

Severe COVID-19, Flu Facilitate Lung Cancer Months or Years Later

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Severe COVID-19 and influenza infections prime the lungs for cancer and can accelerate the disease's development, but vaccination heads off those harmful effects, new research from UVA Health's Beirne B. Carter Center for Immunology Research and UVA Comprehensive Cancer Center indicates.

School of Medicine researcher Jie Sun, PhD, and colleagues found that serious viral infections "reprogrammed" immune cells in the lungs to facilitate the growth of cancer tumors months or even years later. Based on their findings, the scientists are urging doctors to closely monitor patients who have recovered from severe COVID, flu or pneumonia in hopes of catching lung cancer early, when it is most treatable.

"A bad case of COVID or flu can leave the lungs in a long-lasting 'inflamed' state that makes it easier for cancer to take hold later," said Sun, co-director of UVA's Carter Center and a member of UVA's Division of Infectious Diseases and International Health. "The encouraging news is that vaccination largely prevents those harmful changes for cancer growth in the lung."

Setting the Stage for Lung Cancer

Respiratory infections such as flu and COVID are among the most common causes of injury and trauma to the lungs, but scientists have had little understanding of the effects these injuries can have on long-term cancer risk. That prompted Sun and his team to investigate, examining the effects in both lab mice and human patients.

The results were eye-opening: Mice that suffered severe lung infections were both more likely to go on to develop lung cancer and significantly more likely to die from the disease. When the researchers examined data from patients, the findings held true there as well: The scientists found a significant association between prior COVID-19 hospitalization and increased lung cancer incidence. This 1.24-fold increase held true regardless of whether the patients were smokers or had other health conditions, which doctors call "comorbidities."

“These findings have important immediate implications for how we monitor patients after severe respiratory viral infection,” said Jeffrey Sturek, MD, PhD, a UVA physician-scientist and collaborator on the project. “We’ve known for a long time that things like smoking increase the risk for lung cancer. The results from this study suggest that we may need to think about severe respiratory viral infection similarly. For example, in some patients who are at high risk for lung cancer based on smoking history, we recommend close monitoring with routine screening CT scans of the lungs to catch cancer early. In future studies, we may want to consider a similar approach after severe respiratory viral infection.”

Based on their work with mice, the researchers believe they have determined what causes this increased risk. Serious viral lung infections had dramatic effects on immune cells called neutrophils and macrophages that are supposed to protect the lungs. These changes caused wayward neutrophils to begin creating an inflamed, “pro-tumor” environment where cancer can thrive. Further, the scientists identified significant changes to the epithelial cells that line the lungs and the air sacs that let us breathe.

Reassuringly, prior vaccination appeared to prevent the cancer-promoting lung changes. These vaccines train the immune system to battle infections, reducing the severity of illness. The scientists note that the increased cancer risk was seen in patients with severe COVID-19 but not those who had suffered mild cases. Those patients actually saw a slight decrease in risk.

They warn, however, that countless survivors of severe COVID-19 and other serious respiratory illnesses may face increased chances of developing lung cancer in the years ahead.

“With tens of millions of people globally experiencing long-term pulmonary [COVID-19] sequelae, these findings carry significant implications for clinical care,” they write in a new scientific paper outlining their findings. “Individuals recovering from severe viral pneumonia, particularly those with smoking history, may benefit from enhanced lung cancer surveillance, and preventing severe infection through vaccination may confer indirect cancer protection benefits.”

Sun and his colleagues hope that their findings will ultimately help doctors identify patients at risk for viral lung cancer so that they can get treatment sooner. Further, the scientists’ new insights into the biological changes wrought by severe lung infections could lead to better treatments to improve patient outcomes and save lives.

“Our goal is to help doctors identify who may be at higher risk of lung cancer after a severe infection, and develop targeted ways to prevent and treat lung cancer after prior pneumonia,” Sun said. “We also believe that vaccines don’t just prevent acute hospitalization after contracting the virus. They may also reduce the long-term fallout of severe infection, including the kind of immune scarring that can increase cancer risk.”

Finding new and better ways to understand and treat the most complex and challenging diseases is a primary mission for UVA’s new Paul and Diane Manning Institute of Biotechnology. The institute aims to advance cutting-edge medical research such as Sun’s and accelerate how quickly lab discoveries can be translated into lifesaving new treatments.

UVA's Beirne B. Carter Center for Immunology Research (CIC) was founded through the generosity of Beirne B. Carter, and the Beirne Carter Foundation continues to support its efforts. CIC researchers work to provide a better understanding of infection, cancer, cardiovascular conditions, chronic lung diseases, microbiome and autoimmune disorders, helping find new treatments and cures.

UVA Comprehensive Cancer Center, meanwhile, is one of only 57 cancer centers in the nation to earn the National Cancer Center's "comprehensive" designation in recognition of their outstanding patient care and cutting-edge cancer research programs.

Findings Published

Sun and his collaborators have [published their findings in the scientific journal Cell](#). The research team consisted of Wei Qian, Xiaoqin Wei, Andrew J. Barros, Xiangyu Ye, Haibo Zhang, Qing Yu, Samuel P. Young, Eric V Yeatts, Yury Park, Chaofan Li, Sijie Hao, Gislane Almeida-Santos, Jinyi Tang, Harish Narasimhan, Nicole A Kirk, Valeria Molinary, Ying Li, Li Li, Bimal N. Desai, Peter Chen, Kwon-Sik Park, Anny Xiaobo, Jeffrey M. Sturek, Wei Chen, In Su Cheon and Sun.

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