Excessive airway nerves tied to more severe asthma symptoms, study finds

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Researchers Matthew Drake, M.D. (left), and lab manager Emily Blum use a confocal microscope to generate three-dimensional imagery of airway nerves. Their research demonstrated that inflammatory cells can alter nerve structure in the lungs to cause asthma. Credit: Kristyna Wentz-Graff/OHSU

A new study implicates remodeling of nerves in the airways as a key contributor to heightened sensitivity and airway constriction in patients with asthma.

The study published today in the journal *Science Translational Medicine*.

The results provide new insight into a little-understood factor in the development of asthma, a condition that affects about 235 million people worldwide. The study is the first to demonstrate that inflammatory cells can alter nerve structure in the lungs to cause disease.

Airway nerves sense inhaled particles, such as pollen and smoke, in the environment and help regulate airway constriction. In asthma, these nerves become more sensitive, causing patients to develop symptoms of wheezing and cough.

Although previous research had shown that two-thirds of patients with asthma have an overabundance of a type of immune cell, called eosinophils, the effects of eosinophils on airway nerves were not fully understood.

To study airway nerves in asthma, researchers used OHSU's state-of-the-art confocal microscopes to generate three-dimensional imagery capturing a complete picture of airway nerves and their interactions with eosinophils.

"Picture the branches of trees in a forest," said lead author Matthew Drake, M.D., assistant professor of medicine (pulmonary and critical care medicine) in the OHSU School of Medicine in Portland, Oregon. "In previous studies, researchers could only visualize small sections of the branches, which meant you could never see the whole tree or how multiple trees fit together. With our new method, you can see both the forest and the trees."

Using this new 3-D method, Drake's team studied the length of nerves and how often they branch in the airways of healthy patients and in patients with asthma. They found that in asthma, airway nerves are denser.

"In essence, the trees are growing more branches," Drake said. "As a result of those changes, nerves are more easily irritated, which leads to exaggerated responses that constrict the airway."

The research also showed that having more eosinophils increased the likelihood of having denser nerves and that increased nerves connected with more severe asthma symptoms.

"Changes in nerve structure are clearly tied to worse lung function in asthma," Drake said.

However, future studies are needed to determine whether these changes are preventable, or if this process is reversible once it is established, either

by treating with currently available asthma drugs or by developing new medications, Drake said.

More information: Matthew G. Drake et al, Eosinophils increase airway sensory nerve density in mice and in human asthma, *Science Translational Medicine* (2018). DOI: 10.1126/scitranslmed.aar8477

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