## Diversity under a Microscope: As Biodiversity Diminishes, Do Allergies and Asthma Increase?

## Kelley Christensen

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Our planet may be experiencing its sixth known mass extinction event,<sup>1,2</sup> with a precipitous loss of insects,<sup>3</sup> birds,<sup>4</sup> and other species.<sup>5</sup> Unseen by our eyes, even Earth's microbial biodiversity is decreasing.<sup>6,7</sup> Yet human immune systems rely on microbial exposures to build up defenses.<sup>8,9</sup> In a state-of-the-science review published recently in *Environmental Health Perspectives*,<sup>10</sup> researchers assessed studies on the relationships between the inner and outer layers of microbial biodiversity—meaning microbes inside the human body and in the outer environments our bodies encounter and the risk of asthma, wheezing, or allergic sensitization.<sup>11</sup>

The authors originally considered 447 studies; 82 were included in the final review. Of that group, 29 investigated the potential protective effects of outer-layer microbial biodiversity in the development of asthma, wheezing, or allergic sensitization. Another 16 studies discussed associations between outer-layer biodiversity and an increases in the three conditions. Studies of inner-layer biodiversity and their development had mixed results.

Asthma is a relatively common disease with multiple risk factors.<sup>12</sup> The World Health Organization estimated that in 2019, asthma affected more than 262 million people worldwide and caused 455,000 deaths.<sup>13</sup> The development of asthma involves both environmental and genetic factors, as well as allergic and nonallergic processes.<sup>14,15</sup> Wheezing is a common symptom of

asthma, particularly in children, and can also occur with respiratory infections and other obstructive conditions.<sup>16,17</sup>

The researchers were interested in secondary effects of climate change—specifically biodiversity loss, which can result from climate-related ecological shifts—says senior author Jouni J.K. Jaakkola, a professor of public health and environmental health, as well as head of the Center for Environmental and Respiratory Health Research at the University of Oulu in Finland.

"It has been understood for a long time that climate change and loss of biodiversity interact: Climate change causes loss of biodiversity, and loss of biodiversity intensifies climate change," Jaakkola says. "For example, more diverse and species-rich natural forests and grasslands have higher carbon-sequestering potential."<sup>18</sup>

In 2013, Jaakkola's colleague Tari Haahtela was the lead author of a position statement by the World Allergy Organization on the biodiversity hypothesis.<sup>19</sup> The authors proposed that the loss of both outer- and inner-layer biodiversity might play a role in increases in asthma, allergies, and other inflammatory conditions. Researchers have studied whether exposure to higher outer-layer biodiversity is associated with higher inner-layer biodiversity, namely, with a higher abundance of *Acinetobacter*, explains Jaakkola. This group of bacteria, he adds, is reported to be



The state-of-the-science review suggested greater environmental microbial diversity (portrayed here by fungal hyphae, green and blue, which surround fir pollen, yellow, on woody debris) may play a protective role in the development of asthma, wheeze, or allergic sensitization; evidence for such associations with microbial diversity inside the body was mixed. Image: © Eye of Science/Science Source.

positively associated with immunological tolerance through expression of interleukin-10,<sup>20,21</sup> a key anti-inflammatory cyto-kine (protein that affects the immune system<sup>22</sup>).

"These studies also indicated that higher inner-layer biodiversity may also influence the immune system and protect against allergies through induction of Th1-type immune responses, which inhibit the development of Th2 cells," Jaakkola says. Th2 cells produce certain cytokines that mediate allergen responses, including allergic asthma.<sup>23</sup>

Haahtela's hypothesis was based mainly on research findings in immunology and ecology. By 2019, Jaakkola and his collaborators expected to find enough epidemiologic evidence to empirically test the biodiversity hypothesis, and so they began the new review. Given the diverse definitions of the term "biodiversity,"<sup>24</sup> the research team turned to the Convention on Biological Diversity, which defines the concept as "the variability among living organisms from all sources, including, inter alia, terrestrial, marine and other aquatic ecosystems and the ecological complexes of which they are part; this includes diversity within species, between species and of ecosystems."<sup>25</sup>

Marie Pedersen, an associate professor in the Department of Public Health at the University of Copenhagen, notes that the review provides valuable insights for environmental health researchers, policymakers, and health practitioners interested in finding ways to enhance human health by increasing microbial diversity. "This study is important because it addresses biodiversity loss, which is one of the most urgent threats to planetary and human health," says Pedersen, who was not affiliated with the work. Healthy ecosystems provide us with many essentials we take for granted, she notes, including clean air, potable water, healthy soil, and crop pollination.

"Since living organisms interact in dynamic ecosystems, the disappearance of one species can have a far-reaching impact on the food chain that may affect other basic cycles we depend on and, through that loss, increase disease threats,<sup>26–28</sup>" says Pedersen. "It is not known exactly what the consequences of biodiversity loss would be for humans, including the human microbiota that might influence development of asthma and allergies," she continues. "However, climate change, biodiversity, and pollution are closely linked, and we do know that the diversity of nature is essential for a healthy planet and allows us to thrive."

Kelley Christensen is a writer and editor living in Eugene, Oregon, where she is also the director of research communications at the University of Oregon.

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