

Differences in immunity and blood vessels likely protect children from severe COVID-19

December 2 2020



Differences in the immune systems and better blood vessel health were among the factors protecting children from severe COVID-19, according to a new review. Credit: Thiago Cerqueira

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A huge body of global COVID-19 literature was reviewed by experts at the Murdoch Children's Research Institute (MCRI), the University of Melbourne and the University of Fribourg and published in the *Archives of Disease in Childhood* to unravel the reasons for age-related differences in COVID-19 severity and symptoms.

MCRI and University of Melbourne Professor Nigel Curtis said that while a number of hypotheses provided potential explanations as to why adults were at higher risk and [children](#) protected from severe disease and death from COVID-19, most do not explain why COVID-19 severity rises steeply after the age of 60-70 years.

Professor Curtis said in stark contrast to other respiratory viruses, severe disease and death due to COVID-19 was relatively rare in children.

"Most children with COVID-19 have no or only mild symptoms, most commonly fever, cough, sore throat and changes in sense of smell or taste," he said. "Even children with the usual risk factors for severe infections, such as immunosuppression, were not at high risk of severe COVID-19 disease."

Professor Curtis said damage to the thin layer of endothelial cells lining various organs, especially the [blood vessels](#), heart, and lymphatic vessels, increased with age and there was an association between conditions that affect these cells and severe COVID-19.

"We know pre-existing blood vessel damage plays an important role in COVID-19 severity and can lead to blood clots, causing strokes and heart attacks. COVID-19 can infect these endothelial cells and cause blood vessel inflammation," he said.

"The endothelium in children has experienced far less damage compared with adults and their clotting system is also different, which makes children less prone to abnormal blood clotting."

Professor Curtis said diseases associated with chronic inflammation that develop with advanced age including diabetes and obesity were also linked with severe COVID-19.

He said more recent immunization with live vaccines, such as the MMR vaccine against measles, mumps, and rubella, that could boost the [immune system](#) might play a role in protecting children.

Dr. Petra Zimmermann from the University of Fribourg said there were also other important differences in the immune system between children and adults.

"Children have a stronger innate immune response, which is the first-line defense against COVID-19," she said.

"Another important factor is 'trained immunity' which primes innate immune cells after mild infections and vaccinations, leading to a type of 'innate immune memory'.

"Children infected with COVID-19 often have co-infections with other viruses. Recurrent viral infections could lead to improved trained immunity, making kids more effective at clearing COVID-19."

Dr. Zimmermann said different levels of microbiota (bacteria and other germs) in the throat, nose, lung and stomach, also influenced susceptibility to COVID-19.

"The microbiota plays an important role in the regulation of immunity, inflammation and in the defense against illnesses," she said. "Children

are more likely to have viruses and bacteria, especially in the nose, where these bugs might limit the growth of COVID-19."

Dr. Zimmermann said the vitamin D level, with its anti-inflammatory properties, was also generally higher in children.

"The overlap between risk factors for severe COVID-19 and vitamin D deficiency, including obesity, chronic kidney disease and being of black or Asian origin, suggests that vitamin D supplementation may play a role in helping prevent or treat COVID-19," she said.

"In many countries, vitamin D is routinely supplemented in infants younger than one year of age and in some countries even up to the age of three years."

Professor Curtis said understanding the underlying age-related differences in the severity of COVID-19 would provide important insights and opportunities for prevention and treatment of SARS-CoV-2 infections.

More information: Petra Zimmermann et al, Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections, *Archives of Disease in Childhood* (2020). [DOI: 10.1136/archdischild-2020-320338](https://doi.org/10.1136/archdischild-2020-320338)

Provided by Murdoch Children's Research Institute

Citation: Differences in immunity and blood vessels likely protect children from severe COVID-19 (2020, December 2) retrieved 4 May 2024 from <https://medicalxpress.com/news/2020-12-differences-immunity-blood-vessels-children.html>

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