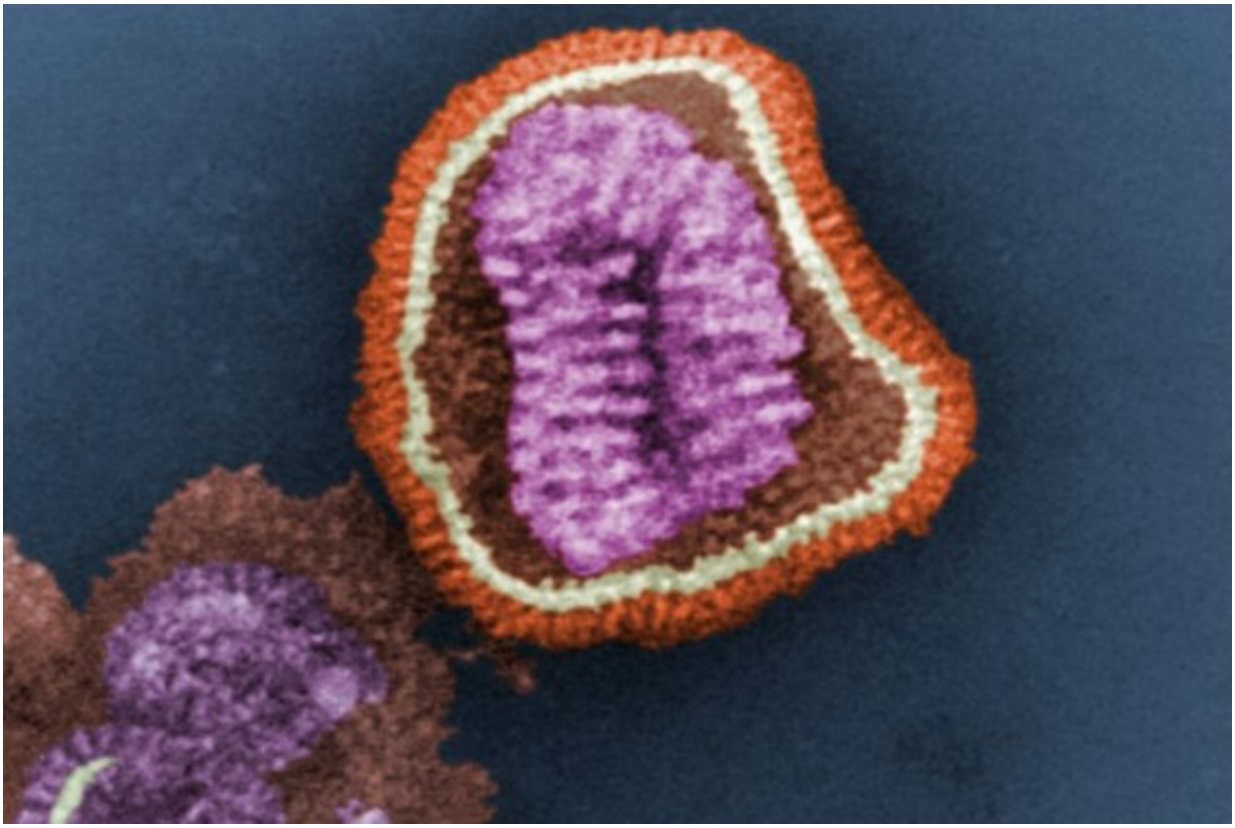
Obesity promotes virulence of influenza

March 3 2020



This digitally-colorized transmission electron microscopic image depicts the ultrastructural details of an influenza virus particle. Credit: CDC, Frederick Murphy

Obesity promotes the virulence of the influenza virus, according to a study conducted in mice published in *mBio*, an open-access journal of the American Society for Microbiology. The finding could explain, in

part, why the influenza virus varies greatly from year to year. This is concerning given that the obesity epidemic is an ever-expanding threat to public health, with currently 50% of the adult population worldwide considered overweight or obese.

"We want to be careful about extrapolating too much from a mouse experiment, but the study does suggest that because of the problem with how cells respond to flu in an obese environment, individuals who are obese don't have good antiviral responses. They are delayed. They are blunted," said principal study investigator Stacey Schultz-Cherry, Ph.D., a faculty member at St. Jude Children's Research Hospital and Deputy Director, World Health Organization Collaborating Centre for Studies on the Ecology of Influenza in Animals and Birds. Dr. Schultz-Cherry is Chair of ASM's Public and Scientific Affairs Committee (PSAC). "Obesity allows the virus to get in, replicate faster and make more mistakes. Some of those mistakes are potentially beneficial for the virus."

Previous research has shown that individuals who are obese have higher influenza viral loads in exhaled breath and that they shed virus longer. Animal studies have demonstrated that the influenza virus can spread deeper into the lungs for longer periods of time when obesity is present. Each year a new influenza vaccine is created because the virus continues to drift and change.Dr. Schultz-Cherry and colleagues hypothesized that the obese microenvironment may allow the influenza virus to change more rapidly.

To find out, the researchers infected lean and obese mice with influenza for 3 days, allowing time for the virus to replicate. They then recovered the viruses from the obese or lean mice and provided them to obese and lean mice respectively, allowed 3 days for replication and then repeated this process. "Basically, we wanted to mimic what would happen during an epidemic where the virus goes from one person to the next," said Dr.

Schultz-Cherry. "What happens if a virus goes from a lean person to a lean person to a lean person versus an obese person to an obese person to an obese person."

The researchers found that as the virus went from obese mouse to obese mouse, the virus underwent changes. Minor variants rapidly emerged in the obese mice and these variants exhibited increased viral replications resulting in enhanced virulence in wild-type mice. "When you get infected with flu, it's not just one virus, it's a population. It's like a little cocktail party and in this case, the cocktail party in the obese mice was a whole different matter," said Dr. Schultz-Cherry. "There were different populations and some of those viruses were more virulent than the strains that went from lean mouse to lean mouse."

When cells interact with influenza, the body typically mounts an interferon response to stop the virus from replicating and spreading. The new research showed that this emergency response was blunted in obese mice. The increased diversity of the influenza viral population in obese mice correlated with decreased type I interferon responses and treatment of obese mice with recombinant interferon reduced viral diversity, suggesting that the delayed antiviral responses exhibited in obesity may permit the emergence of a more virulent influenza virus population.

The researchers said they would next like to study what is happening at the population level in humans. "Do we see this increased viral diversity in obese people in what they are shedding? Is obesity part of why we now see so much viral drift each season and why we have to continually update our vaccines?" said Dr. Schultz-Cherry. The researchers will also tease apart what is happening at the cellular level to impact the virus itself.

Provided by American Society for Microbiology