

COMMENTARY

Global network could avert pandemics

Good surveillance is key to responding to a bird flu pandemic. **Jean-Paul Chretien, David L. Blazes** and their colleagues propose a new network of labs modelled on existing military facilities.

Since late 2003, an avian influenza epidemic has caused human deaths in Vietnam, Thailand, Cambodia, Indonesia, China and, this year, Turkey and Iraq. So far, most or all of these human infections were acquired directly from birds; if the virus becomes easily transmissible from person to person, we could face a devastating pandemic. To avert this, we must be able to quickly identify and contain avian influenza outbreaks, in birds and people, wherever they occur. This is challenging in developing countries, which often lack basic laboratories and epidemiologic capabilities. We are concerned that surveillance is weak in those countries that need it most.

How can we improve influenza preparedness in critical, but resource-poor settings? There is an existing model, based on a network of US military overseas laboratories, that we believe is worth copying. These laboratories work with host countries and the World Health Organization (WHO) to improve detection of and response to avian influenza and other emerging infections. US Naval Medical Research Unit-2 (NAMRU-2) in Jakarta helped to detect avian influenza in Indonesia last July, and plays an important role in monitoring the disease. NAMRU-3 in Cairo, Egypt, identified avian influenza in birds in Central Asia last summer, provided on-the-ground expertise in Turkey after human cases occurred there, and identified the first human case in Iraq.

Closing down

NAMRU-2 and NAMRU-3 are two of the few remaining overseas infectious-disease research laboratories that the US military established decades ago. The world needs such laboratories now, more than ever, as platforms for sustained epidemic detection and response — for avian influenza, and as-yet-unknown diseases. The time has come to build on their experience and create a new generation of multilateral, WHO-aligned laboratories as a front-line defence against future pandemics.

During the Second World War, the Navy established NAMRU-2 in Guam to study infectious-disease threats in the Pacific. Relocated several times for strategic and diplomatic reasons, the laboratory settled in Indonesia in 1970 after helping the government



A US Army veterinarian conducts training in Kenya on collecting avian specimens for influenza testing.

to control a plague outbreak there. Since then, NAMRU-2 has operated continuously in collaboration with the Indonesian Ministry of Health and other governmental and non-governmental organizations.

The NAMRU laboratories and the Armed Forces Research Institute of Medical Sciences, a US Army-affiliated facility in Bangkok, Thailand, were each set up following joint US and host-country concerns over a specific disease, but they have since conducted broad-ranging research. With state-of-the-art capabilities, access to areas with high disease rates, and strong cooperation between US and host-country personnel, the laboratories conducted field studies that led to vaccines for hepatitis A and Japanese encephalitis, treatments for malaria, cholera, typhoid fever and leptospirosis, and other lasting contributions. The laboratories never lost sight of important local diseases that posed little threat to US troops, and retained their welcome even when diplomatic relations worsened. As testimony to this, NAMRU-3 continued operations despite a diplomatic break between the United States and Egypt after the Six-Day War in 1967.

The US military built two more infectious-disease laboratories that remain today, in

Kenya and Peru. But during the second half of the century, more labs were closed than opened. Laboratories in Panama, Puerto Rico, Brazil, Congo, Uganda, Ethiopia, Malaysia and other countries folded for various reasons, including budget cuts and changing strategic needs. In the late 1970s, the United States even contemplated closing, or turning over to civilian contractors, all of its overseas military research laboratories. That plan was dropped after vigorous opposition from leaders in tropical medicine, in universities, government and industry, and from the host countries.

Under surveillance

In 1992, public-health experts warned that the loss of overseas laboratories left the United States, and the world, more vulnerable to emerging infections¹. In response, President Bill Clinton, in 1996, directed the Department of Defense to address emerging infections as a national-security threat. The military added a mission to its research-oriented overseas laboratories: develop surveillance networks to detect emerging infections, and contain epidemics before they spread. The US Department of Defense Global Emerging Infections Surveillance and Response System (DoD-GEIS) was

established to support and coordinate these efforts, among others².

Building on the existing military laboratories, DoD-GEIS developed surveillance networks that monitor host-country populations in clinics, hospitals and communities in areas where disease epidemiology was largely unknown. From the beginning, influenza, with its ever-present pandemic threat, was the top priority. Current DoD-GEIS influenza surveillance networks include patient enrolment sites in more than 20 countries in South America, the Middle East, sub-Saharan Africa and central and southeast Asia³. In several countries, including Indonesia, the networks are the WHO's only information source on circulating strains, essential for vaccine development and pandemic preparedness. Collaboration with the US Centers for Disease Control and Prevention has strengthened these networks in Indonesia and elsewhere. The laboratories also respond to outbreaks of other diseases at the request of host countries or the WHO by sending their own field epidemiologists to the scene, or by providing definitive testing. They often identify diseases where they were not previously known to occur.

Training personnel from the host country in surveillance and outbreak response is important. Graduates of outbreak courses, often Ministry of Health staff, have gone on to apply the lessons to real epidemics. And in Peru and Egypt, the military laboratories assisted host countries in developing nationwide surveillance systems, which are now under host-country control.

Fill in the gaps

We believe that these efforts have improved epidemic preparedness in many places, especially where they complement activities of the WHO and its partners. But critical gaps remain. We cannot be optimistic that a deadly and easily transmissible disease emerging in sub-Saharan Africa, or a rural part of Asia or South America, would be detected, characterized and contained before spreading. But we do have a model for improving the situation. A network of new, state-of-the-art laboratories, built upon lessons learned by the military laboratories, could help to detect and contain

epidemics in key areas worldwide (see table).

The United States may decide in the future to establish more broad-based overseas laboratories, but we should not expect one country to build and sustain the network entirely on its own. Affiliation with a single country can complicate work where relations between sponsor and host are strained. And as we have seen, even a wealthy country with vested interest in global epidemic preparedness may withdraw support for productive overseas laboratories. Multilateral support would buffer against funding fluctuations. An instructive example is the International Centre for Diarrhoeal Disease Research in Dhaka, Bangladesh. Supported by dozens of donor countries and organizations, and governed by a multinational board, this centre has conducted important research on cholera and other diseases for 28 years.

Despite multilateral support, the laboratories must address host-country needs. The longevity of existing military laboratories is owed, in part, to bilateral development of laboratory priorities. For example, the laboratories monitor diseases important to host countries that might not pose direct threats to US troops, including yellow fever (against which US forces are vaccinated), cholera and hepatitis C. The laboratories must also balance global needs for public disease notification with local sensitivities over patient specimens and information; otherwise, host countries may be reluctant to acknowledge outbreaks.

We emphasize that the multilateral laboratories would support, not duplicate, the WHO's work. Through its Global Outbreak Alert and Response Network (GOARN), the WHO connects existing institutions and networks to identify, confirm and respond to outbreaks of international importance. But it is not part of GOARN's mission to fund the construction of new laboratories. The mission of the multilateral laboratories would be to develop regional surveillance and response capacity in resource-poor regions, but they would seek recognition from the WHO. Once again, the military laboratory experience, with

DoD-GEIS as a full GOARN partner, has demonstrated the benefits of being linked to a global professional network.

Official WHO affiliation is also important when persuading countries to report surveillance results. For example, NAMRU-3 is assisting several countries in Asia, the Middle East and Africa in establishing national

influenza surveillance systems. With technical assistance comes an obligation to make information and viral isolates available to the WHO's global monitoring efforts.

Be prepared

The global threat of avian influenza has motivated wealthy countries into action. The US Congress allocated US\$3.8 billion during this fiscal year to prepare for a pandemic; some of these funds will support overseas surveillance and response activities. At the International Pledging Conference on Avian and Human Pandemic Influenza in January, co-hosted by the Chinese government, the European Commission and the World Bank, donor countries and international health organizations pledged \$1.9 billion to fight avian influenza and prepare for a pandemic, surpassing expectations. This is an important time, during which plans for systems and laboratories will be developed. We

have an unprecedented opportunity to influence global epidemic preparedness, especially in developing countries. We urgently need more capacity to do so, and in our view there is a model waiting to be adapted.

The support of the WHO, with its unparalleled network of human and technical resources, is needed for this effort. We encourage the WHO to charter a working group to flesh out the model presented here, compare it with alternatives, and judge how feasible it is.

Our proposed network is not risk-free for the sponsoring countries; uncontrollable factors can hamper overseas activities. Sponsors may feel they risk less with discrete projects than with broad-based laboratories that cover many projects and staff and require long-term support. But the next pandemic — which may or may not involve influenza — could begin anywhere in the world. Making long-term investments in laboratory and epidemiologic capabilities could help us to detect and control it. ■

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1. Institute of Medicine. *Emerging Infections. Microbial Threats to Health in the United States* (eds Lederberg, J. & Oaks, S. C.) (National Academies Press, Washington DC, 1992).
2. DoD-GEIS www.geis.fhp.osd.mil
3. Canas, L. C. et al. *Mil Med* 165, 52-56 (2000).

OVERVIEW OF PROPOSED LABORATORIES	
Who would fund them	Multiple governments, other funding organizations
What the host country role would be	Drive priority setting Contribute some of the staff
What other sponsors' roles would be	Negotiate priorities Contribute staff for multi-year positions Foster links with other specialized laboratories
What they would do	Develop surveillance networks Respond to outbreaks Train personnel (in developing and wealthy countries) Conduct research
How they would relate to the WHO	Join WHO network as partners Seek Collaborating Center status