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RSV, COVID-19, and Influenza A: Are We on the Verge of Viral Armageddon?

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I dedicate this column to the late Dr. Andrew (Andy) Shennan, the founder of the perinatal program at Women's College Hospital (now at Sunnybrook Health Sciences Centre). To my teacher, my mentor and the man I owe my career as it is to, thank you. You have earned your place where there are no hospitals and no NICUs, where all the babies do is laugh and giggle and sleep.

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At first, it seemed that the NICU (and PICU) would be spared the carnage our adult ICU colleagues witnessed, and indeed, this has been the case. Until now.

With each pandemic wave, we learned more about this virus, and it would seem that C-19 learned much more about us. If actions speak louder than words (or science!), an outside observer might conclude that C-19 has learned a lot more about us than we have about it. That public health messaging has been inconsistent, politically influenced, and sometimes downright wrong has not been helpful; this has been magnified by a myriad of influential mouthpieces spewing what can only be described as scientific garbage. Worse, some of these mouthpieces are scientists and physicians.

It was not long before our obstetrical colleagues identified pregnant women as at risk for severe C-19 disease (1), but it did not appear that the fetus was in danger. This assurance was short-lived, and evidence now suggests that conclusion was wrong. C-19 can severely damage the placenta (2) and has resulted in an increase in stillbirths (and other maternal complications) following C-19 infection during pregnancy (3). How and if the maternal infection affects the newborn is less clear, but the evidence is not painting a pretty picture.

Adverse neurological outcomes at up to 1.5 years of age have been found in children born to C-19-infected mothers, although the mechanism is unclear (4). This is in contrast to previous studies indicating that adverse neurological outcomes were rare and may reflect C-19's evolving from primarily pulmonary involvement to vascular epithelial disease.

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Recently a C-19-infected mother delivered a baby at the institution where I practice. The baby was admitted to NICU for "distress." An echocardiogram revealed two coronary arteries completely clotted with accompanying myocardial dysfunction. Myocardial damage was irreparable, and the baby died. This is an extremely rare occurrence and cannot, in this case, be blamed on C-19 with any certainty. Given the effects of C-19 on the vascular epithelium and that it is known to alter cardiac DNA (5), the question of C-19's involvement, in this case, is valid in this author's opinion.

Each C-19 mutation seems to bring something new to the virus's formidable arsenal, and recent mutations seem to produce more severe diseases in children. Children's hospitals across North America are bursting at the seams, and in Ontario, adult ICUs are being prepared to accept paediatric patients as young as 14. The waitlists in children's hospital emergency rooms may be well over 12 hours, and NICUs are admitting month-old babies because there are no available PICU beds. Patients in PICU are, for the most part, not there due to C-19. Or are they?

This brings us to RSV. In addition to the RSV season starting early, RSV-infected children are being admitted to hospitals in record numbers. The reason why may lead right back to C-19.

We know that some viruses, measles, for instance, are immune-suppressive (6). Like HIV, C-19 is both immune-suppressive and immune-evasive (7,8). This has some researchers describing C-19 as "airborne HIV." While the mechanisms of transmission and immune suppression/evasion are different, the result is the same: increased susceptibility to other pathogens and a decreased ability to fight them. Even though newer C-19 variants do not typically involve severe pulmonary infection, the virus does damage the lungs, even in mild cases (not requiring hospitalisation) (9), back to RSV.

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Children who have recovered from C-19 infection are both more susceptible to infection with a reduced ability to fight them and may also have lung damage that exacerbates any pulmonary infection. Logically, this leads to more children becoming infected with RSV and more children with severe disease requiring hospitalisation. Indeed, the RSV hospitalisation rate is much higher this season than is typical, and many more are requiring PICU care (10). Unfortunately, PCR testing for C-19 is ramping down in many jurisdictions and is at the discretion of the attending clinician. Therefore, empirical evidence of prevous C-19 infection in RSV patients is lacking but begs further investigation to support this premise.

As if C-19 and an early and severe RSV season were not bad enough, flu season is also early this year and is predicted to be severe (11). Currently, RSV/C-19 coinfection seems to be low and did not result in severe disease (10), but as the season ramps up, this may change. The small number of C-19/RSV coinfections in the aforementioned study may be reassuring, but C-19's uncanny ability to change the game should temper that reassurance.

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We in the NICU do not typically think about Influenza A (IA), but its prevalence may be underestimated. Since there is no approved flu vaccine for those under six months of age, these children are at much greater risk of severe IA disease, and the best treatment for these children is prevention. A flu shot during pregnancy bestows a significant advantage on the newborn infant. While in the NICU, most infants are reasonably protected if within an incubator or while on respiratory support.

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This season's triple viral threat threatens to cripple healthcare systems already on the brink of collapse. A recently published study examining RSV/IA coinfection found that a hybrid composed of both viruses was formed even though RSV and IA are completely different. This hybrid showed immune-evasive capability and raised the possibility of the emergence of a new respiratory pathogen. It is not known how the hybrid virus behaves in the presence of RSV prophylaxis.

This is particularly concerning. IA is an upper to middle respiratory tract infection, whereas RSV travels more deeply into the lungs. A hybrid virus may be able to bring influenza deep into the lungs resulting in viral pneumonia. A pathology C-19 has shown to be very difficult to treat (12). Since no RSV vaccine is currently available, this also raises the question of whether or not a hybrid virus could reduce the effectiveness of existing flu vaccines. C-19 has aptly demonstrated that more hosts infected means more mutations, particularly within immune-compromised patients who harbour active viruses longer than those with fully functioning immune systems (13). A combined severe RSV and flu season would allow both viruses to replicate in real life what has been seen in the lab. Let us hope not.

To date, the NICU has been spared the brunt of C-19's arsenal, and although variants seem to be targeting younger people, that may remain the case. We are more likely to face the sequelae of gestational infection in newborns. And RSV.

As this is ostensibly a respiratory column, I would be remiss if I were not to suggest that high-frequency jet ventilation is ideal for treating RSV patients requiring mechanical ventilation. A low jet rate is most helpful in clearing secretions.

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