infection with *S. aureus*, possibly MRSA. The possibility of MRSA must be considered when initiating antimicrobial agents to treat TSS.

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Are SARS Superspreaders Cloud Adults?

To the Editor: The primary mode of transmission of severe acute respiratory syndrome (SARS) appears to be through exposure to respiratory droplets and direct contact with patients and their contaminated environment. However, in summarizing their experiences during the SARS outbreaks in Toronto and Taiwan, McDonald et al. (1) note that certain persons were very efficient at transmitting SARS coronavirus (SARS-CoV), and that in certain settings these so-called "superspreaders" played a crucial role in the epidemic. Airborne transmission by aerosols may have occurred in many of these cases. The same observation has been made by others (2–4), but the causes of these superspreading events and the reasons for the variable communicability of SARS-CoV are still unclear. Possible explanations include specific host characteristics (e.g., altered immune status, underlying diseases), higher level of virus shedding, or environmental factors (1–3).

We hypothesize that superspreading events might be caused by coinfection with other respiratory viruses. Such a mechanism has been identified in the transmission of *Staphylococcus aureus*. Eichenwald et al. (5) showed that newborns whose noses are colonized with this bacterium disperse considerable amounts of airborne *S. aureus* and become highly contagious (i.e., superspreaders) after infection with a respiratory virus (e.g., adenovirus or echovirus). These babies caused explosive *S. aureus* outbreaks in nurseries. Because they are literally surrounded by clouds of bacteria, they were called "cloud babies" (5). We have shown that the same mechanism also occurs in certain adult nasal carriers of *S. aureus* ("cloud adults") (6,7). Reports indicate that viral infections of the upper respiratory tract facilitate the transmission of other bacteria, including *Streptococcus pneumoniae*, *S. pyogenes*, *Haemophilus influenzae*, and *Neisseria meningitidis* (8). Moreover, superspreading events have also been reported in outbreaks of viral diseases such as Ebola hemorrhagic fever and rubella (3).

Some observations suggest that coinfection with other respiratory viruses might cause superspreading events with airborne transmission of SARS-CoV. First, other viral pathogens, including human metapneumovirus, have been detected together with SARS-CoV in some patients with SARS (4). Second, few patients with SARS are superspreaders, and upper respiratory symptoms such as rhinorrhea and sore throat are a relatively uncommon manifestation of SARS (with prevalences of 14% and 16%, respectively) (4). Thus, some

patients with SARS and upper respiratory symptoms might be coinfected with other respiratory viruses and become superspreaders. Interestingly, the report on a SARS superspreading event in Hong Kong explicitly states that the superspreader had presented with a "runny nose" (in addition to fever, cough, and malaise) (3). Therefore, upper respiratory symptoms might be a marker for highly infectious SARS patients. Future investigations, based upon either existing specimens from the last outbreak or newly collected specimens from any future outbreak, should focus on whether an association exits between SARS superspreading events and coinfection with other respiratory viruses.

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Route of Infection in Melioidosis

To the Editor: Melioidosis is an emerging tropical infectious disease, the incidence of which is unknown in many developing countries because of the lack of diagnostic tests and medical practitioners' lack of awareness of the disease. It is a potentially fatal disease caused by the soil bacterium *Burkholderia pseudomallei*. Clinical manifestations, severity, and duration of *B. pseudomallei* infection vary greatly (1).

Melioidosis develops after subcutaneous infection, inhalation, or ingestion of contaminated particles or aerosols. Infection has occurred after near-drowning accidents (1–3) and transmission of *B. pseudomallei* in drinking water (4). The route of *B. pseudomallei* infection is at least 1 of the factors that influences disease outcome, thus contributing to the broad spectrum of clinical signs associated with melioidosis. Researchers use different routes of delivery of *B. pseudomallei* in experimental models to study the pathogenesis of the disease and the induction of host protection. Infection by different routes exposes a pathogen to different components of the host immune system and may subsequently influence disease outcome. Despite this difference, no comprehensive investigation has compared the pathogenesis of melioidosis established by different routes of infection.

Following intravenous (IV) injection, BALB/c mice are highly susceptible, and C57BL/6 mice are relatively resistant to *B. pseudomallei* infection (5). Using this murine model, we compared the pathogenesis of *B. pseudomallei* infection after introducing the bacterium by IV, intraperitoneal (IP), intranasal, oral, and subcutaneous (SC) routes of infection. The virulence of 2 *B. pseudomallei* strains (NCTC 13178 and NCTC 13179) was compared in BALB/c and C57BL/6 mice by using a modified version of the Reed & Meunch (1938) method. Compared to BALB/c mice, C57BL/6 mice are less susceptible to *B. pseudomallei* infection, regardless of the portal of entry, thus validating the model of differential susceptibility for various routes of infection (Table). However, as demonstrated by others (5–7), C57BL/6 mice are not completely resistant to infection by *B. pseudomallei*. Systemic melioidosis can be generated in C57BL/6 mice by using different routes of infection, if a high dose is used. When injected IV into BALB/c mice, NCTC 13178 is highly virulent since the 50% lethal dose (LD_{50}) is <10 CFU. However, if BALB/c mice are injected SC with NCTC 13178, the LD_{50} value increases 100-fold to 1 x 10^3 CFU. This value is equivalent to the LD_{50} of the less virulent NCTC 13179 delivered SC The results emphasize that virulence depends on the route of infection.

The pathogenesis of *B. pseudomallei* NCTC 13178 infection was compared after infection by the IV, IP, SC, intranasal, and oral routes. BALB/c and C57BL/6 mice were administered 570 CFU (equivalent to 60 x LD_{50} delivered IV) or 3 x 10^5 CFU (equivalent to 60 x LD_{50} delivered IV), respectively. At 1, 2, and 3 days postinfection, bacterial loads were measured in blood, spleen, liver, lungs, lymph nodes (right and left axillary and inguinal), and brain by using methods described previously (5).

A tropism for spleen and liver was demonstrated following infection by