Interviews

In these interviews, Donald B. Middleton discusses the important questions in respiratory research, how to design vaccination strategies, and building sustainable global respiratory surveillance systems in the face of future outbreaks. Tina Q. Tan shares her hopes for the future of pediatric respiratory care.

Featuring: Donald B. Middleton and Tina Q. Tan

Donald B. Middleton

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Q1 You have spent decades working in both family medicine and influenza vaccine research. How has working directly with patients influenced the kinds of respiratory research questions you believe are most important to investigate?

Prevention of disease in patients of all ages is clearly the motivator for all primary care clinicians. Luckily, over time, we have had more tools that are available to achieve this goal. Illnesses with high morbidity and mortality, like influenza, are frightening. Proven, effective vaccines like Tdap (tetanus, diphtheria, and pertussis) are basic parts of my armamentarium. Every year, I embrace vaccines that are fine-tuned to whatever particular virus variants are likely to circulate. Over the years, I have seen remarkably enhanced influenza vaccine development with much improved vaccine effectiveness (VE), but more is needed. Every winter, I would treat many babies with rotavirus infection who were dehydrated, vomiting, and having severe diarrhea, but now I see almost none. We also need new vaccines to produce long-lasting protection against agents like pertussis and respiratory syncytial virus (RSV). On the downside, lately, convincing individuals to be vaccinated has become more difficult. Research that helps answer how to persuade individuals that vaccination is safe and effective for them, their families, and society is paramount.

> **Prevention of disease in patients of all ages is clearly the motivator for all primary care clinicians**

Q2 Throughout your career, respiratory viruses have evolved from being viewed as largely seasonal challenges to major drivers of healthcare system pressure and public policy. How have you personally seen the clinical and societal perception of respiratory disease change over time?

The failure of our public leaders to commit to appropriate vaccination for everyone is deplorable and has led many individuals and parents to reject vaccination. Individuals seem to think that they are immune to infection, or that infection will be mild, or that treatment will be

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available, so there is no need to vaccinate. These opinions are sadly wrong. The commitment to the protection of society through vaccination of everyone against communicable diseases seems to have lost part of its punch. But not for me.

Q3 Recent US studies have explored waning influenza vaccine protection across a single respiratory season, particularly among older adults and high-risk groups. What practical lessons should clinicians and policymakers take from this research when designing vaccination strategies?

The 2020 reference provided is from Jill Ferdinands et al.[1] She is a remarkable researcher with whom I and others were able to work to produce a VE study in 2021. In that study,[2] we showed that the rate of VE waning was actually worse in adults aged 65 years and over; a decline of approximately 10% every 30 days post-vaccination. At that rate, influenza VE, which typically begins at around 50–60%, could decline by more than half by season's end. We did not know what percentage of the study participants received an enhanced influenza vaccine, which might reduce this dangerous VE drop. Most of the time, influenza starts in November. So, to provide better protection throughout the influenza season, given the 1–2-week delay in effectiveness post-vaccination, I like to vaccinate my older patients (including myself) in early-to-mid-October. The clinician must be committed to making certain that older patients do not fall through the cracks to end up being unvaccinated. A good motto is "If you are older, wait until it's colder."

Q4 Recent respiratory research[3] in the US has also focused on co-circulation of influenza, RSV, and SARS-CoV-2, and the challenge this creates for diagnosis, triage, and healthcare capacity planning. Which findings from these studies do you think will have the greatest long-term impact on respiratory care systems?

Co-circulation of respiratory viruses and bacterial pathogens like pertussis is not a new issue. The new issue is that with the advent of clinically useful diagnostic tests, multiple other viruses besides influenza have been recognized to cause significant diseases, including death, across all ages. An emphasis on co-circulation of respiratory viruses came with the arrival of SARS-CoV-2; its death rate eclipsed the death rate from influenza. The thought that these two potentially deadly agents would cocirculate was alarming. Every year, multiple viruses, some seasonal (RSV) and some not (SARS-CoV-2), including others like human metapneumovirus, which also infects all ages, co-circulate. Many of these agents tend to cause prolonged coughing, lasting several weeks. The cough from bacterium *Bordetella pertussis* tends to get lost in the thought that only viruses can create this problem. Although recently, the influenza B/Yamagata has disappeared from circulation, I do not see the spontaneous disappearance of most of the other agents which constantly evolve. All health systems should maintain some method of diagnostic detection to provide focused treatment whenever possible.

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Q5 Many countries are now rethinking respiratory surveillance after COVID-19. Based on your experience with influenza monitoring programs, what elements are essential for building sustainable global respiratory surveillance systems that can respond to future outbreaks?

Hopefully, many countries have bolstered their detection and reporting systems. Local education about how to detect and report a disease is helpful, including home tests for influenza and SARS-CoV-2. Patients and clinicians must suspect particular agents, like influenza, and take steps to diagnose properly. Most laboratories report to a central agency like a health department, which then reports to a national infection control agency like the CDC. Both health departments and national bodies must then distribute warnings about circulating agents. The WHO remains critically important to provide warnings and control measures.

Q6 Vaccine confidence has become an increasingly important global health issue in respiratory medicine. How can healthcare professionals better communicate uncertainty, effectiveness, and risk in ways that improve public engagement without oversimplifying the science?

References to supportive websites like Immunize.org or the American Academy of Pediatrics (AAP), discussing disease consequences, and explaining the length of time vaccines are studied for safety and effectiveness can all help. I simply tell a hesitant patient that I vaccinate myself and my family, that I like them, and that they need vaccination too.

Q7 Emerging technologies such as universal influenza vaccines, mRNA-based respiratory vaccines, and AI-assisted outbreak prediction are rapidly changing the field. Which of these developments do you believe has the greatest potential to transform respiratory medicine over the next decade?

I do not endorse any single approach. New technologies and new combinations are coming for many vaccines, like the pneumococcal vaccine and Lyme disease. However, mRNA vaccines have great potential to be widely effective. Influenza and SARS-CoV-2 protection can be combined in one injection, and others could be added down the line. The mRNA Lyme vaccine is under investigation. Many hope for better mRNA cancer vaccines. So, I think that is where I would put my money. AI may help to truncate outbreaks, but patients and clinicians first need to explore AI recommendations and second need to have reassurance against errors in advice. AI must also be informed: false anti-vaccine information must not be repeated.

Q8 Finally, if you were advising the next generation of clinicians and researchers entering respiratory and infectious disease medicine today, what unanswered questions or underexplored areas do you believe deserve far more attention in the years ahead?

The public's trust in the science of vaccination needs to be restored. A growing number of hesitant medical practitioners need to reaffirm their faith in vaccination. How to accomplish these tasks is the major issue facing us now. For clinicians, vaccine fatigue must be rejected. More improvements of current vaccines should be embraced. Vaccines to stop other diseases like human metapneumovirus should be embraced.

> **"Co-circulation of respiratory viruses and bacterial pathogens like pertussis is not a new issue"**

References

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