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Bronchoscopy in the Age of COVID-19

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The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to 95,333 confirmed cases as of March 5, 2020.[1] In this issue of the Journal, the American Association for Bronchology and Interventional Pulmonology (AABIP) has provided an initial statement on the use of bronchoscopy and respiratory specimen collection in patients with suspected or confirmed COVID-19 infection.[13] This statement has received expedited peer review by the Journal in an effort to disseminate high quality information in a clinically useful timeframe that ultimately will help patients. At this point in time much remains unknown, and evidence-based guidance regarding bronchoscopy precautions and SARS-CoV-2 infection will require updating as new information becomes available. But as William Osler reflected, "Medicine is a science of uncertainty and an art of probability." So even though there is much that is still uncertain, we need to act prudently in a timely manner rather than waiting for perfect information. The AABIP statement is an initial step in this process and it will be updated accordingly at the website of the AABIP (https://aabronchology.org/). Subsequent updates will also be reviewed and published in the Journal with free access to all in an expedited manner.

The AABIP statement highlights the fact that while interventional pulmonology is a procedurally oriented discipline, it remains important for physicians to be cognizant of epidemiological concepts and the context within which procedures are performed. Bronchoscopy is a tremendous tool for diagnosis and treatment of a variety of conditions, but it can also transmit disease if appropriate precautions are not followed. In the cases of SARS-CoV-2, there are risks to both patients and healthcare providers. The AABIP statement appropriately highlights this and emphasizes that bronchoscopy is not an appropriate tool for diagnosis of SARS-CoV-2 infection – the benefits are far outweighed by the risks.

There are also more nuanced aspects to the epidemiology that should impact how we think about bronchoscopy in the age of COVID-19. One way to characterize infectious epidemics is to calculate the basic reproduction number, also called the basic reproductive ratio (R_0). R_0 is not a rate, but rather a ratio. It is the ratio of the expected number of cases directly generated by a case in a population in which all members are susceptible to the infection.[2] Note that this definition makes certain assumptions – specifically that all members of the population are susceptible so R_0 technically is not changed by interventions such as vaccination. This number attempts to quantify the potential for transmissibility of an infectious agent. While R_0 is a valid biological metric, the value itself is usually estimated with

mathematical models that are in turn based on key assumptions, so interpretation of its value is complex and estimated values for the same pathogen can vary widely depending on the models used.[3] While R_0 is conceptually useful, the more relevant number is the effective reproduction ratio (R) which is different. This is the number of cases generated in the current population at a moment in time, but it does not assume complete susceptibility in the population. The effective reproduction ratio can change with vaccination. Both R_0 and R are not solely determined by the pathogen, although the pathogen of course has a large impact. Other factors such as population density, behavior patterns, and interventions can change R. For most situations, when $R > 1$ the infection will be able to spread within a population while if $R < 1$ it will not be able to spread. Estimates of the median daily reproduction number in Wuhan declined from 2.35 before travel restrictions to 1.05 after travel restrictions.[1] Other investigators have estimated R to be 2.2 (95% CI 1.4 to 3.9).[1,4] Over time R will hopefully decrease as interventions take effect. In the prior SARS pandemic of 2003, R was estimated initially at 2.75 but with interventions R dropped below 1 rapidly.

However, the previous SARS epidemic also demonstrates another important point, namely that even when R was lower than 1, super-spreader events occurred and the epidemic continued. In Toronto, most early SARS cases occurred in hospitals, with movement of SARS patients between hospitals contributing to the outbreak.[5,6] In Taiwan, Hong Kong, and Singapore, transmission often occurred through transmission in hospital wards. While the typical infected patient transmitted to < 1 other patient, occasional outliers transmitted to multiple individuals (threshold value defining a super-spreader was 8 in SARS).[7]

How can we apply the epidemiology and the lessons from the SARS epidemic to bronchoscopy? Screening based on symptoms, even in a best case scenario, is not sensitive. If a routine bronchoscopy patient (e.g. for a lung nodule) is infected but asymptomatic and therefore remains undetected, then healthcare providers will be unprotected. Now this is true in many areas of healthcare delivery, not just the bronchoscopy laboratory. But unlike other areas of healthcare, the act of bronchoscopy is likely to increase the probability of transmission to bronchoscopy personnel due to respiratory droplets. Those same bronchoscopy personnel provide care to other particularly vulnerable patients every day, setting up a super-spreader situation since infected individuals have close contact with a particularly vulnerable population with frequent comorbidities, including cancer and immunosuppression.[8,9] In addition data is still scant on whether SARS-CoV-2 can

survive outside the body for long. The coronavirus that caused Middle East respiratory syndrome demonstrated the ability to survive outside the body for up to 60 minutes. A report of a cluster of 19 cases in a shopping mall suggests that the virus might have spread via indirect transmission, but the evidence is not definitive at this time.[10]

One possible step to at least partially address this risk is to test all patients prior to undergoing *any type* of bronchoscopy and/or increase the level of healthcare provider protection in the bronchoscopy area. This of course is only possible once testing becomes more widely available such that all other higher priority patients can be tested. Another intervention is to consider delaying elective cases when possible. The available data suggests that for diagnosis and staging of cancer a brief delay could be implemented without much adverse impact.[11] In the absence of widely available testing, one option would be to implement a two week delay combined with self-quarantine for elective cancer diagnosis and staging cases. Patients who remain asymptomatic would have their elective bronchoscopy. After a brief 2 week down time, the daily flow of elective cancer cases would return to more normal levels so that delays in cancer care would not be excessive while balancing the need for containment of the pandemic. Which interventions to implement and when to implement them will be context dependent, depending in large part on the prevalence of disease in each locale and the available resources, so individualization to each particular hospital's context is important.

Current testing paradigms are based on the probability of identifying a true positive patient, which is a very reasonable strategy especially given limited resources. But good decisions are based on an assessment of probabilities *and* consequences. A rare event with disastrous consequences warrants a different decision threshold.[12] Super-spreader events provide insight into the probabilities and consequences in this context. Transmission of SARS-CoV-2 in the healthcare environment is always a concern because of the vulnerable population we serve. But the risk of transmission to staff is even higher in the bronchoscopy area and the consequences would be worse than in other healthcare settings. It is a weak link in our defense system, and we should tend to it.

The current AABIP statement on the use of bronchoscopy and respiratory specimen collection in patients with suspected or confirmed SARS-CoV-2 infection is timely and can help synthesize current expert-based recommendations. It will have to be a living document that will evolve as our knowledge evolves.

However, the COVID-19 epidemic impacts not just bronchoscopy in patients with suspected or confirmed SARS-CoV-2 infection, it should impact how we think about bronchoscopies for other indications even in patients where we have no suspicion of the disease. This will require additional data collection and analysis as well as timely and prudent decision making that incorporates not only probabilities but consequences as well. Bronchoscopy in the age of COVID-19 needs to change, but the underlying concepts of epidemiology and decision theory can still serve us well as we work together to address these problems.

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