Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Experience of a global laboratory network in responding to infectious disease epidemics

The challenge of emerging infections transcends national borders. Influenza A (H5N1), severe acute respiratory syndrome (SARS), and diseases that continue to re-emerge such as cholera, drug-resistant malaria, and dengue can expand rapidly from local to regional or global threats. We were pleased to see that Georgios Pappas and colleagues,[1] in their global review of human brucellosis epidemiology, discussed serious problems in tracking and containing the disease, which apply to many emerging infections: lack of appropriate diagnostic capabilities in developing countries, cross-border disease spread from countries with high incidence, and emergence of new endemic foci because of socioeconomic and other changes.

Several of us have proposed a network of new, broad-based laboratories as a way to address such challenges for emerging infections of international importance.[2] These laboratories would assist host countries in developing surveillance systems and responding to epidemics, strengthen global epidemic detection and response efforts of WHO in key regions, and form links with specialised institutions worldwide to support these activities.

We offered, as a model for the proposed network, US military overseas infectious disease research laboratories. Following World War 2, the US military and host countries established these laboratories to study infectious diseases of bilateral concern.[3] Broad-based laboratory proficiencies and access to key populations facilitated important research (see, for example, references 4–8). Currently, there are five such Department of Defense (DoD) Overseas Laboratories: Naval Medical Research Center Detachment (NMRCD; Lima, Peru), Naval Medical Research Unit-3 (NAMRU-3; Cairo, Egypt), US Army Medical Research Unit-Kenya (USAMRU-K; Nairobi), Armed Forces Research Institute of Medical Sciences (AFRIMS; Bangkok, Thailand), and Naval Medical Research Unit-2 (NAMRU-2; Jakarta, Indonesia).

In 1996, a Presidential directive instructed federal departments and agencies to strengthen US detection, response, and prevention for emerging infections.[9] The DoD, in turn, codified the missions of emerging infection surveillance, outbreak response, and host country capacity building for these research-oriented laboratories. The DoD-Global Emerging Infections Surveillance and Response System (DoD-GEIS) was established to support and coordinate these activities at the Overseas Laboratories and in the Military Health System.[10] The DoD-GEIS network of Overseas Laboratories currently maintains surveillance activities in more than 20 countries. These include a global influenza surveillance system[11] and surveillance for malaria, dengue, diarrhoeal diseases, other febrile illnesses, and antimicrobial resistance. The Overseas Laboratories respond to outbreaks on invitation by host countries or WHO.

Between Oct 1, 2003 and Feb 28, 2006, the Overseas Laboratories responded to 66 outbreaks in 22 countries

Disease or agent	Number of outbreaks
Bartonellosis	1
Brucellosis	1
Chikungunya	10
Cholera	4
Crimean-Congo haemorrhagic fever	1
Cryptosporidium	1
Cyclospora	2
Dengue fever or haemorrhagic fever	10
Ebola haemorrhagic fever	1
Enterotoxigenic *Escherichia Coli*	2
Enterovirus meningitis	1
Hepatitis (viral)	4
Influenza	9
Japanese encephalitis	1
Leishmaniasis (cutaneous)	2
Leptospirosis	1
Marburg haemorrhagic fever	1
Plague (bubonic)	1
Q fever	1
Typhoid fever	2
Yellow fever	2
Unknown aetiology	
Febrile syndrome	2
Gastrointestinal syndrome	3
Respiratory syndrome	3
Total	66

Table: **DoD-GEIS overseas outbreak responses, October, 2003, to February, 2006**

(table; we provide country of occurrence only for selected outbreaks because of host country sensitivities). They provided laboratory and field support, laboratory support only, and field support only for 36, 26, and four responses, respectively, identifying the causal agent in 55 of 62 (89%) responses involving laboratory support. 62 responses targeted human outbreaks only. The four others included veterinary (with or without human) response.

Among human outbreaks, size ranged from fewer than ten cases (eg, Crimean-Congo haemorrhagic fever in Sudan) to thousands (eg, chikungunya in Kenya). Response to outbreaks involving animals included influenza A (H5N1) in Egypt, Iraq, Kazakhstan, and Turkey. Overall, the three most common diseases were chikungunya (ten outbreaks in Comoros, Indonesia, Kenya, and Somalia), dengue fever or dengue haemorrhagic fever (ten outbreaks in Eritrea, Indonesia, Peru, Sudan, and Yemen), and influenza (nine outbreaks in Cambodia, Egypt, Indonesia, Iraq, Kazakhstan, Kenya, Nepal, and Turkey). Laboratory testing did not identify the causal agent but excluded SARS in two outbreaks (in Iraq and Peru) where it was suspected initially because of patient travel history or clinical features.

Several outbreak responses helped to identify disease emergence or re-emergence. These include influenza A (H5N1) in Egypt, Indonesia, Iraq, Kazakhstan, and Turkey; a large outbreak of cutaneous leishmaniasis in a forested region of Ghana (an unusual focus, since the disease usually occurs in arid or semi-arid areas); outbreaks of chikungunya in Lamu and Mombasa, Kenya (the first confirmed outbreaks along the Kenyan coast); emergence of dengue haemorrhagic fever in Iquitos, Peru; re-emergence of dengue in Lima, Peru (after a 60-year absence); and isolation of a novel virus associated with a haemorrhagic fever outbreak in Bolivia (further viral characterisation is pending). Several outbreaks involved diseases recognised by the International Health Regulations[12] as capable of rapid international spread. These include ebola and Marburg haemorrhagic fever in Sudan and Angola, respectively; cholera in Kenya; yellow fever in Peru and Sudan; and dengue and influenza A (H5N1) as described above.

The Overseas Laboratories collaborated with WHO or the US Centers for Disease Control and Prevention in 22 outbreak responses. Host country collaborations are integral to the success of the Overseas Laboratories. Host country Overseas Laboratory staff provide understanding of local language and culture, and maintain continuity since US personnel rotate every few years. Outbreak responses provide opportunities for training and technology transfer with Ministry of Health personnel, strengthening partnerships and readiness for future outbreaks.

The model presented here—broad-based laboratories with epidemiologic capabilities, links to wider networks, and strong host country collaborations—has proven useful in responding to outbreaks of epidemic, endemic, and emergent diseases. The DoD Overseas Laboratories also devote considerable resources to applied research (such as clinical trials of vaccines and drugs), development of host country surveillance systems, and training of host country and US military medical personnel, activities that facilitate outbreak response. We encourage government and public health leaders to consider establishing facilities similar to these in countries where the need is most critical.

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1 Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. *Lancet Infect Dis* 2006; **6:** 91–99.
2 Chretien JP, Gaydos JC, Malone JL, Blazes DL. Global network could avert pandemics. *Nature* 2006; **440:** 25–26.
3 Gambel JM, Hibbs RG, Jr. U.S. military overseas medical research laboratories. *Mil Med* 1996; **161:** 638–45.
4 Meegan JM. The Rift Valley fever epizootic in Egypt 1977–78. 1. Description of the epizootic and virological studies. *Trans R Soc Trop Med Hyg* 1979; **73:** 618–23.

5 Innis BL, Snitbhan R, Kunasol P, et al. Protection against hepatitis A by an inactivated vaccine. *JAMA* 1994; **271:** 1328–34.

6 Hoke CH, Nisalak A, Sangawhipa N, et al. Protection against Japanese encephalitis by inactivated vaccines. *N Engl J Med* 1988; **319:** 608–14.

7 Hoffman SL, Punjabi NH, Kumala S, et al. Reduction of mortality in chloramphenicol-treated severe typhoid fever by high-dose dexamethasone. *N Engl J Med* 1984; **310:** 82–88.

8 Fryauff DJ, Baird JK, Basri H, et al. Randomised placebo-controlled trial of primaquine for prophylaxis of falciparum and vivax malaria. *Lancet* 1995; **346:** 1190–93.

9 Presidential Decision Directive NSTC-7. Washington DC, WA, USA: The White House, 1996.

10 Department of Defense Global Emerging Infectious Surveillance and Response System. http://www.geis.fhp.osd.mil/ (accessed July 28, 2006).

11 Canas LC, Lohman K, Pavlin JA, et al. The Department of Defense laboratory-based global influenza surveillance system. *Mil Med* 2000; **165** (suppl 2)**:** 52–6.

12 World Health Assembly. Resolution WHA58.3. Revision of the International Health Regulations. Geneva: World Health Organization, 2005.

Human brucellosis in Croatia

We read with interest the review by Georgios Pappas and colleagues of the new global map of human brucellosis.[1] In this review the authors stated that Croatia is free from human brucellosis, which is consistent with published data.[2,3] However, we report that human brucellosis occurred in 2004 in a rural area of southern Croatia near the border of Bosnia and Herzegovina, a country with recognised natural foci of brucellosis.[1,4] Brucellosis has been a notifiable disease in Croatia since 1960. No documented case of human brucellosis had been reported previously in southern Croatia.[5] In the area where brucellosis occurred in 2004, goat and sheep breeding is an important economic activity.

The first patient became ill in June 2004. He lived in the rural area of Split-Dalmatia county, and had had regular contact with sheep and goats. In the same area, a familial outbreak (father, mother, and two sons [aged 7 and 9 years]) occurred during July and August 2004. This family had a herd of 210 goats. During the spring of 2004 they observed several abortions in their goats.

The sixth patient, a sheep breeder and slaughterer, lived in the most southern Croatian county, close to the Bosnia and Herzegovina border. Because brucellosis had never been observed in south Croatia, physicians were unfamiliar with the clinical features, and brucellosis initially was not recognised as a possible cause of his illness. He became ill in May, was hospitalised three times, and, finally, in September 2004, was diagnosed as having brucellosis.

All patients presented with prolonged fevers, night sweats, body aches, arthralgias, and weakness. The patients were diagnosed by culture and/or by serological methods. All six cases were positive by the standard agglutination test for brucella antibodies, with titres ranging from 1/160 to 1/640. *Brucella* spp organisms were isolated by culture from the blood of all but one patient. Isolates were identified by standard bacteriological techniques as *Brucella melitensis*. To confirm the identity of the cultures, DNA extracted from isolated colonies was used as a template to amplify

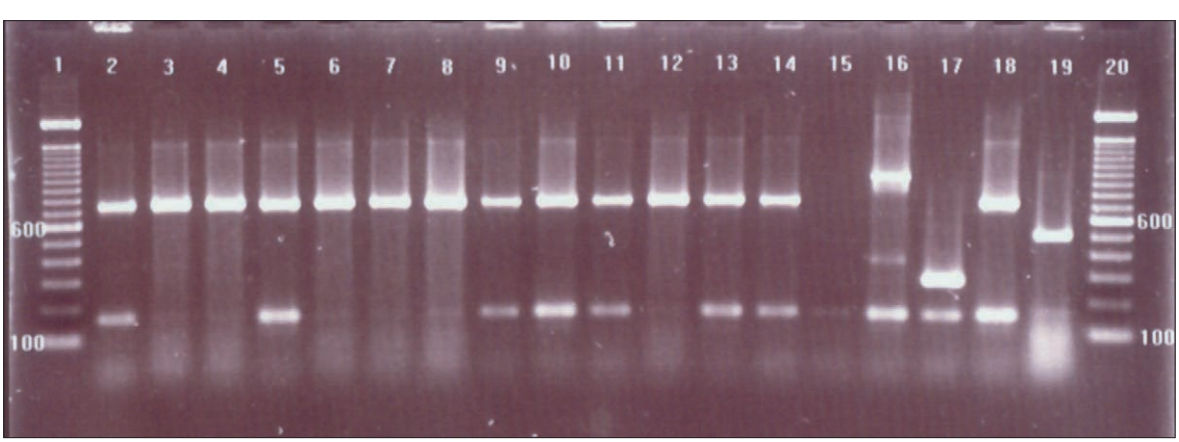

Figure: **Agarose gel electrophoresis and ethidium bromide staining showing amplified products of 731 bp of *B melitensis***
Lanes 1 and 20=Ready-Load (Invitrogen Ltd, Paisley, UK); 100 bp DNA ladder; lanes 2–3=sheep blood isolates; lanes 4–9=goat blood isolates; lanes 10–14=isolates obtained from bloods of five patients; lane 15=negative control; lane 16=positive control *Brucella ovis* 63/290; lane 17=positive control *Brucella suis* 1330; lane 18=positive control *B melitensis* 16M; lane 19=positive control *Brucella abortus* 544.