1918 flu antibodies resurrected from elderly survivors

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Ninety years after the sweeping destruction of the 1918 flu pandemic, researchers at Monroe Carell Jr. Children's Hospital at Vanderbilt have recovered antibodies to the virus – from elderly survivors of the original outbreak.

In addition to revealing the surprisingly long-lasting immunity to such viruses, these antibodies could be effective treatments to have on hand if another virus similar to the 1918 flu breaks out in the future.

The study, led by James Crowe Jr., M.D., professor of Pediatrics and director of the Vanderbilt Program in Vaccine Sciences, Christopher Basler, Ph.D., at the Mount Sinai School of Medicine, and Eric Altschuler, M.D., Ph.D., at the University of Medicine and Dentistry of New Jersey-New Jersey Medical School, is published online in the journal *Nature*.

The influenza pandemic of 1918 killed nearly 50 million people worldwide, many of whom were young, healthy adults. With fears of another looming flu pandemic stoked by the emergence of "bird flu" in Asia, researchers have wanted to study the 1918 virus and the immune response to it.

In 2005, researchers from Mount Sinai and the Armed Forces Institute of Pathology in Washington, D.C., resurrected the 1918 virus from the bodies of people killed in the outbreak. The bodies, and the virus, had been preserved in the permanently frozen soil of Alaska.

When the investigators approached Crowe, whose lab had developed methods of making antibodies, to try to make antibodies to the 1918 flu, he was skeptical, but agreed to try.

The researchers collected blood samples from 32 survivors age 91-101 years and found that all reacted to the 1918 virus, suggesting that they still possessed antibodies to the virus.

Crowe's team was then able to isolate exceedingly rare B cells – the immune cells that produce antibodies – from eight of those samples and grow them in culture. Seven of those samples produced antibodies to a 1918 virus protein, suggesting that their immune systems were waiting on standby for a long-awaited second outbreak.

"The B cells have been waiting for at least 60 years – if not 90 years – for that flu to come around again," Crowe said. "That's amazing…because it's the longest memory anyone's ever demonstrated."

Crowe's team then fused cells showing the highest levels of activity against the virus with "immortal" cells to create a cell line that secretes monoclonal (or identical) antibodies to the 1918 flu. The antibodies reacted strongly to the 1918 virus and cross-reacted with proteins from the related 1930 swine flu but not to more modern flu strains.

To test if these antibodies still work against 1918 flu in a living animal, Crowe's collaborators at the Centers for Disease Control and Prevention infected mice with the 1918 flu and then administered the antibodies at varying doses. Mice receiving the lowest dose of 1918 antibody – and those receiving a non-reactive "control" antibody – died. All mice given the highest doses of 1918 antibodies survived.

Although aging typically causes immunity to weaken, "these are some of the most potent antibodies ever isolated against a virus," Crowe said.

"They're the best antibodies I've ever seen."

The findings suggest that B cells responding to a viral infection – and the antibody-based immunity that results – may last a lifetime, even nine or more decades after exposure.

These antibodies could be used as potential treatments for future outbreaks of flu strains similar to the 1918 virus. And the technology could be used to develop antibodies against other viruses, like HIV.

Most importantly, said Crowe, "the lessons we are learning about the 1918 flu tell us a lot about what may happen during a future pandemic."

Source: Vanderbilt University