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Nasopharyngeal Detection of Severe Acute Respiratory Syndrome-Associated Coronavirus RNA in Health-Care Workers

The risk of developing severe acute respiratory syndrome (SARS) after exposure was conventionally determined by the prospective follow-up for symptomatic disease or the retrospective seroprevalence study of the exposed population. The average number of secondary cases resulting from a single case of SARS ranged from two to four.[1] Transmission mostly resulted from contacts with patients with overt disease rather than from asymptomatic or mildly symptomatic patients. Seroprevalence appeared to be low (0%, 0.43%, and 1.2%) for healthy individuals, and about 1% for health-care workers, approximately 1% for asymptomatic family contacts under quarantine, and 0.19% for asymptomatic contacts overall.[2–7] Systematic use of reverse transcriptase polymerase chain reaction (RT-PCR) in the early identification of patients with higher risk for developing SARS has not been reported. In this issue of *CHEST* (page 95), Ho et al[8] report on the nasopharyngeal shedding of SARS-coronavirus (CoV) RNA from 27 of 217 frontline health-care workers (12.4%) after encountering SARS patients for 1 week. Twenty five of those health-care workers were characterized by low mean (± SD) viral loads (312 ± 204 to 386 ± 203 copies per milliliter), a lack of or paucity of symptoms, and the absence of seroconversion during follow-up. This is in contrast to the two subsequently symptomatic health-care workers with significantly higher mean viral loads (16,900 ± 7,920 copies per milliliter) and subsequent seroconversion. The authors excluded contamination with PCR amplicon carryover by using 13 nonfrontline health-care workers as negative control subjects in addition to the usual PCR-negative control subjects. Since the word *colonization* is used to describe the establishment of a microbial agent in the host without inducing a specific immune response or invasion, as manifested by disease or distant dissemination, the authors concluded that SARS-CoV can "colonize" a significant proportion of exposed individuals, with disease manifestation occurring in only 2 of 27 initially colonized individuals (7.4%).

However, using the term *colonization* to describe this interesting phenomenon is premature, because the viral culture and virus-specific cell-mediated immune response of these colonized individuals were not performed as part of the workup. The amount of viral shedding is the end result of the interaction between a replication-competent virus in susceptible host cells at the nasopharynx and the innate immune system of the host defense. Populations of virus often contain particles that are not capable of completing an infectious cycle. Though a single virus particle can theoretically initiate an infection, many perfectly competent virions fail because of nonproductive interactions with the extracellular matrix at the cell surface. Even virions that have successfully entered the cell may be delivered to a wrong compartment, thereby resulting in an abortive infection. Thus, viral RNA can be detected by RT-PCR with no viable viruses isolated on a cell culture. Only a sufficient amount of viral replication occurs and results in cytolysis with the induction of host proinflammatory damage will lead to symptomatic disease and subsequent seroconversion.[9]

In these patients with more severe disease, a higher level of viral shedding is expected, and is manifested as a higher viral load on quantitative RT-PCR and even as a positive viral culture finding. Only 40.4% of those RT-PCR-positive respiratory secretions have a positive viral culture finding.[10] A lower amount of viral replication may result in low-level viral shedding with a negative cell culture and asymptomatic or mildly symptomatic infection with or without seroconversion.[11] It is important to remember that some commercial sex workers employed in areas that are highly endemic for HIV do not seroconvert despite repeated sexual exposure to HIV-1; they did, however, have local HIV-specific immune responses in the genital tract.[12] It would be interesting if we can determine whether these RT-PCR-positive health-care workers have similar local

or systemic cell-mediated immune responses to SARS-CoV. Before more conclusive studies are performed, these cases should preferably be regarded as abortive infections since cellular invasion must have occurred before viral shedding occurs.

The findings of this study have important implications for the protection of health-care workers who are looking after patients with highly contagious diseases such as SARS. Routine virologic surveillance by nucleic acid amplification tests may facilitate early quarantine and randomization to clinical trials for early preemptive therapy with hyperimmune globulin, topical or systemic interferon, or combinations of agents.[13–15] It is important to remember that total compliance with infection-control measures can never be achieved due to the intrinsic human nature of making errors from time to time. The successful treatment of these patients with early shedding may offer greater protection for health-care workers. Although Ho et al[8] cannot find any relationship between the ACE2 polymorphism and abortive infection or protection against symptomatic disease, other markers such as ACE1, HLA-B*4601, and HLA-B*0703 have all been associated with the severity of illness. More work should be performed to understand the continuum of exposure, infection, and disease manifestation in patients with SARS.

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