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Science FINDINGS

INSIDE

"Science affects the way we think together."
Lewis Thomas

50 Shades of Green: Exposure to Plant Diversity Protects Against Human Immune System Diseases

A playground in Portland, Oregon. Novel research by USDA Forest Service scientists and researchers in New Zealand found a correlation between greater exposure to plant diversity and reduced risk of childhood asthma and acute lymphoblastic leukemia. USDA Forest Service photo.

IN SUMMARY

Mammals, including humans, have evolved in concert with the world of microbes. From birth to childhood and throughout adult life, the human immune system is shaped by exposure to microbes. Global loss of biodiversity is a pressing ecological concern, and scientists have begun to study whether reduced contact with the natural world adversely affects the human microbiota and its role in regulating our immune systems.

Most studies that explore the relationship between exposure to nature and improved public health outcomes have focused on the intensity rather than the diversity of exposure. Scientists with the USDA Forest Service, Pacific Northwest Research Station and Massey University's Research Centre for Hauora and Health in Wellington, New Zealand investigated the role of exposure to plant biodiversity in protecting against childhood asthma and acute lymphoblastic leukemia, the most common type of cancer in children.

The findings suggest that exposure to plant diversity may play an important role in protecting against both diseases. Planting a variety of trees and shrubs to increase children's exposure to plant diversity may represent cost-effective public health interventions that could help reduce the risk of developing these childhood immune system diseases, and potentially others.

"In some Native languages the term for plants translates to "those who take care of us."

—Robin Wall Kimmerer

Beyond the animals and plants we can readily see, ecosystems are teaming with organisms we can't see, namely microbes—bacteria and other micro-organisms. As these unseen life forms obtain the energy they need, they cycle essential elements, such as carbon and nitrogen through the biosphere, helping make planet Earth habitable for mammals.

Mammals, including humans, have evolved in concert with this world of microbes. The human immune system is shaped by exposure to microbes. We are born with an immature immune system which, as we are exposed to microbes from birth through childhood, matures and acquires memory that protects against future disease. Our immune systems continue to be shaped by microbial exposures throughout life.

Scientists have begun to study whether reduced contact with the natural world adversely affects the human microbiota and its role in regulating our immune systems. This concept, known as the biodiversity hypothesis, is based on the idea

Plant leaves harbor a diverse microbial community, as seen in this plate of agar stamped with the leaf of a greenhouse-grown tomato plant. Photo courtesy of the Britt Koskella Laboratory; University of California, Berkeley.

Key Findings

- A large study of children in New Zealand found that children exposed to more vegetation, or greenness, were 6 percent (95 percent confidence interval, 1.9 to 9.9 percent) less likely to develop asthma. Children who were also exposed to greater plant diversity were 6.7 percent (95 percent confidence interval 1.1 to 11.5 percent) less likely to develop the disease.
- Risk of developing asthma increased, however, with exposure to some exotic conifers as well as gorse (*Ulex europaeus*), an invasive shrub.
- Exposure to plant diversity during the first 2 years of a child's life was associated with a 35 percent (95 percent confidence interval 11 to 53 percent) reduced risk of developing childhood acute lymphoblastic leukemia, the world's most common pediatric cancer.

of a link between the global loss of biodiversity and an increase, particularly in high-income countries, of immune system diseases.

"We've drastically changed the environment in which all human beings live, and there are consequences to that," says Geoffrey Donovan, research forester with the USDA Forest Service, Pacific Northwest Research Station. "One is that we see an increase in immune diseases in Western countries. Our immune systems need to be exposed to these microbes we've evolved with, yet we're increasingly removed from them."

Scientists have calculated the total leaf surface area of the world's terrestrial plant species to be 393 million square miles—twice the land surface area of the planet. Plants provide important habitat for microbes, which are present on their leaves as well as in their roots and soil. The more diverse the plant communities, the greater the microbial diversity.

For more than a decade, Donovan, whose background is in forest economics, has studied the benefits trees can provide for people who live in cities, including energy conservation, crime reduction, and stormwater mitigation. One study found that women who live in houses surrounded by more trees are less likely to have underweight babies. After noticing that most studies testing relationships between vegetation and human health tend to focus on the quantity of the vegetation, or simply "greenness," Donovan began to wonder if the composition of that vegetation—the diversity of plants—might influence the health of human immune systems.

"A link between biodiversity and immune health is intuitively appealing," Donovan says. "Yet, as far as we know, few studies have demonstrated a direct link between exposure to biodiversity and specific health outcomes, or that exposure to plant diversity can protect against specific immune diseases."

While on sabbatical in New Zealand, Donovan partnered with Jeroen Douwes, professor of public health and director of Massey University's Research Centre for Hauora and Health in Wellington. Demetrios Gatziolis, fellow research forester with the Pacific Northwest Research Station, also joined this unique partnership.

Pooling Donovan's expertise in forest economics, Douwes' in epidemiology and public health, and Gatziolis' in spatial analysis as a remote-sensing scientist and modeler, the trio launched their study. Their goal: to investigate the role of plant biodiversity in protecting against childhood asthma and acute lymphoblastic leukemia (ALL), the most common type of cancer in children.

"Despite having studied asthma for many, many years, we're still struggling to know specifically what causes it," Douwes says. "And that's a real problem because if you don't know what causes asthma, it's very difficult to come up with interventions."

The scientists' findings show that exposure to diverse vegetation is associated with a lower risk of developing asthma and a reduced incidence of ALL.

"To our knowledge, these are the first studies showing that exposure to vegetation diversity can protect against a specific adverse health outcome," Douwes says.

The results point to simple public health interventions that could help reduce the risk of the two childhood immune diseases, and potentially other diseases with similar characteristics. These include planting a variety of trees and shrubs to increase children's exposure to plant diversity.

An Abundance of Quality Data

The data that the scientists used for these two studies are a researcher's dream.

"What is so unique about the asthma study is that we were able to follow a cohort of nearly 50,000 children born in 1998 for 18 years using routinely collected data," Donovan says.

Without the availability of these extensive data, a field study with more than 50,000 children (the number of children in New Zealand born in 1998) would be cost prohibitive.

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Aerial photograph (left) of the area around the airport in Wellington, New Zealand. The same area (right) showing different types of land cover (e.g., forest, grassland, shrubs), a measure of plant diversity. Scientists analyzed this type of geospatial information along with health data to understand the relationship between plant biodiversity and the incidence of immune system diseases.

In New Zealand, national data about education, income, benefits, migration, justice, and health are collected by several entities and linked together to form the Integrated Data Infrastructure. The system, maintained by Statistics New Zealand, holds 166 billion pieces of information. The government agency removes personal information from the data to protect individual privacy.

"We don't have anything like that in the U.S.," Donovan says. "The [U.S.] healthcare system is fragmented; there's no national health system."

In the United States, which is much larger than New Zealand, such government agencies vary from state to state, making consistent data collection complicated.

New Zealand's Integrated Data Infrastructure provides useful information about the well-being of people in general. But spatial analysis is required to describe how diseases like asthma and ALL vary by location.

"Without it, you cannot see how specific parameters that are associated with well-being are distributed within a city, or across neighborhoods," Gatziolis says. "In other words, you're getting a blurry picture."

Gatziolis most often applies his expertise to forest inventory and analysis where he uses satellite imagery to generate better performing––more precise and accurate––models.

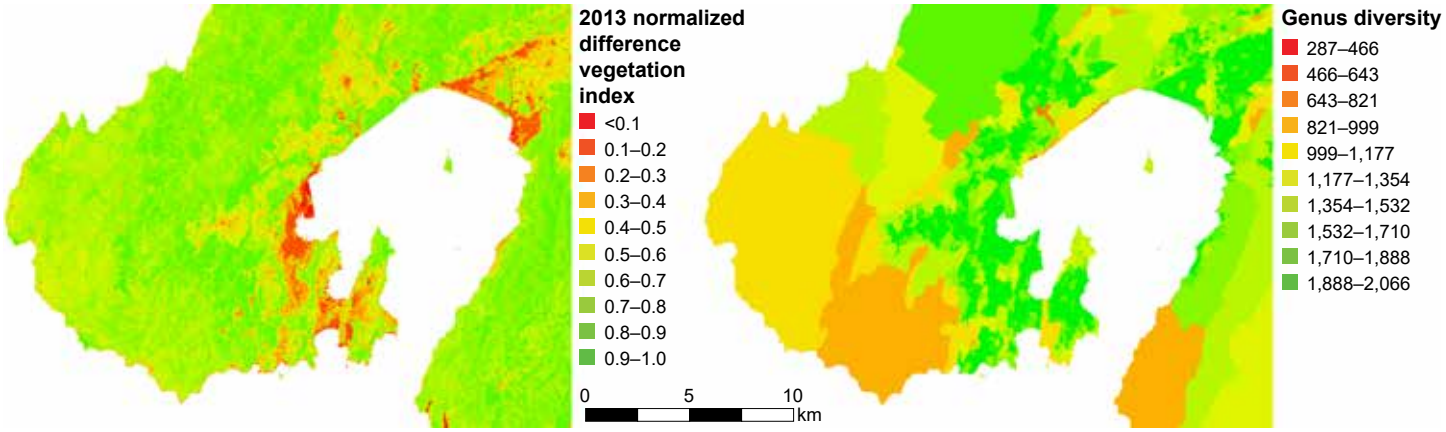
His expertise in spatial data analysis allowed the scientists to link attributes of well-being to specific elements of the environment, including vegetation. As a result, it helped bring the relationship between biodiversity and immune system diseases into clearer focus.

Reducing the Risk of Asthma

Asthma is the most common chronic disease among children globally. The 2019 New Zealand Health Survey estimated that 13 percent of children nationwide have asthma. The same year in the United States, the Centers for Disease Control and Prevention (CDC) estimated that nearly 8 percent of children under age 18 have asthma. The financial burden of the disease is high. Developed countries spend an estimated 1 to 2 percent of their healthcare budget on asthma.

To assess whether exposure to the natural environment is linked to childhood asthma in New Zealand, the scientists included measures of vegetation and plant biodiversity. To measure the level of vegetation in a child's neighborhood, they used a metric called the normalized difference vegetation index, which is derived from satellite imagery. Because the vegetation index doesn't distinguish between types of vegetation, they used a database that categorizes New Zealand land cover into 35 classes, such as grassland, trees, and natural forests, to measure plant diversity.

The researchers found that children in greener neighborhoods as well as those who live in neighborhoods with more plant diversity were less likely to develop childhood asthma. These associations remained after adjusting for potentially confounding factors, such as air pollution and socioeconomic status.



Patterns of vegetation (left) and plant diversity (right) in Wellington, New Zealand. Children exposed to more vegetation and plant biodiversity were less likely to develop childhood asthma.

Children exposed to higher levels of greenness (one standard deviation) had a 6 percent reduction in risk compared with those exposed to lower levels of greenness. Also, children who were exposed to higher levels of plant diversity had a 6.7 percent reduction of risk compared to those exposed to lower levels of diversity. The scientists noted that the reduction in risk could be smaller or larger (1.9 to 9.9 percent for greenness and 1.5 to 11.5 percent for plant diversity). Combined, the risk of developing childhood asthma among children who grew up in an environment with more green space as well as more biodiversity was reduced by nearly 13 percent.

"You may look at that number and think that's not that much," Douwes says. "But in a country like New Zealand, where one in seven children has asthma, a 13 percent reduction means you could potentially prevent a lot of children from getting ill in the first place."

Microbes and Leukemia

As with asthma, the findings indicate that whether a child develops ALL is also related to plant diversity. The scientists hypothesize that microbial exposure is the underlying immunological mechanism that contributes to both diseases. Childhood leukemia, which is the world's most common pediatric cancer, is characterized by two stages. First, a child has a genetic mutation for the disease, and second, exposure to an ordinary infection (such as a cold or the flu) may trigger the development of leukemia. However, exposure to certain bacteria can also encourage the immune system to mature in such a way that leukemia does not develop.

"So, you have this paradox," Donovan explains. "You're exposed to certain bacteria, which can improve your immune system so that when you're exposed to another infection that would have otherwise caused the leukemia to develop, you're fine."

Donovan's interest in studying ALL and plant diversity was sparked by a single line in a paper that said most cases of child leukemia were potentially preventable through early exposure to microbes.

"I was really taken by that because ALL is the most common cause of pediatric cancer in the world, and it's on the rise," he said. "If this disease can be reduced, it would mean a lot less suffering for children and their families."

Donovan again partnered with Douwes to see if there was a similar link between ALL and exposure to plant diversity. They used the same New Zealand dataset that was used for the asthma study, but this time they followed all children born between 1998 and 2013 for 5 years. They identified 264 cases in which children had ALL by age 5.

LAND MANAGEMENT IMPLICATIONS

- Loss of biodiversity may have profound implications for public health.
- Exposure to vegetation and plant diversity may help protect against childhood asthma. Similarly, exposure to plant diversity may protect against childhood acute lymphoblastic leukemia.
- Increasing human exposure to plant diversity to prevent certain immune system diseases from developing is relatively cost effective and easy to implement.

Despite fewer children with ALL compared with the number of children with asthma in the other study, the correlation between plant diversity and disease protection was strong. Controlling for other variables associated with ALL (number of older siblings, ethnicity, age of mother, sex, and birthweight), exposure to plant diversity during the first 2 years of a child's life was associated with a 35 percent reduction (95 percent confidence interval 11 to 53 percent) in the risk of developing ALL.

By comparison, having an older sibling was linked to a 47 percent risk reduction, which supports findings from other research that children who have older siblings are less likely to get immune diseases because their siblings serve as a source of microbial exposure. Having a mother older than 33 was linked to a 48 percent increase in the risk of developing ALL.

The amount of vegetation a child was exposed to was not associated disease protection, which suggests that plant diversity is the more important factor at play. The risk of developing other cancers that were included in the study was not associated with plant biodiversity, which suggests the effects are specific to ALL.

Biodiversity and Public Health

Few, if any, public health interventions have been shown to reduce immune system diseases such as asthma and ALL.

"We can't get rid of house dust mites in countries like New Zealand, just like we can't get rid of a whole bunch of other allergens that people get exposed to," says Douwes. "But we can introduce people to environments where they might get exposed to diverse microorganisms; and that will help mature their immune system to a stage where they actually won't develop the allergies."

It is relatively inexpensive and easy to increase exposure to vegetation and plant diversity. And the likelihood that the public health benefits of increasing plant diversity could well outweigh the costs was not lost on Donovan.

The U.S. national expenditure on health in 2020 reached an all-time high of $4.1 trillion—nearly 20 percent of gross domestic product. For asthma alone, a study by the CDC estimated that 15.4 million Americans were treated for disease each year between 2008 and 2013 at an annual cost of $81.9 billion. In New Zealand, the cost of asthma is more than $1 billion per year. In both countries, children living in poorer neighborhoods are more likely to get asthma, as are African Americans and the indigenous Māori people of New Zealand.

"What excites me is that we can manage resources in ways which can improve our health, and we can do it cost effectively," Donovan says. "Trees are cheap; healthcare is expensive."

A young child's exposure to diverse microbes can be helped along by landscape design that prioritizes plant diversity.

"Clever urban landscape design was introduced with the idea that it would benefit people because it would beautify a place," Douwes says. "We now have reasonably hard data to suggest that it may also benefit people's health in addition to having mental health benefits."

Individuals can also take actions, such as planting trees, establishing more plants around the places they live, or visiting parks with a variety of plants and trees on a regular basis.

However, not all plants provide equal benefits. Exposure to some plants may exacerbate the problem. The New Zealand asthma study showed the risk of developing asthma increased with exposure to radiata pine (*Pinus radiata*), the most common exotic conifer in New Zealand and the country's dominant commercial tree species. Risk of asthma also increased with exposure to gorse (*Ulex europaeus)*, a shrub similar in appearance to Scotch broom that is considered invasive in New Zealand.

Working Backwards

As far as the scientists know, their studies represent the first evidence to establish links between childhood asthma and ALL and plant biodiversity, which serves as a proxy for microbial exposure. However, they caution that it's important to understand that these studies established an *association* rather than a *cause.*

Exposure to gorse (yellow flowering shrub in foreground) and radiata pine (midground), both nonnative species in New Zealand, were found to increase likelihood of developing asthma. Photo courtesy of Jon Sullivan/Flickr.

"The results are suggestive of a causative link, certainly, but no more than that," Donovan says.

Donovan describes the research process as a story that starts at the end point and works backward. The endpoint is that results show changes in disease patterns, a difference in the incidence of childhood asthma and ALL.

"Now you work your way backwards and try and work out why that is," he says. "If that's true, a load of other things should also be true. We need to find out if they are true."

Further research could eventually establish a causal link between plant biodiversity and the two diseases. The scientists are in the processes of developing studies that lead in that direction. One study in Portland, Oregon, for example, will test skin and fecal samples to see if there is greater microbial diversity in people who live with more diverse plants and trees near their homes. In New Zealand, Douwes is developing a similar study to measure skin and fecal samples of children before and after repeated visits to a protected natural area in Wellington and compare them with samples from a control group that lacks increased exposure to plant diversity.

However, both scientists emphasize that it isn't necessary to wait to establish a cause before pursuing interventions.

"We always have to make decisions based on imperfect information," Donovan says, "that's the nature of the human condition."

Previous research has already shown that efforts to increase vegetation can provide additional benefits, such as sequestering carbon, reducing energy consumption, and increasing home values.

"Increasing exposure to plant biodiversity is something that has real promise in terms of bringing health benefits," Douwes says, "and we can start now."

Urban landscaping, such as this in Seattle, Washington, may serve multiple functions, including enhancing public health. Photo courtesy of Guy Kramer.

"Every one of us is a zoo in our own right—a colony enclosed within a single body. A multi-species collective. An entire world."

—Ed Yong, science journalist

For Further Reading

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