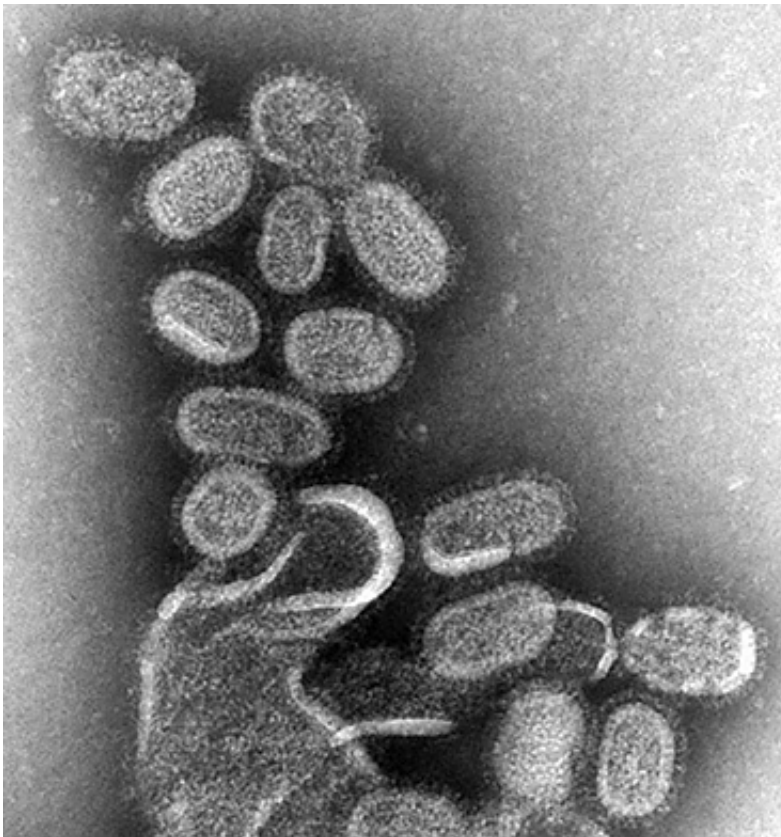


Immune response turned up, not down, by flu during pregnancy, study finds

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Electron microscopy of influenza virus. Credit: CDC

Pregnant women have an unusually strong immune response to influenza, an unexpected finding that may explain why they get sicker from the flu than other healthy adults, new research from the Stanford University School of Medicine and Lucile Packard Children's Hospital Stanford has

found.

The results were surprising because immune responses are thought to be weakened by pregnancy to prevent the woman's body from rejecting her fetus.

The study, which will be published online Sept. 22 in the *Proceedings of the National Academy of Sciences*, is the first to examine the reactions of immune cells taken from [pregnant women](#) to [influenza](#) viruses, including the H1N1 strain that caused the 2009 [flu](#) pandemic.

"We were surprised by the overall finding," said Catherine Blish, MD, PhD, assistant professor of [infectious diseases](#) and the study's senior author. "We now understand that severe influenza in pregnancy is a hyperinflammatory disease rather than a state of immunodeficiency. This means that treatment of flu in pregnancy might have more to do with modulating the [immune response](#) than worrying about viral replication."

In the study, immune cells taken from 21 pregnant women and 29 healthy, nonpregnant women were exposed to different flu viruses in the lab. The immune cells were obtained by collecting blood samples from the women before and seven days after they received flu vaccines. Cells taken from pregnant women six weeks after their babies were delivered were also tested. The researchers studied responses to two flu viruses: pandemic H1N1 and a strain of seasonal influenza, H3N2.

Pregnancy enhanced the immune response to H1N1 of two types of [white blood cells](#): natural killer and T cells. Compared with the same cells from nonpregnant women, H1N1 caused pregnant women's NK and T cells to produce more cytokines and chemokines, molecules that help attract other immune cells to the site of an infection.

"If the chemokine levels are too high, that can bring in too many immune cells," Blish said. "That's a bad thing in a lung where you need air space." Getting the flu during pregnancy, especially pandemic strains such as those that caused the pandemics of 1918, 1957 and 2009, carries a heightened risk for pneumonia and death, she noted.

Both strains of flu also caused NK and T cells to be activated in a greater variety of ways in pregnant than nonpregnant women, the study found.

Today, pregnant women with influenza are usually treated with drugs to slow the replication of the flu virus in their bodies. Although this is a useful treatment, the new findings suggest that it isn't the only good option, the study's authors said.

"If our finding ends up bearing out in future studies, it opens the possibility that we can develop new immune-modulating treatment approaches in the setting of severe influenza, especially in pregnant women," said Alexander Kay, MD, instructor in pediatric infectious diseases and the study's lead author.

The researchers are curious about whether the response of pregnant women's [immune cells](#) to other viruses would be similarly heightened, an idea they have yet to test.

"I suspect this is peculiar to influenza for a variety of reasons," Blish said. Having influenza during pregnancy quadruples a woman's risk for delivering her baby prematurely, she said.

"I wonder if this is an inflammatory pathway that is normally activated later in pregnancy to prepare the body for birth, but that flu happens to overlap with the pathway and aberrantly activates it too early," Blish said.

Blish and Kay plan to continue the research by studying pregnant and nonpregnant women who have contracted flu infections in their day-to-day lives.

And they hope that their research will remind women who are pregnant or planning a pregnancy to get their flu shots. "Flu vaccination is very important to avoid this inflammatory response we're seeing," Kay said. "But only 50 percent of pregnant women are currently vaccinated for influenza."

More information: Enhanced natural killer-cell and T-cell responses to influenza A virus during pregnancy, *Proceedings of the National Academy of Sciences*: www.pnas.org/cgi/doi/10.1073/pnas.1416569111

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