Screening Laboratory Requests

To the Editor: In August 1999, the Laboratory Response Network (LRN) was established to better integrate and improve laboratory capacity for responding to public health threats (1). However, while experts have focused on clinical indications for testing for agents of bioterrorism, laboratory methods for microbial identification, and needs for integrated communication networks (2–4), little attention has been given to how sentinel laboratories can effectively screen clinicians’ requests for testing pathogens designated as global health threats.

In times of crisis, clinicians often pressure laboratorians to perform testing for patients whose probability for disease is very low or for nonvalidated sample types. In 2001, a few cases of anthrax triggered large numbers of nationwide requests to test nasal swabs for *Bacillus anthracis* despite the absence of data to support this clinical practice outside epidemiologic investigations (5). Similarly, a false-positive result for severe acute respiratory syndrome (SARS) in 2003 from the National Microbiology Laboratory in Canada created public alarm that SARS was reemerging, when the virus was actually that of a coronovirus and Semliki Forest viruses replication by antiviral compounds: synergistic effect of interferon-alpha and ribavirin combination. Antiviral Res. 2004;61:111–7.

10. Ajayakajhajorn C, Mammen MP Jr, Endy TP, Getayacamin M, Nisalak A, Nimmannitya S, et al. Randomized, placebo-controlled trial of nonpegylated and pegylated forms of recombinant human alpha interferon 2a for suppression of dengue virus viremia in rhesus monkeys. Antimicrob Agents Chemother. 2005;49:4508–14.

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References

1. Schuffenecker I, Iteinan I, Michault A, Murri S, Frangeul L, Vaney MC, et al. Genome microevolution of chikungunya viruses causing the Indian Ocean outbreak. PLoS Med. 2006;3:e263.

2. Laras K, Sukri NC, Larasati RP, Bangs MJ, Kosim R, Djauzi, WT, et al. Tracking the re-emergence of epidemic chikungunya virus in Indonesia. Trans R Soc Trop Med Hyg. 2005;99:128–41.

3. Lloyd G Alphaviruses. In: Zuckerman AJ, Laras K, Sukri NC, Larasati RP, Bangs MJ, Kosim R, Djauzi, WT, editors. Principles and practice of clinical virology. 5th ed. Chichester (UK): John Wiley & Sons Ltd; 2004. p. 517–9.

4. Wong CK, Lam CW, Wu AK, Ip WK, Lee NL, Chan IH, et al. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. Clin Exp Immunol. 2004;136:95–103.

5. Jiang Y, Xu J, Zhou C, Wu Z, Zhong S, Liu J, et al. Characterization of cytokine/chemokine profiles of severe acute respiratory syndrome. Am J Respir Crit Care Med. 2005;171:850–5.

6. Peiris JS, Yu WC, Leung CW, Cheung CY, Ng WF, Nicholls JM, et al. Re-emergence of fatal human influenza A subtype H5N1 disease. Lancet. 2004;363:617–9.

7. Avila-Aguero ML, Avila-Aguero CR, Um SL, Soriano-Fallas A, Canas-Coto A, Yan SB. Systemic host inflammatory and coagulation response in the Dengue virus primo-infection. Cytokine. 2004;27:173–9.

8. Green S, Vaughn DW, Kalayanarooj S, Nimmannitya S, Suntayakom S, Nisalak A, et al. Elevated plasma interleukin-10 levels in acute dengue correlate with disease severity. J Med Virol. 1999;59:329–34.

9. Briolant S, Garin D, Scaramozzino N, Green S, Vaughn DW, Kalayanarooj S, et al. Elevated plasma interleukin-10 levels in acute dengue correlate with disease severity. J Med Virol. 1999;59:329–34.

10. Ajayakajhajorn C, Mammen MP Jr, Endy TP, Getayacamin M, Nisalak A, Nimmannitya S, et al. Randomized, placebo-controlled trial of nonpegylated and pegylated forms of recombinant human alpha interferon 2a for suppression of dengue virus viremia in rhesus monkeys. Antimicrob Agents Chemother. 2005;49:4508–14.
absence of positive results, no confirmatory testing was indicated. Although SARS no longer poses a credible threat and human-to-human transmission of H5N1 has not been well delineated, our experiences with these 2 pathogens demonstrate how a sentinel laboratory can effectively intervene in the initial phases of a public health threat. We found that having a laboratory professional contact the clinician and systematically ask the scripted questions was a pragmatic tool for the first phase of response and resulted in cancellation of most tests. We acknowledge that optimal validation of this algorithm would require randomly selecting and testing rejected specimens during a phase of high disease prevalence. Although low disease prevalence during our study period precluded validation testing, we recommend that such testing be performed.

Our systematic approach to screening requests to test for agents with the potential to threaten global health can prevent arbitrary decision making, reduce inappropriate testing, and increase the value of laboratory consultation. The principles guiding our testing protocols for SARS and avian influenza can be generalized to future global health threats. Responsible and judicious use of diagnostic testing will be crucial for minimizing the risk of providing clinicians with misleading results that could severely disrupt the public health system and lead to an unnecessary expenditure of limited resources. With the emergence of highly pathogenic avian influenza, we anticipate further demands on laboratory and public health resources that will necessitate effective, pragmatic tools to enhance the value of laboratorian-clinician consultation before tests are performed on site or referred to an LRN laboratory.

Figure. Laboratory algorithm used to screen test requests for avian influenza H5N1 or severe acute respiratory syndrome (SARS)

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References
1. Centers for Disease Control and Prevention. The laboratory response network partners in preparedness [cited 2006 Jun 8]. Available at http://www.bt.cdc.gov/lrn
2. Pien BC, Saah JR, Miller SE, Woods CW. Use of sentinel laboratories by clinicians to evaluate potential bioterrorism and emerging infections. Clin Infect Dis. 2006;42:1311–24.
3. Klietmann WF, Ruoff KL. Bioterrorism: implications for the clinical microbiologist. Clin Microbiol Rev. 2001;14:364–81.
4. Snyder JW. Role of the hospital-based microbiology laboratory in preparation for and response to a bioterrorism event. J Clin Microbiol. 2003;41:1–4.
5. Kiratisin P, Fukuda CD, Wong A, Stock F, Preuss JC, Ediger L, et al. Large-scale screening of nasal swabs for Bacillus anthracis: descriptive summary and discussion of the National Institutes of Health’s experience. J Clin Microbiol. 2002;40:3012–6.
6. Enserink M. Infectious diseases. Unexplained false alarm may hold lessons. Science. 2003;302:767.
7. Enserink M, Normile D. Infectious diseases. Search for SARS origin stalls. Science. 2003;302:766–7.
8. Yu AC. The difficulties of testing for SARS. Science. 2004;303:469–71.
9. Centers for Disease Control and Prevention. Updated interim guidance for laboratory testing of persons with suspected infection with avian influenza A (H5N1) virus in the United States [cited 2006 Sep 19]. Available from http://www2a.cdc.gov/han/Archive/Sys/ViewMsgV.asp?AlertNum=00246
10. Centers for Disease Control and Prevention. Clinical guidance on the identification and evaluation of possible SARS-CoV disease among persons presenting with community-acquired illness [cited 2006 Jun 12]. Available from http://www.cdc.gov/ncidod/sars/clinicalguidance.htm

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