance and reporting systems, which started in 2007.

As Mexico's strategic reserve of antivirals would cover only 1% of the population for community cases and up to 80,000 hospitalized cases, the nation is implementing a central logistics and delivery system to assure their efficient allocation. The country also expects to have 20 million doses of the H1N1 vaccine available by December. As even this would cover only a fraction of the population, the government will prioritize health-care workers, then individuals at risk of severe disease, such as pregnant women and people with chronic underlying illnesses. **Stefano Bertozzi, executive director at the Center for Evaluation Research and Surveys at the National Institute of Public Health in Cuernavaca**

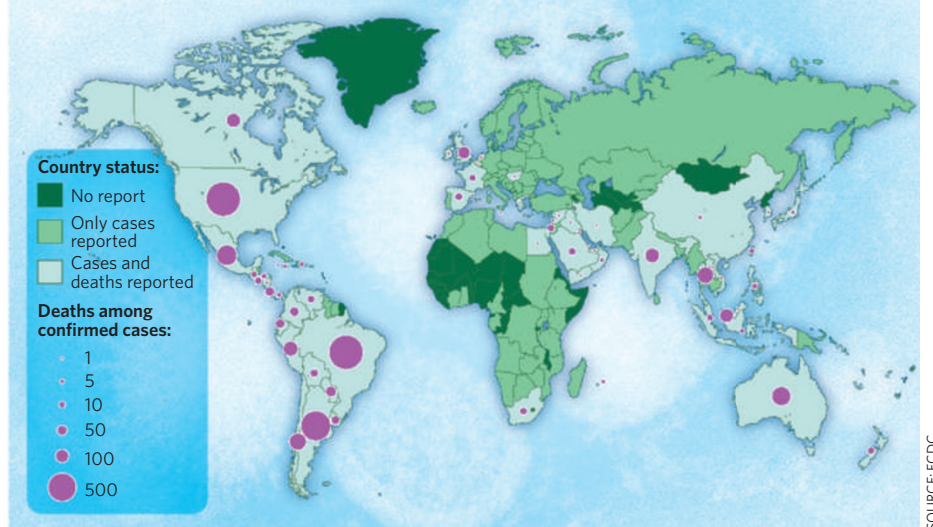
AUSTRALIA

POPULATION 21 MILLION

The timing of the epidemic has differed across the country, which has meant that we needed different public-health measures and messages in individual states. The pandemic virus seems to be outcompeting the seasonal flu viruses. The great majority of flu cases around the country are now pandemic H1N1.

One interesting question is whether this pandemic virus will completely replace any of the seasonal flu strains. If it doesn't, that's going to complicate the production of future seasonal flu vaccines, as we will need a vaccine against four strains instead of the current three. The Australian government has ordered 21 million

REPORTED FATALITIES FROM PANDEMIC INFLUENZA



SOURCE: ECDC

doses of dedicated pandemic virus vaccine, so if we need two doses per person, that covers half the population. There has been a lot of discussion about who should get it first, and when.

We are seeing similar patterns of disease severity to those reported worldwide, with most cases being mild. But there have been a significant number of cases with severe disease, not just in the at-risk groups, but also in healthy people. Our indigenous population is being hit harder, and we are seeing disproportionate numbers hospitalized with severe disease.

An important message for other countries that have intensive-care facilities is to expect significant pressure on them. There is a need for mechanical ventilators, and we have seen heavy use of scarce extracorporeal membrane oxygenation units.

Anne Kelso, director of the World Health Organization Collaborating Centre for Reference and Research on Influenza in Melbourne

JAPAN

POPULATION 128 MILLION

Japan stopped counting cases on 25 July and launched a new cluster surveillance system that is directly in the hands of the health ministry. Our Infectious Disease Surveillance Center no longer has any disease data feed, making it difficult to analyse epidemiological trends or disease burden. But we have received hundreds of

reports through routine sentinel-based surveillance of clusters of disease from many regions and big cities, so there is extensive spread.

The demand on public-health services to report and investigate all cluster cases is overwhelming public-health staff and leading to a breakdown in the normal public-health diagnostic service in local laboratories.

With the rising numbers of cases we are seeing a corresponding increase in deaths. As elsewhere, it is younger people who are affected with more severe disease requiring hospitalization, but the overall hospitalization rate is no greater than that of human seasonal influenza. Japan has an ageing population with large numbers of people older than 65, many with at-risk underlying health conditions, but so far pandemic H1N1 seems to be largely sparing the elderly.

The country's pandemic plan was based almost entirely on a severe pandemic of H5N1 avian influenza, which limited medical consultations to just a few hospitals.

The government seems to be relaxed with the low level of epidemic by the less virulent virus since May, and seems to have yet to draw any lessons from the pandemic. As a result, local and regional authorities have now independently started to prepare for the coming flu season.

Masato Tashiro, director of the Department of Viral Diseases and Vaccine Control at the National Institute of Infectious Diseases in Tokyo



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KING'S COLLEGE, LONDON

ARGENTINA

POPULATION 40 MILLION

The current epidemiological situation is a generalized spread of the virus throughout the country, although with a marked downward trend in the number of reports of the levels of influenza-like illness. The epidemic started in mid-May in Buenos Aires, and three weeks later spread to the city's larger metropolitan area. Activity peaked on 25 July, with influenza A representing 80% of the circulating respiratory viruses; 65% were H1N1-pandemic confirmed. Very few isolates were H3 and H1 seasonal.

Health systems in Argentina were overloaded because of government advice to people to consult a physician on first signs of flu symptoms such as fever or cough.

The major challenge at the lab level was in diagnosing the first cases produced by a new, unknown virus. Later, the challenge was for lab capacity to meet demand. Information transmitted to the public was not always clear enough, and the mass media had a negative role, including providing contradictory information and producing fear.

Wilma Savy, head of the respiratory virus service at the National Institute for Infectious Diseases in Buenos Aires

VIETNAM

POPULATION 85 MILLION

The first cases in Vietnam were at the end of May, a bit later than in many other parts of Asia, probably because Vietnam does not have a major international airport hub. We are now seeing an increase in disease and a small number of severe cases. Vietnam was a hotspot for H5N1 avian influenza in 2003 and 2004, and the pandemic preparation that resulted from both this and SARS has made a massive difference to the current situation.

Prior to avian flu, few hospital staff had community-acquired pneumonia on their radar; attention was concentrated on malaria, dengue fever and tuberculosis. Now clinicians have a much greater awareness of the need to look out for clusters of respiratory illnesses. There has also been greater interaction and collaboration between clinical and other researchers, and between centres across the country.

Access to vaccines and drugs remains an important issue. There is a global shortage of vaccines, and the rich countries have bought up all the first stocks. This is a really urgent issue; if we can get this right now, then many of the past issues around sharing of samples, data and general openness on emerging infectious diseases will be helped, maybe resolved. If we get it wrong, we will be back to square one. If ever there was a time for the rich world to reach

out and ensure equity of access to drugs and vaccines, it is now.

Jeremy Farrar, Vietnam director for the Wellcome Trust Major Overseas Programme, director of Oxford University's Clinical Research Unit in Ho Chi Minh City, and coordinator of the South East Asia Infectious Disease Clinical Research Network

UNITED STATES

POPULATION 301 MILLION

US health-care systems have been stretched and have no surge capacity. The system cannot handle this pandemic, even if it remains moderate in severity. The same applies to many of the supplies we get. Ask anybody who has tried to order an N95 respirator recently; there aren't any. We recently surveyed a group of world-class pharmacists to identify the essential drugs needed daily to keep patients from dying. They came up with a list of more than 30 — all generics, and most made offshore, mainly in Asia, and China and India in particular. Nobody is thinking what might happen to US or global supply chains when pandemic flu hits these countries, where the primary workforce are the young, who are most affected by the virus.

The United States has a federal programme for vaccine procurement but it is administered at the state level, and the two do not always mesh up. It is still not clear how this vaccine is going to be rolled out, or whether it will be here in time.

I worry most that, given current existing public concerns about vaccines, in the autumn we might see mounting public responses and concerns about pandemic-vaccine safety, and people refusing to be vaccinated. Expect the unexpected over the next six months.

Michael Osterholm, director of the University of Minnesota's Center for Infectious Disease Research and Policy in Minneapolis

INDIA

POPULATION 1.1 BILLION

The virus is now transmitting in city clusters. Large numbers of people are turning up at designated testing facilities, swamping an already stretched surveillance system, so there is little room for monitoring mutations and reassortment. This should be done. One way would be to bring in academic labs outside of the government testing system, but sharing of clinical materials and trust is low.

Deaths have sparked a fair amount of concern and panic. Poor communication of risks by the government and the public-health system is largely to blame.

Even if this pandemic remains moderate, the impact in India is likely to be severe, owing to its high population density, low awareness of

the pandemic and the propensity of the virus to infect the young (50% of Indians are under 25 years of age). Moreover, there is a high load of other infectious diseases as well as chronic conditions, groups that are at higher risks of severe forms of pandemic H1N1 disease. The health-care infrastructure is poor.

Despite this bleak outlook, India has strengths for tackling the virus, including that the government has pandemic plans in hand, and that we have a vibrant generic-pharmaceutical industry as well as a decent capacity for manufacturing vaccines. There is little clarity, however, as to India's vaccine plans, and the regulatory process is archaic, so it is not even clear whether pandemic vaccine could be rapidly approved for use in the country. The government says it has enough Tamiflu for 3 million people.

Shahid Jameel, head of the virology group at the International Centre for Genetic Engineering and Biotechnology in New Delhi

SUB-SAHARAN AFRICA

POPULATION 800 MILLION

H1N1 has not yet been reported in Nigeria, or any of the other sub-Saharan African countries with which we collaborate — Niger, Burkina Faso or the Central African Republic, although the Democratic Republic of Congo has one confirmed case. But surveillance is still very poor, and the virus may well often escape detection. International media attention to the pandemic is probably more than it deserves from an African public health point of view. Any diversion of resources from other important programmes needs to be carefully evaluated for long-term cost-benefit and sustainability.

Systems for lab surveillance and reporting of respiratory illnesses have improved since H5N1, which has hit nine sub-Saharan African countries since it first spread to the continent in 2006. With international support Nigeria, for example, has set up a central national laboratory for human influenza surveillance in Abuja, as well as several decentralized satellite labs.

There is no culture of testing for respiratory viruses, however, and the effort that went into H5N1 control is losing steam. The H5N1 virus was perceived as a major threat to the poultry industry, whereas the disease burden of pandemic flu seems low. Don't expect much mobilization for a virus where most cases are mild. ■

Claude P. Muller, head of the Institute of Immunology at the WHO Collaborative Center for Reference and Research on Measles Infections in Luxembourg

Interviews by Declan Butler

See www.nature.com/swineflu for more on pandemic flu.