COVID 2023 – The More We Know, the Less We Know: A year in review

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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.

As we come to the end of the fourth year of the pandemic that never ends (yes, we're still in it), it gives me no pleasure to be writing my fourth column on COVID-19 (C19). My displeasure notwithstanding, the body of knowledge and plethora of studies and papers on the subject continue to grow. Denial is not science, and wishful thinking is neither treatment nor cure.

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Early in the pandemic, neonatology and pediatrics took some comfort in the (mistaken) belief that this virus posed little or no danger to infants or children. From all appearances, it seemed that children's hospitals would be spared the chaos overwhelming the adult healthcare system and our colleagues who work within it. This was indeed true (at least for a while). Children did not suffer the same life-threatening symptoms as adults, many showing no symptoms at all. Most public health officials went so far as to proclaim that children posed no risk to adults because they did not spread the virus. This (again mistaken) belief persisted until the evidence to the contrary could not be ignored. The consequences of this overconfidence were disastrous.

The Chief Medical Officer of Health (CMOH) for British Columbia, Canada, was one of those insisting children posed no risk and that they were not responsible for driving the rapidly increasing numbers infected. This faulty assumption led to the reopening of schools for in-person learning. The public were told this would not significantly impact the number of infections amongst the general public. To validate this assumption, the CMOH et al. studied "waste blood" (blood remaining after routine laboratory tests are completed). Samples were tested for C19 prior to school opening and continued after the fact. The results revealed that the C19 positivity of waste blood samples skyrocketed shortly after schools reopened. In what can only be described as an egregiously unethical move, the message given to the public at large did not change despite the study's findings (1). Regarding children and C19, this was only the beginning of a cascade of research demonstrating how wrong these assumptions were. Not only can children transmit C19, but they are also not immune to sequelae stemming from C19 infection.

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Recently, a study of autopsies was conducted on 23 people who had died suddenly and unexpectedly. The cohort included four children aged 2, 3, 14 months, and 7 years respectively. The deaths of the 2- and 3-month-old infants were initially thought to be due to sudden infant death syndrome (SIDS). The mother of the 7-year-old child had C19, but her child showed no symptoms of C19 infection and also tested negative on a rapid antigen test (RAT). Her daughter's death occurred approximately 30 days after her mother's initial C19 diagnosis. In all cases, PCR testing showed the presence of C19, although 9 of the deceased had no C19 in the nasopharynx. The greater the concentration of C19 virus in the lungs, the less was present in the nasopharynx. All subjects had either no symptoms of C19 infection or very mild ones. Despite this, it is thought the disease entered a latent phase that led to death (2). Because C19 was (is) thought to be of little consequence to children under 12, testing them for C19 was often not done. Clearly, this is not the case.

"At first, it was thought that C19 did not cross the placenta, but this has also been found to be untrue, albeit rare. Not only has the virus been detected in fetuses, but it is also associated with cerebral bleeds."

C19 poses risks during pregnancy as well. Infection during the first and second trimesters (but not the third trimester) increases the risk of stillbirth (3). One investigation found an increase from 2.3 per 100k in non-infected women to 5.8 per 100k for those having been C19 infected. The risk also changed with the C19 variant, with Delta presenting the highest risk and others less so. No data is available for the most recent variants (4). Other research has found an increased risk of preeclampsia and preterm birth in those infected, although the risk of preterm birth appears only to be if infection occurs after 34 weeks PMA (5).

At first, it was thought that C19 did not cross the placenta, but this has also been found to be untrue, albeit rare. Not only has the virus been detected in fetuses, but it is also associated with cerebral bleeds. These findings were from aborted fetuses; thus, it is not clear whether or not they were deleterious. Nevertheless, there are reports of brain damage in babies born to C19-infected mothers, and the virus has been found in the children's brains (5). These are rare findings, but it has been previously reported in this column that some infants born of C19-infected mothers failed to meet developmental milestones between 6 and 8 months of age compared to none in the non-infected comparators (5).

"The severity of last year's RSV season (with 2023 at least initially promising a similar one) certainly gives credence to the possibility of long-term immune system damage."

Once thought to be a primarily respiratory infection, it is now well known that C19 attacks vasculature. As the virus continues to mutate into more and more variants, it appears to target the lungs far less and favour other (all) organs. The speed at which mutations occur makes the prospect of herd or natural immunity impossible. Research on C19 and the risk of repeat infection is all over the map. Some report a decreased risk, while others say each infection increases the risk of repeat infections and secondary infections with once-rare pathogens. The severity of last year's RSV season (with 2023 at least initially promising a similar one) certainly gives credence to the possibility of long-term immune system damage. The damage it does to the immune system (6) is eerily similar to HIV, so much so have some refer to C19 as "airborne HIV." (Many researchers categorically deny this, although it is too early to determine how valid this comparison is in the author's opinion.)

"There are also reports of latent tuberculosis (TB) becoming active, raising the possibility of increased transmission of TB. TB-C19 coinfection may also increase the likelihood of severe disease, although there is insufficient data to confirm this."

The latest "gift that keeps on giving" is discovering viral reactivation post-C19 infection. Epstein Barr and varicella are most notable, but there are also reports of cytomegalovirus, hepatitis B, and other viral reactivations (7), some of which can adversely affect the fetus. (Anecdotally, one physician I correspond with says he has seen more shingles in the past year than in 30 years of practice.). There are also reports of latent tuberculosis (TB) becoming active, raising the possibility of increased transmission of TB. TB-C19 coinfection may also increase the likelihood of severe disease (8), although there is insufficient data to confirm this (9). TB-related deaths have increased since the pandemic, but the mechanism driving the increase is multifactorial (9).

The fact that C19 and TB present with very similar symptoms may lead to missed diagnosis and, thus, delayed treatment. Delaying TB treatment is known to increase the risk of death from the disease (8).

In pregnancy, TB increases the risk of obstetrical complications, premature birth, birth defects, and perinatal mortality. Placental transmission is relatively rare (10), but if the prevalence of TB increases, we are likely to see more cases.

"Even so, 2019-2021 meta-analyses of C19 and perinatal outcomes revealed an increase in maternal death, preeclampsia, fetal distress, caesarian delivery, low 5th minute APGAR, preterm birth, low birthweight, stillbirth, and NICU admission compared to non-infected mothers."

As the bulk of this column does not directly relate to neonatal and pediatric practice, one may ask how it is relevant to them. Research on C19 related to pregnancy, infants, and children is sparse relative to the adult population, but it is growing. For the most part, in the acute phase, life-threatening C19 infection is rare in the pediatric population. Since C19 was initially believed to pose little or no threat to children and infants, the research did not focus on this cohort. Even so, 2019-2021 meta-analyses of C19 and perinatal outcomes revealed an increase in maternal death, preeclampsia, fetal distress, caesarian delivery, low 5th minute APGAR, preterm birth, low birthweight, stillbirth, and NICU admission compared to non-infected mothers (11).

A tangential effect of C19 has been increased pediatric admissions for respiratory illness. This is compounded by C19 illness and long-C19 among hospital staff, exacerbating a severe staffing shortage. Supply chains continue to be disrupted, with many items used in the NICU being substituted or on backorder.

For those on "X," I recommend following AJ Leonardi, MBBS, Ph.D. (@fitterhappierAJ) for all the latest C19. While a magnet for controversy, he has been bang-on in his assessments from day one. While C19 research has been and continues to be prolific, so much of the information available is contradictory that reaching any conclusion with a high degree of certainty is challenging.

This book is still being written, and it promises to be long. C19 has opened an epidemiologic Pandora's box. One thing is for sure: C19 is far from done with humankind.

Be well everyone, Happy Holidays, and wishes for a wonderful new year for all. (C19 notwithstanding!)

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