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EDITORIAL COMMENTARY

Optimizing and Unifying Infection Control Precautions for Respiratory Viral Infections

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The coronavirus disease 2019 (COVID-19) pandemic has focused an intense spotlight on respiratory precautions for healthcare workers managing patients with respiratory viral infections. Prevailing wisdom before the pandemic was that most respiratory viruses are transmitted by large respiratory droplets and fomites. These droplets were believed to have a carrying radius of 3–6 feet before rapidly falling to the ground by virtue of gravity. Surgical masks were presumed to provide adequate protection in most situations by providing a barrier between patients' emissions and the mucous membranes of providers' mouths and noses.

Notwithstanding this framework, the United States Centers for Disease Control and Prevention's (CDC) infection control guidelines include a hodgepodge of different personal protective equipment recommendations for different respiratory viruses [1]. These span the gamut from respirators, eye protection, gowns, and gloves to care for patients with emerging pathogens such as Middle East Respiratory Syndrome (MERS), avian influenza, and now, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); surgical masks alone to care for patients with influenza; gloves and gowns alone without masks or eye protection to care for patients with respiratory syncytial virus (RSV); and nothing at all to care for immunocompetent adults with parainfluenza.

This curious mix of recommendations appears to be the product of a handful of studies conducted predominantly in the 1980s and 1990s that evaluated the additive benefit of one or more of these precautions against one of these viruses, mostly RSV. None of the cited studies compared infection rates between viruses or provided evidence why one virus should be treated differently from another. Many of the source studies only reported on nosocomial infection rates in patients but did not consider infections in healthcare workers. And almost all the studies focused on pediatric populations. The suitability of these studies to support current infection control recommendations is dubious.

For example, 2 key studies are cited to support the use of gloves and gown alone without a mask or eye protection to care for patients with RSV. The first was a quality improvement initiative in a children's hospital designed to increase providers' compliance with gloves and gowns over the course of 3 RSV seasons from 1982 to 1985. The investigators reported that an increase in glove and gown use from 39% to 81% of audits was associated with a 3-fold decrease in nosocomial RSV infections [2]. The investigators did not assess whether adding masks and eye protection could further decrease infections and the study only evaluated infections in patients; infections among staff members were not assessed.

The second study was a prospective comparison of nosocomial RSV rates among children assigned to wards with different precaution sets over 3 RSV seasons [3]. Nosocomial RSV rates ranged from 26% of patients when using no precautions, 28% with gloves and gowns alone, 19% with cohort nursing alone, and 3% with gloves and gowns combined with cohort nursing. The fact that the only successful strategies included cohort nursing belies the importance of staff as vectors of infection, yet the study did not report on staff infection rates. This study also did not evaluate the marginal benefit of masks and eye protection. Instead, the investigators cited a study that reported that nose and eye protection was associated with striking decreases in both staff and patient infections [4] but explained that they decided not to include nose and eye protectors in their strategies because "they are not popular with clinical staff and are frightening to children" [3].

It is very difficult to reconcile the CDC's patchwork of legacy recommendations for different respiratory viruses with the wealth of data now demonstrating the primacy of the respiratory route in respiratory viral transmission [5, 6]. It has become evident that the majority

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of viral transmission is attributable to small aerosol inhalation rather than contact with fomites or large ballistic droplet inoculation of mucous membranes [7]. People routinely emit respiratory particles in a continuum of sizes, but most respiratory emissions are in the aerosol size range; these aerosols can carry the full range of seasonal and emerging respiratory viruses, and both animal and human studies confirm that virus-laden aerosols can efficiently transmit influenza, RSV, rhinovirus, coxsackievirus, SARS-CoV-2, and other viruses, particularly over short distances [8–12].

The studies that informed CDC's guidelines discounted aerosol-based transmission because of the protective effect of distance. Investigators assumed that because aerosols can travel well beyond 6 feet, the rarity of transmission beyond 6 feet ruled out aerosol-based transmission and proved instead the primacy of large droplets and fomites [13]. We now know, however, that distance is protective against both aerosol-borne and droplet-borne pathogens. This is because infection risk is a function of infectious dose; the more virus one is exposed to by virtue of concentration or duration, the greater the likelihood of infection [6, 14, 15]. Distance diminishes infection risk with aerosol-borne pathogens because aerosols diffuse with distance from the source and get diluted by the surrounding air, leading to progressively lower viral concentrations, particularly if the space is well ventilated. A parallel phenomenon explains why fomite-based transmission is comparatively rare: Each successive step in the transmission pathway from the source person to the exposed person decreases viral burden (eg, source individual's nose to hand, hand to door handle, door handle to exposed person's hand, exposed person's hand to mucous membranes) [16]. The fact that higher inocula of some viruses (eg, influenza) are required to cause infection via mucous membrane contact vs inhalation further diminishes the risk of fomite-based transmission [17].

The predominance of aerosol inhalation in the transmission of respiratory viruses bespeaks the necessity of effective respiratory protection for healthcare workers seeing patients with respiratory viral infections. A new study in this issue of *The Journal of Infectious Diseases* by Landry et al helps elucidate the relative effectiveness of surgical masks vs poorly fitting N95 respirators vs fitted N95 respirators and the extent to which room ventilation can mitigate the risk of mask failure [18].

Investigators from Australia's Monash University nebulized very high concentrations of a benign bacteriophage within a sealed room with no ventilation, and then measured live virus concentrations within the nostrils and on the skin of a single volunteer who spent 40 minutes in the room wearing a gown, gloves, face shield, and alternately a surgical mask, an N95 respirator that failed fit testing, and then an N95 respirator that passed fit testing. Each condition was repeated up to 5 times with and without a portable high-efficiency particulate air (HEPA) filtration unit in the room (providing 13 air changes per hour) and with the volunteer next to the aerosol generator vs distanced from the generator (0.85 m vs 2.7 m from the aerosol source). The investigators found that in the absence of HEPA filtration, virus counts within the nostrils were high with both a surgical mask and a poorly fitted N95 respirator but trended lower with an N95 that passed fit testing ($P = .06$). Once the HEPA filter was activated, nasal viral recovery remained high with surgical masks but was significantly lower and near zero with a fitted N95 respirator both near and far from the aerosol generator. Gloves and gowns were associated with significantly lower viral recovery from hands and forearms but not from the uncovered neck.

Key contributions from this study include documentation of the superiority of fitted N95 respirators over surgical masks, the importance of fit testing to minimize viral exposure to the respiratory tract, the synergistic benefits of good ventilation and N95 respirators, and documentation that gowns and gloves reduce viral contamination of the hands and forearms. Importantly, the investigators used viral culture to confirm that live virus, not just nonviable genetic material, reached the volunteer's nostrils. Limitations of the study, however, include the use of a proxy pathogen rather than common respiratory viruses, documentation of viral colonization of the nostrils rather than clinical infection, and the use of only one test subject. Notably, the finding that virus was isolated in the volunteers' nostrils despite wearing a fitted N95 respirator in the absence of a portable HEPA filter should not cause alarm, as the investigators nebulized supraphysiologic amounts of virus that far exceed the amount of virus typically exhaled by infected patients, and the study room was sealed to eliminate all ventilation whereas most clinical spaces in the U.S. are required to have at least 6 air changes per hour.

The investigators' demonstration that surgical masks provide substantially less protection against viral inoculation of the respiratory tract compared to fitted N95 respirators echoes the wealth of real-world studies that document failures of surgical masks worn by healthcare workers and/or patients to prevent transmission [19–21], as well as case-control studies that found respirators to be more protective than surgical masks [22–24]. An opposing signal comes from 2 trials that randomized healthcare workers to surgical masks vs N95 respirators when seeing patients with respiratory viral syndromes [25, 26]. Both studies found that influenza rates were high and similar between groups. In retrospect, however, we now recognize that the majority of healthcare worker infections are acquired in the community and the majority of SARS-CoV-2 and influenza infections are transmitted by asymptomatic and presymptomatic individuals [27–29]. Future studies comparing

N95 respirators vs surgical masks will ideally require providers to wear their assigned face covering during all patient interactions when community infection rates are high, regardless of patients' symptoms, and incorporate epidemiologic analyses or whole genome sequencing to exclude community-acquired infections.

In the interim, it is high time to modify infection control guidelines for respiratory viruses to recognize that that their transmission is more alike than different and that most transmission is attributable to aerosol inhalation. We recommend switching from the current confusing and non-evidence-based mosaic of different precautions for different viruses to one universal set of respiratory viral precautions that includes wearing gowns, gloves, eye protection, and fitted respirators in well-ventilated spaces.

Notes

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