nasal cultures in 6 of the 11 members of the 2 families. In this niche, it was able to persist and cause a series of infections in a relatively large number of family members. Even though the *S. aureus* isolated from active lesions were not available for testing, the recovery of identical PVL-positive organisms from nasal cultures strongly suggests the presence of a pathogenic clone that probably caused the recurrent infections in the 6 affected family members. Our investigation highlights the high transmissibility of this PVL-producing *S. aureus* clone, its high attack rate, and its virulence. The intervention in this outbreak might have prevented not only subsequent recurrences of cutaneous infections but also further spread of this clone and the manifestation of even more serious infections such as necrotizing pneumonia. Increasing awareness among community-based healthcare providers of PVL-producing *S. aureus* infections is important to facilitate rapid and adequate response in similar clinical events in the future.

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Chikungunya Fever, Hong Kong

To the Editor: Chikungunya virus disease, caused by a mosquitoborne alphavirus, is endemic to Africa and Southeast Asia. It typically causes an acute febrile illness, with joint pain and a skin rash. Chronic arthropathy may develop (*1*,*2*). No treatment or vaccine is available, and relatively little research has been conducted into its pathogenesis, compared with that of other arboviruses, such as dengue. Recent reports have described a massive outbreak of chikungunya disease occurring on islands in the Indian Ocean, off the east coast of Africa (*1*). Reemergence of chikungunya has also been reported from Indonesia (*2*).

During March 2006, a 66-year-old Chinese man from Hong Kong visited Mauritius where he was bitten by mosquitoes 2 days before returning to Hong Kong. On the return trip, he experienced fever (39°C), severe finger joint and muscle pains, mild headache, and a skin rash, and he sought treatment at the Prince of Wales Hospital (PWH) Infectious Diseases Clinic on the second day of his illness. Physical examination showed a generalized erythematous rash over the trunk and limbs and petechiae over the lower limbs. Mild finger joint stiffness was observed, but no joint swelling. No lymphadenopathy or eschar was detected. Level of C-reactive protein was elevated at 10.4 mg/L. Results of screens for malaria and dengue were negative. Results of other routine assessments were unremarkable. His symptoms subsided gradually within a week.

Serum specimens taken on days 2 and 6 were positive for chikungunya virus RNA by in-house reverse transcription (RT)-PCR at the Public Health Laboratory Service (PHLS) (targeting the nonstructural protein-1 [NSP-1] gene) and PWH laboratory (targeting both NSP-1 and the envelope glycoprotein [E1] gene). An

additional serum sample taken on day 8 of illness, received by PHLS only, was also positive for chikungunya RNA. Both laboratories confirmed RT-PCR results by sequencing. At PWH, phylogenetic analysis was performed to determine the likely origin of the virus. In-house immunofluorescent slide serologic assays developed at PHLS found chikungunya immunoglobulin G (IgG) titers <10, 160, and 320 in the serum samples taken on days 2, 6, and 8 of illness, respectively, and detected chikungunya IgM in the day 8 serum. The acute cytokine immunologic response to this virus was also tested (online Appendix available from http://www.cdc.gov/ncidod/EID/vol12no11/06-0574_app.htm).

Sequencing and phylogenetic analysis was consistent with an imported infection, almost certainly originating from the current chikungunya outbreaks in the Indian Ocean. Phylogenetic analyses of the NSP-1 and E1 regions, indicated that this virus is most closely related to previous African rather than South-east Asian chikungunya viruses (see online Appendix Figures 1 and 2, available from http://www.cdc.gov/ncidod/EID/vol12no11/06-0574_appG1.htm and http://www.cdc.gov/ncidod/EID/vol12no11/06-0574_appG2.htm). The persistence of viremia up to at least day 8 of illness was unusual. Standard texts state that viremia may be present during the first 2–4 days of illness, with neutralizing antibodies appearing by days 5–7 (*3*).

The most striking finding from the cytokine analysis (Table) is the high level of interferon-γ (IFN-γ)– inducible protein-10 (IP-10/CXCL-10), up to 26 and 16 times the upper limit of the normal range at days 2 and 6 after disease onset, respectively. Serum concentrations of interleukin-8 (IL-8), monocyte chemoattractant protein (MCP) 1 (MCP-1) and monokine induced by IFN-γ (MIG/ CXCL9) are also elevated in both samples. Notably, serum IFN-γ, tumor necrosis factor-α (TNF-α), and IL-1β, 6, 10, and 12 concentrations remain within normal limits in both samples, although the concentrations at local inflammatory sites (e.g., joints) are unknown. CXCL10 and MCP-1/CCL2 concentrations decreased during clinical recovery. Thus, the cytokine profile demonstrates that the levels of Th1 chemokine CXCL10 was highly elevated and that the levels of chemokines IL-8/CXCL8, CCL2, and CXCL9 were moderately elevated. In contrast, IFN-γ and other inflammatory/Th2 cytokines were not elevated during the illness.

Interpretation of the significance of these cytokine results is necessarily speculative. Some comparison can be made with other viral infections. In severe acute respiratory syndrome–associated coronavirus (SARS-CoV) (*4*,*5*) and H5N1 influenza (*6*) infections, very high blood levels of CXCL10 and moderately high CCL2, CXCL9, and CXCL8 concentrations, or their enhanced expressions in vitro, have been reported. In dengue fever, which has similar clinical manifestations as chikungunya fever, only elevated CXCL8, IL-6, IL-10, and TNF-γ concentrations have been shown consistently (*7*,*8*), although CXCL10 expression has not been studied.

The function of CXCL10 is to act as a chemoattractant for Th1 cells in the activation of cell-mediated immune response. Its expression can be up-regulated by the Th1 cytokine IFN-γ during acute inflammation. CXCL10 has been implicated in the pathogenesis of SARS-CoV and H5N1 influenza infections, in which persistently high CXCL10 concentrations seem to correlate with disease severity and progression (*4*–*6*). CCL2, CXCL9, and CXCL8, have also been found to have a pathogenic role in H5N1 influenza, SARS-CoV, and dengue infections. Notably, the level of antiviral cytokine IFN-γ was not elevated in our chikungunya case, though admittedly, this is only 1 case. This finding may represent a way that the chikungunya virus evades host defenses and may provide a rationale for the use of IFN as a therapeutic option (*9*). Such IFN therapy has been suggested and tried, experimentally, for SARS-CoV (*5*) and dengue infections (*10*).

Table. Serum cytokine profiles of patient with chikungunya infection, days 2 and 6 of illness*

	Time after onset of illness	
Serum cytokine profile (ng/L)	2 d	6 d
IFN-γ, N<15.6	UD	UD
IL-1β, N<7.2	2.4	1.5
IL-6, N<3.1	UD	1.3
IL-10, N<7.8	1.7	1.7
IL-12 p70, N< 7.8	3.6	1.4
TNF-α, N< 10.0	UD	UD
CXCL8, N<10.0	45.3	54.3
CXCL10†, N = 232–1,019	26,319	16,156
CCL2†, N = 18–152	445	257
CXCL9†, N = 37–463	1,138	1,605
CCL5, N = 10,349–46,704	24,745	60,671

*N, normal range; IFN, interferon; IL, interleukin; UD, undetected; TNF, tumor necrosis factor.
†Both 2 d and 6 d and led samples above normal range.

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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 common respiratory illness in a nursing home (*6*). The problem is further complicated when laboratories other than the LRN lack standardization, have greater access to nucleic acid amplification-based testing, and develop tests for global health threats outside a quality-regulated system. False-positive results caused by contamination or cross-reactivity with a microorganism of low virulence can disrupt a public health system, adversely affect patient care, and increase costs (*6–8*); false-negative results may prompt clinicians to discontinue containment procedures and potentially risk transmitting a virulent microorganism. At our sentinel laboratory, we recognized these challenges and took steps to promote judicious use of testing for agents designated as global health threats. We report use of an algorithm to evaluate test requests for SARS-associated coronavirus and highly pathogenic avian influenza H5N1; however, the algorithm can be used to screen testing requests for any pathogen that has potential to threaten public health.

During outbreaks of SARS and H5N1, a laboratory protocol was established to notify the on-call laboratory professional when a sample was received for testing for 1 of these pathogens (Figure). The protocol required the laboratorian to communicate directly with the clinician, using a script with questions based on criteria established by the Centers for Disease Control and Prevention, to determine the medical necessity for testing (*9,10*). Samples from patients not meeting these criteria were rejected. Testing for SARS used an in-house real-time PCR assay with a standard laboratory protocol. Samples accepted for H5N1 testing were screened by a nonspecific hemagglutinin influenza PCR assay and, if results were positive, were to be forwarded to an LRN laboratory. Positive results were to be reported only after confirmation by an LRN laboratory. Laboratory professionals were specifically trained about the sensitivity, specificity, positive predictive value, and negative predictive value of test methods in relation to sample type, time between symptom onset and specimen collection, and disease prevalence.

Of 41 samples (40 SARS and 1 H5N1) received for testing, 26 (63%) samples were not tested because clinician responses failed to satisfy the screening criteria. The remaining 15 (37%) samples met criteria for testing and all had negative results. In the