COVID-19: BEYOND TOMORROW

VIEWPOINT

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What Is an Aerosol-Generating Procedure?

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has brought renewed urgency to the question of what constitutes an aerosolgenerating procedure. Public health agencies have long noted that certain medical procedures increase transmission risk for respiratory pathogens because they generate aerosols. In contrast with respiratory droplets, aerosols are minute respiratory particles that are small enough and light enough to remain suspended in the air for long periods of time, travel beyond 6 ft from the source patient, and penetrate or circumnavigate surgical masks. Therefore, health care workers are cautioned to wear N95 respirators during aerosolgenerating procedures in patients with possible SARS-CoV-2 infection, and if possible, to use airborne infection isolation rooms with 12 or more air changes per hour and negative air flow to minimize the amount of infectious aerosols in the room and to prevent their spread beyond the room.

However, in practice, there is no consensus on which procedures are aerosol generating. The World Health Organization stipulates that intubation, noninvasive positive pressure ventilation, tracheotomy, cardiopulmonary resuscitation, bronchoscopy, and sputum induction are definite aerosol-generating procedures because epidemiologic studies have associated these procedures with greater risk for health care worker infections.¹ By contrast, high-flow oxygen and nebulization are only designated as possible aerosolgenerating procedures because associations between these procedures and health care worker infections have been equivocal.

With the emergence of SARS-CoV-2, professional societies have unilaterally declared a plethora of additional procedures as aerosol generating, including nasogastric tube placement, thoracentesis, esophagogastroduodenoscopy, colonoscopy, cardiac catheterization, exercise tolerance tests, pulmonary function tests, percutaneous gastric tube placement, facial surgery, second stage of labor, and others. To our knowledge, most of these designations were made on theoretical grounds rather than formal quantifications of aerosol generation or epidemiologic studies demonstrating increased risk for infection. None of these procedures appear on the official lists of aerosol-generating procedures published by the World Health Organization or the US Centers for Disease Control and Prevention.^{2,3}

To add to the confusion, a recent study documented that controlled intubations and extubations in asymptomatic patients generate a negligible amount of aerosols and indeed a tiny fraction of the amount generated by volitional coughing.⁴ The same has been documented of bronchoscopy and noninvasive ventilation.⁵ How then do we explain the studies associating these procedures with increased risk for health care worker infections?

The answer lies in the evolving science of respiratory transmission. It has become clear that the traditional dichotomy between droplet vs aerosol-based transmission is overly simplistic. In practice, people routinely produce a profusion of respiratory particles in a range of sizes that include both droplets and aerosols as well as particles in between.⁶ Respiratory particles of all sizes can carry virus and all are potentially capable of transmitting infection. The amount of respiratory particles one emits varies by activity. Quiet breathing generates a small but steady flow of aerosols. Loud speaking, heavy breathing, and coughing produce far more. Larger respiratory particles will rapidly fall to the ground within a narrow radius of the source patient. Smaller respiratory particles can remain suspended in the air but will diffuse and get diluted by the surrounding air leading to progressively lower concentrations of virus the further one is from the source patient.

This translates into 4 factors that explain transmission risk during medical procedures. The first is forced air. Any time air is forced over moist respiratory mucosa, it will generate more virus-laden respiratory particles. This may explain the increased risk of infection associated with noninvasive positive pressure ventilation and cardiopulmonary resuscitation. However, by the same logic, coughing, spirometry, and heavy breathing should also be considered aerosol generating because these activities also increase the velocity and volume of air being forced over respiratory mucosa.

The second factor is symptoms and disease severity. Symptomatic patients are more likely to have active infection, more likely to have a large burden of virus, and more likely to be spreading virus into the surrounding air because they are coughing, sneezing, or breathing heavily. In one study, close contacts of symptomatic patients were 10 to 20 times more likely to get infected compared with close contacts of asymptomatic patients.⁷

The third factor is distance. Respiratory emissions are densest closest to their source. The further one gets from the source, the more time and space there is for respiratory emissions to diffuse and dilute in the surrounding air. This decreases the potential inoculum and lowers the probability of infection. This has been borne out by multiple case-control studies and helps explain why long-range SARS-CoV-2 transmission is rare in wellventilated spaces.^{8,9} By contrast, in poorly ventilated spaces, virus-laden aerosols can accumulate, leading to higher inocula and greater risk for infection even over greater distances from the source patient.

The fourth factor is duration. The more time one is exposed to virus-laden aerosols, the greater the probability of infection. This has been demonstrated in case-control studies of health care worker infections and epidemiologic studies of transmission rates in train travelers, and, in combination with proximity, helps to explain the very high rate of transmission in households.^{9,10}

Combining multiple factors increases risk. Sustained proximity to a highly symptomatic patient in the setting of forced air exposes one to large amounts of respiratory emissions and confers a high risk for infection. By contrast, limited exposure to an asymptomatic patient at a distance is associated with a very low risk of infection, all the more so if masks are worn by the source patient (to filter respiratory emissions) and health care worker (to decrease exposure). Good ventilation is likely a mitigating factor insofar as it can lower the concentration of virus-bound aerosols in enclosed spaces. However, ventilation alone is unlikely to provide adequate protection for clinicians who need to be very close to highly symptomatic patients because they will still be exposed to the full brunt of the patient's undiluted emissions.

These factors explain the intubation paradox, the fact that controlled intubations generate negligible amounts of aerosols (far less than volitional coughing), but intubation has repeatedly been associated with increased risk for health care worker infections.^{1,4} The answer is that intubating a patient with viral respiratory failure forces the operator to be very close to the respiratory tract of a highly symptomatic patient, often while also forcing gas over the respiratory mucosa for the purposes of preoxygenation or preintubation respiratory support. In other words, it is not intubation per se that generates aerosols and facilitates transmission but the circumstances surrounding the procedure, including patient factors (eg, severe illness, high viral loads, coughing, heavy breathing, superemissions) as well as forced air, profound proximity to the respiratory tract, and for some procedures, prolonged exposure. As such, the term *aerosolgenerating procedure* is a misnomer. It is not the procedure that increases risk but sustained proximity to the respiratory tract of a highly symptomatic patient.

Clarity regarding the factors that lead to increased transmission risk should allow hospitals and health care workers to make more logical choices about respiratory protection and negative airflow rooms. Surgical masks alone are likely adequate for controlled procedures in asymptomatic patients in settings with low SARS-CoV-2 prevalence. However, higher-level respiratory protection may be necessary for health care workers practicing in high-prevalence settings who need to be close to patients' respiratory tracts, present when large amounts of air are being forced across the respiratory mucosa (positive pressure ventilation, high-flow oxygen, coughing, heavy breathing, spirometry), or treating highly symptomatic patients even in the absence of traditionally defined aerosolgenerating procedures.

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REFERENCES

1. Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PLoS One*. 2012;7(4):e35797. doi:10.1371/journal.pone.0035797

2. World Health Organization. Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed. Published June 29, 2020. Accessed November 2,

2020. https://www.who.int/publications/i/item/ WHO-2019-nCoV-IPC-2020.4

3. Centers for Disease Control and Prevention. Which procedures are considered aerosol generating procedures in healthcare settings? Updated November 18, 2020. Accessed November 25, 2020. https://www.cdc.gov/coronavirus/2019ncov/hcp/faq.html

4. Brown J, Gregson FKA, Shrimpton A, et al. A quantitative evaluation of aerosol generation during tracheal intubation and extubation. *Anaesthesia*. 2020. doi:10.1111/anae.15292

5. O'Neil CA, Li J, Leavey A, et al; Centers for Disease Control and Prevention Epicenters Program. Characterization of aerosols generated during patient care activities. *Clin Infect Dis*. 2017; 65(8):1335-1341. doi:10.1093/cid/cix535

6. Morawska L, Johnson GR, Ristovski ZD, et al Size distribution and sites of origin of droplets expelled from the human respiratory tract during expiratory activities. *J Aerosol Sci*. 2009;40(3):256-259. doi:10.1016/j.jaerosci.2008.11.002 7. Luo L, Liu D, Liao X, et al. Contact settings and risk for transmission in 3410 close contacts of patients with COVID-19 in Guangzhou, China: a prospective cohort study. *Ann Intern Med.* 2020; 173(11):879-887. doi:10.7326/M20-2671

8. Doung-Ngern P, Suphanchaimat R, Panjangampatthana A, et al. Case-control study of use of personal protective measures and risk for SARS-CoV 2 infection, Thailand. *Emerg Infect Dis.* 2020;26(11):2607-2616. doi:10.3201/eid2611.203003

9. Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schünemann HJ; COVID-19 Systematic Urgent Review Group Effort (SURGE) study authors. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *Lancet.* 2020;395(10242):1973-1987. doi:10.1016/S0140-6736(20)31142-9

10. Hu M, Lin H, Wang J, et al. The risk of COVID-19 transmission in train passengers: an epidemiological and modelling study. *Clin Infect Dis*. 2020;ciaa1057. doi:10.1093/cid/ciaa1057