

Why do more women have asthma than men? Blame hormones

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Obstruction of the lumen of a bronchiole by mucoid exudate, goblet cell metaplasia, and epithelial basement membrane thickening in a person with asthma. Credit: Yale Rosen/Wikipedia/CC BY-SA 2.0

Women are twice as likely as men to have asthma, and this gender difference may be caused by the effects of sex hormones on lung cells. Researchers at Vanderbilt University and Johns Hopkins found that testosterone hindered an immune cell linked to asthma symptoms, such



as inflammation and mucus production in the lungs. The study in human cells and rodents appears November 28 in the journal *Cell Reports*.

"When we started this study, we really thought that ovarian hormones would increase inflammation, more so than testosterone making it better," says senior author Dawn Newcomb, of the Vanderbilt University Medical Center. "I was surprised to see that testosterone was more important in reducing inflammation."

Prior studies have found that, before puberty, boys have approximately 1.5 times higher rate of <u>asthma</u> than girls (DOI: <u>10.1016/j.jaci.2015.05.046</u>). That trend reverses after puberty, when women are twice likely to have asthma as men. This pattern continues until women hit menopause, and then the asthma rates in women start to decline. Increased <u>asthma symptoms</u> are regulated by many different factors, including exposure to allergens and viral infections, and the researchers suspected that sex hormones might also be involved.

Newcomb and her colleagues looked at human and <u>mouse cells</u> to further study the trend in gender differences that they had observed. They focused on <u>lung cells</u> called Group 2 <u>innate lymphoid cells</u>, or ILC2 cells. These cells make cytokines, proteins that cause inflammation and mucus production in the lungs, which makes it harder to breathe. The researchers collected blood from people with and without asthma and found that those with asthma had more ILC2 cells than those without. Of that group, asthmatic women had more ILC2 cells than asthmatic men.

ILC2 cells are also found in the lungs of mice, but they are rare. They make up only about 10,000 of the 10 million cells in a mouse lung. Similar to the results that they found in humans, Newcomb and colleagues always found that they were getting fewer cells from male mice than female mice. They used these mouse cells to experiment with



the effects of hormones on ILC2 cells.

When the researchers added ovarian hormones, like estrogen and progesterone, to the ILC2 cells, they did not see much of a change or increase in the ability of the cell to make cytokines. However, when they added testosterone, they saw that the hormone prevented the <u>cells</u> from expanding and reduced the production of cytokines.

While this study focused on testosterone, Newcomb hopes to expand further studies to explore the effects of more <u>sex hormones</u> on asthma. "Sex hormones are not the only mechanism but, rather, one of many mechanisms that could be regulating airway inflammation," she says. "This is not the only important mechanism in asthma."

More information: *Cell Reports*, Newcomb et al.: "Testosterone attenuates group 2 innate lymphoid cell-mediated airway inflammation" <u>www.cell.com/cell-reports/full ... 2211-1247(17)31590-5</u>, <u>DOI:</u> <u>10.1016/j.celrep.2017.10.110</u>

Dawn C. Newcomb et al. Estrogen and progesterone decrease let-7f microRNA expression and increase IL-23/IL-23 receptor signaling and IL-17A production in patients with severe asthma, *Journal of Allergy and Clinical Immunology* (2015). DOI: 10.1016/j.jaci.2015.05.046

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