Children and SARS-CoV-2/COVID-19 science and commentary from the AAMC

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Dear colleagues, we are all part of a division that puts science to work. We are all either directly working in STEM or work and learn with people who are. Throughout the pandemic I have recommended that everyone go to the primary sources of data, rather than try to derive information from secondary or tertiary sources, or worse.

Many of you have school-age children, or younger, and have valid concerns for their safety from SARS-CoV-2 and the possibility that they may spread the virus to higher risk people in your household. I found the commentary below from the Association of American Medical Colleges (AAMC) very useful, along with the link to the science it describes. For those with PhDs and MS degrees in the relevant fields, the paper is straight forward and clear; for those who do not, it will be challenging to incomprehensible. But the commentary I have bolded covers the important, and (to me) comforting, concepts you may like to be aware of.

Regards,
Shane

It has been established that children and infants have reduced SARS-CoV-2 infection rates when compared with adults. Moreover, research has shown that children are at a substantially lower risk for developing COVID-19 compared with adults. What is happening on the cellular level and the molecular level that accounts for this difference? On Aug. 18, researchers published a manuscript in *Nature Biotechnology* that shed some light on why **younger age groups have relatively superior protection from SARS-CoV-2 infection**. For this study, investigators characterized the "single-cell transcriptional landscape" in the upper airways of SARS-CoV-2 negative and positive children and adults, spanning an age range of 4 weeks to 77 years old. **Investigators chose the upper airway (nose) as a location to examine because this region has been shown to have high susceptibility for SARS-CoV-2 infection.** For the study design, the authors chose to focus on early infections, so only mild and/or moderate COVID-19 cases were considered for the study. **What did the investigators find?** When using single-cell RNA sequencing data to compare the cellular composition in the upper respiratory tract of children and adults, the authors found "striking" differences between pediatric and adult study participants — including the number and type of cells found in each cohort. **"While immune cells were rarely detected in nasal samples from healthy adults, samples from SARS-CoV-2-negative children contained high amounts of almost each immune cell subset, with an overall dominance of neutrophils**," the authors noted. Secondly, the cellular and molecular events after SARS-CoV-2 infection differed between the two cohorts. **In adults, "SARS-CoV-2 infection was associated with immune cell influx, while the proportion of immune and epithelial cells remained nearly stable in children."** Notably, **children had significantly higher basal expression of genes encoding proteins that promote response to viral infections and viral sensing.** [Editor's comment: This study used a dataset of over 265,000 cells to map out the differences in gene expression and

cell composition in SARS-CoV-2 negative and positive children vs. adults. **The data convincingly show that, compared to adults, the epithelial and immune cells of the upper airways of children are so-called "pre-activated and primed for virus sensing."** The authors believe that this is likely **a general feature of children's mucosal immune response and accounts for the relatively low rates of SARS-CoV-2 infection in children.** As for a nascent pathway, the authors hypothesize that "primed virus sensing and a pre-activated innate immune response" in children leads to efficient early production of interferon — a family of proteins involved in alerting the cellular immune system to viral infection of host cells — in the infected airways. This in turn might cause a reduction in virus replication and faster clearance of SARS-CoV-2. The authors propose that their data may provide a mechanism that **explains "why children are better able to control early-stage infection as compared to adults and therefore have a lower risk of developing severe COVID-19." As vaccines are still not authorized for children younger than 12, this data is encouraging, to say the least.**

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