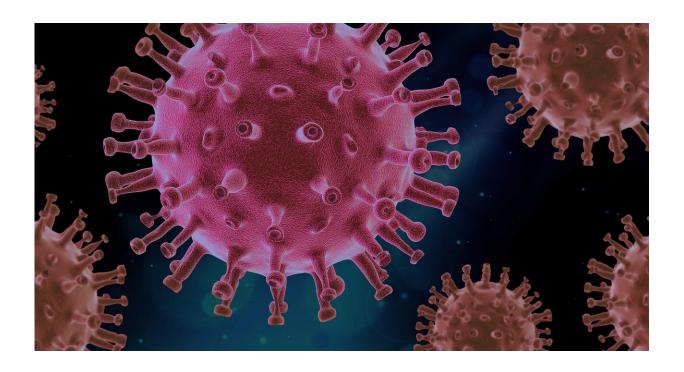


Slower clearance of coronavirus infection may explain why men fare worse than women

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Researchers at Montefiore Health System and Albert Einstein College of Medicine may have solved a mystery surrounding the novel coronavirus pandemic: Why men infected by the virus generally show more severe symptoms and are more likely than women to die from COVID-19. In collaboration with the Kasturba Hospital for Infectious Diseases in Mumbai, India, the scientists showed for the first time that men clear the



virus from their bodies slower than women and found a possible explanation: a potential male-only "reservoir" for coronavirus.

Their study was uploaded today to MedRxiv, a website created by Cold Spring Harbor Laboratory to make research quickly available to the scientific community before undergoing the usual peer review process. It has become widely used to share information quickly during the COVID-19 pandemic.

"COVID-19 studies worldwide have consistently shown a higher incidence and greater severity of the disease in men compared with women," says Aditi Shastri, M.D., assistant professor of medicine at Einstein, a clinical oncologist at the Montefiore Einstein Center for Cancer Care, and lead author of the Montefiore-Einstein study. "Our collaborative study found that men have more difficulty clearing coronavirus following infection, which could explain their more serious problems with COVID-19 disease."

The viral-clearance analysis involved 68 people (48 men and 20 women) with symptoms of COVID-19 who were examined at India's Kasturba Hospital for Infectious Diseases, in Mumbai. After undergoing initial nasal swab tests indicating active infection, individuals were re-tested with serial swabs until the tests turned negative, indicating the time taken to clear the coronavirus. The women cleared the virus significantly earlier than men: a median of four days for women vs. six days for men.

Next, three Mumbai families were identified in which men and women had tested positive for coronavirus infection on swab testing. Again, the women in all three families cleared the coronavirus earlier than male members of the same family.

Why do men have trouble shaking off their infections? Seeking a molecular explanation, the researchers focused on how coronavirus



infection occurs. To infect cells, coronaviruses must first latch onto well-known proteins, called ACE2 receptors, that sprout like tiny antennae from the surfaces of cells. Cell types expressing copious levels of ACE2 on their surfaces would theoretically be most susceptible to infection.

The researchers consulted three independent databases with information on ACE2 expression in different tissues. They saw that the testes, along with the lungs and kidneys, were among the areas of the body with the highest ACE2 expression. By contrast, ACE2 could not be detected in tissue of the ovaries.

Dr. Shastri stresses that the novel coronavirus' ability to infect and multiply in testicular tissue needs to be confirmed, but says it wouldn't surprise her. A recent study from China compared the levels and ratios of sex hormones in male COVID-19 patients vs. healthy men of the same age. The results indicated that the COVID-19 patients had experienced impaired testicular function—evidence that the testes may be significantly affected when men develop COVID-19. Such a COVID-19 complication could have important medical and public health implications, she notes, and deserves to be investigated by clinical trials.

The study's Montefiore-Einstein senior authors are Amit Verma, M.B.B.S., professor of medicine and of developmental & molecular biology at Einstein and director of hematologic malignancies at Montefiore; and Ulrich Steidl, M.D., Ph.D., professor of cell biology and of medicine and the Diane and Arthur B. Belfer Faculty Scholar in Cancer Research at Einstein, and associate chair for translational research in oncology at Montefiore.

The study's other senior author is Jayanthi Shastri, M.D., a microbiologist and infectious disease specialist. As director of Kasturba Hospital's molecular diagnostic laboratory, Dr. Jayanthi Shastri led Mumbai's effort to serially monitor and analyze coronavirus infection in



individuals and their family members.

More information: Aditi Shastri et al. Delayed clearance of SARS-CoV2 in male compared to female patients: High ACE2 expression in testes suggests possible existence of gender-specific viral reservoirs, (2020). DOI: 10.1101/2020.04.16.20060566

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