

## Why children aren't sick with COVID

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*A study reports that the immune cells present in the nasal mucosa of children are already activated and can therefore neutralize the coronavirus very quickly and drastically reduce its infectious potential.*

The risk gap is simply huge: for example, a study found that the death rate from infection reached 8.3% in those 80 and over, this rate was only 0.001% in 5-9 years-old children, a difference of 10,000 times (1).

This increased resistance is not due to the absence of infection, but rather to a very rapid neutralization of the virus which leads to its elimination.

For example, one study found that children who lived under the same roof as their infected parents had an immune response similar to that of their parents (specific antibodies to the coronavirus), yet were negative when tested for the presence of the virus by PCR (2).

### ONLY EXPLANATION

The only possible explanation is that the virus can indeed be transmitted to children, but children usually clear it very quickly and do not develop major symptoms of the disease.

A recent study suggests that this rapid neutralization of the coronavirus by children is mediated by the innate immune system present in the nasal mucosa, the main gateway for the virus (3).

Using the technique of single cell RNA sequencing, which makes it possible to draw up an exhaustive inventory of genes that are active in a specific type of cell, the researchers compared the expression of these genes in cells taken from the noses of children and adults whether or not infected with the coronavirus.

This approach has shown enormous differences in the immune composition of the nasal mucosa between children and adults. While immune cells are absent in the mucous membrane of uninfected adults, the noses of children contain large amounts of all of the immune cells responsible for the innate response, especially neutrophils. In other words, even without having been exposed to the virus, the nasal mucosa of children is ready to face foreign agents.

One of the consequences of this immune mobilization is that the nasal mucosa of children can quickly produce several antiviral proteins, in particular interferons. These molecules appear to be extremely important in neutralizing the coronavirus, as a high



proportion of severe cases of COVID-19 is directly linked to the presence of genetic defects that compromise this response (4).

The immediate production of interferons, made possible by the presence of a pre-activated immunity in the nasal mucosa of children, could therefore explain why young people are better able to control the infection from the start and, by extension, have less risk of developing complications of the disease.

### DELTA VARIANT

At present, there is no indication that this pre-activated immune response is less effective against the delta variant, the main form of the coronavirus currently in circulation. This variant is much more contagious than the original strain, but data collected in the United Kingdom (where this variant has been circulating for several months) does not seem to show an increase in the mortality rate associated with this variant, including in children. More children are currently hospitalized in the United States, but the increase appears to be due to a significant increase in the number of infections (due to the low vaccination rate), and not to the greater danger of the virus for children.

With a few rare exceptions, adults remain the preferred targets of the virus and most at risk of being severely affected by the disease.

- (1) O'Driscoll M et al. Age-specific mortality and immunity patterns of SARS-CoV-2. *Nature* 2021 ; 590 : 140-145.
- (2) Tosif S et al. Immune responses to SARS-CoV-2 in three children of parents with symptomatic COVID-19. *Nat Comm.* 2020 ; 11 : 5703.
- (3) Loske L et al. Pre-activated antiviral innate immunity in the upper airways controls early SARS-CoV-2 infection in children. *Nature Biotech.* (Published online, August 18<sup>th</sup> 2021)
- (4) Zhang Q et al. Inborn errors of type I IFN immunity in patients with life-threatening COVID-19. *Science* 2020 ; 370 : eabd4570.