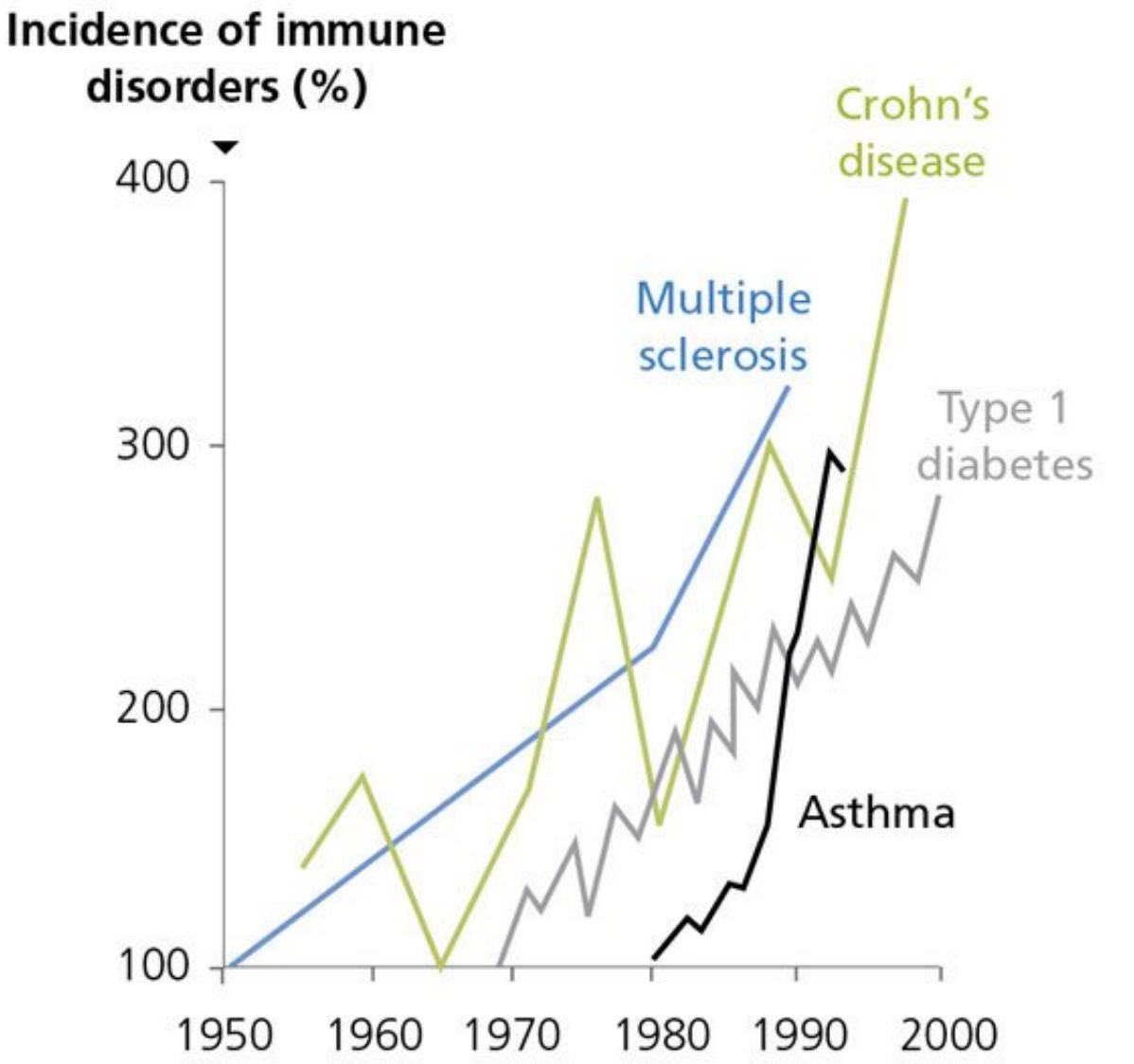
Letting Biodiversity Get Under Our Skin

We live at the crossroads of three global megatrends, three barreling and intertwined juggernauts of modernity. The first is the massive migration of humanity to the world's cities. I grew up in a small town, walking deer trails beneath the shade of maples and oaks. Now I live with my kids in a city where the path beneath our feet is ever more likely to be paved. My story is our story. By 2050, two-thirds of all humans on Earth will live in cities.

The second is the loss of biodiversity. Species are disappearing, both from the places where we live and from the earth as a whole. If our hairy ancestors were to visit our cities and suburbs, they would wonder how the escalators work, but they would also question where the plants and animals have gone. What have we done with all the birds? Some, like the Carolina parakeet, are just gone. Others live on, but at a distance—geographically removed from our daily lives, far away from the majority of people.

And then there's the third trend—the one that, at first glance, seems not to belong with the others. The prevalence of allergies and chronic inflammatory diseases among urban populations in developed countries has skyrocketed in recent years. Incidences of asthma, Crohn's disease, multiple sclerosis, and even depression (which can have an immune component) are on the rise.

The parallels in geography and timing between urbanization, the loss of biodiversity, and the rise in immune-system problems raise an intriguing—and troubling—question. Could our distance from nature and our chronic immunological discontent be related? Some now say . . . yes.



Bach, J.F. 2002. *New England Journal of Medicine* doi.full/10.1056/NEJMra020100.

In May 2012, a team of Finnish ecologists, allergy specialists, molecular biologists, and immunologists led by Ilkka Hanski at the University of Helsinki announced the results of a study comparing the allergies of adolescents living in houses surrounded by biodiversity to those of adolescents surrounded by

simplicity—the modern landscape of cement and grass. (1) They found that those individuals who lived in houses surrounded by a greater diversity of life were themselves covered with different kinds of microbes. They were also less likely to show the telltale immunological signs of allergies.

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In the years to come, we may regard these results as a new threshold to our understanding biodiversity. What Hanski and others have posited—that the loss of contact with a diversity of other species is making us sick—is almost unprecedented in the long history of our medical understanding of the body. It is the opposite of the germ theory of disease. If the germ theory is the idea that the presence of bad species can make you sick, the growing sense seems to be that the opposite can also be true. We can get sick because of the absence of good species—or even just the absence of the diversity of species.

The possible link between biodiversity and human health has been tossed around for a while. Half a dozen theories—biophilia, nature deficit disorder, the deficiency theory of disease, the dilution effect, and more—describe the ways in which the loss of a connection to biological richness might cause us to ail. Elements of these theories are at the core of modern ecology. Less biodiverse systems—be they grasslands, forests, or the biomes of tiny life on our skin and in our guts—are less resilient and at greater risk of invasion (whether by pathogens or weeds) than more diverse systems.

Allergies were not part of the story until the early 1980s, and even then they were considered separately, as though part of another tale with a different beginning and different ends. Epidemiologists began to notice differences between the immune systems of city kids and farm kids. Farm kids were less likely to have allergies. A million things are different between cities and farms—education, refrigeration of food, exercise, exposure to the sun, exposure to

toxins—and any one of them might affect children's immune systems. Many explanations were suggested. But David Strachan, an epidemiologist at St. George's University of London, had a curious idea, which he called the hygiene hypothesis. The key was bacteria; the lock was our immune system. Perhaps urban kids were too distant from microbial nature for their immune systems to develop properly. Farm kids work in the dirt. They touch farm animals. They are exposed to more life, be it cows, chickens, or—as Strachan suspected—the microbes that cows and chickens harbor. It was a wild, speculative idea. It also increasingly appears to have been right.

Progress in testing the hygiene hypothesis has been incremental rather than revolutionary. Farm kids, particularly those who interact with farm animals, do suffer from fewer allergies. And in general, it is beginning to seem as though exposure to bacteria and/or parasitic worms early in life may be necessary to forestall the development of allergies. In West Africa, children who had parasitic worms were at increased risk of allergies when those worms were removed. In Detroit, houses with dogs had more kinds of bacteria than those without. Pregnant women living in those same doggy houses were less likely than women in dogless houses to show evidence of allergy in their umbilical-cord blood. (The presence of an allergic response (atopy) in umbilical-cord blood has been shown to predispose children to allergies once they are born.) In laboratories, mice without skin bacteria failed to develop normal immune systems. Add skin bacteria back, and their defenses were restored.

None of these effects is simple. They come with caveats and clauses, but we should not expect an ecological interaction to be easy to understand. No one going to a play with hundreds of characters expects it to be short. Yet, as complex as the connections might be, consensus has begun to emerge that some aspect of "dirty" living is good.

Bacteria seem to be part of the useful dirtiness, but which bacteria? Or maybe

the question is, how many? Or what mix? Studies tend to refer to "missing microbes" as if they were some great mass—a heaving, metabolizing pile of life that, Buddha-like, needs to be rubbed for health. But it's not yet been established whether we are missing interactions with lots of microbes, lots of kinds of microbes, or something else. The trouble is, thousands of bacteria can be found on the average human body, perhaps tens of thousands in the average house—and far more in backyards, farms, and the wild. Microbiologists have barely scratched the surface in their attempts to calculate the sublime magnitude of their quarry.

What can be said with certainty is that, as we have become more urban and as we have transformed the world, we have also become experts at replacing habitats filled with many species with habitats populated by just a few. We plant inert cement where forests once grew. We clean and scrub our houses with antibiotic wipes. We overuse antibiotics to clean out pathogens in our bodies. We overuse antimicrobials to clean everything else. One can now even buy underpants preloaded with chemicals that clean away the bacteria below the belt.

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The word "clean" seems wholesome, but what it usually means is kill. We kill some species and favor others. We once cleaned the predators and snakes from around our homes. Now that the snakes and predators are gone, we clean what is invisible. As we do, we kill the life most susceptible to our weapons. In their place grows a more depauperate and resistant wildness—nature despite us, not for us—a jungle of potentially dangerous weeds. We are reducing diversity in our daily lives, even on our bodies, in exactly the same way that we are reducing it in the world. We manage our own flesh as we manage the earth.

This parallel caught Hanski's attention, and he wondered whether he could take the hygiene hypothesis a step further. Could the loss of biodiversity—the number of kinds of species, not the presence of some particular form—lead our immune systems to break in such a way that they can no longer distinguish wholesome friends from ancient enemies? It was an idea already suggested in the work on dogs in houses, but Hanski thought he could carry it a step further, out-of-doors.

The Wright brothers did not take off in a thunderstorm, and Hanski, for his part, chose to begin his work where he could control as many extraneous factors as possible. Hanski is highly regarded for the care he takes in designing studies; he chooses circumstances that reduce the wilderness to its simplest elements, whether that means studying flies on dead animals, beetles in dung, or the waxing and waning of populations of butterflies in patches of grass. It was the elegance of this approach that won him the Crafoord Prize, the most prestigious prize in ecology. Not content to rest on his laurels, Hanski set out to expand his work on why rare species decline—and to begin probing the consequences of those declines.

In studying households, Hanski wanted to work with houses he could know in minute detail. He would work in his native Finland, where biodiversity was low to start with, low enough to be knowable, if not yet known. He chose to study a city and region in Finland where few people move very far, where the microbes they are born around might be similar to those among which they die. He then focused on adolescents to control the impact of age. If biodiversity was in fact affecting allergies, Hanski would maximize his chances of seeing the effect.

Hanski randomly selected 118 adolescents in an equal number of homes within a 100 kilometer–by–150 kilometer area. Some of the homes were, by chance, in the city, and others stood alone out in woods or on farms. Hanski and his crew visited those houses, armed with needles and plant presses.

They drew blood from each adolescent and screened the samples for evidence of allergies.

To measure the diversity of bacteria on the adolescents' skin, Hanski and his crew swabbed their forearms, then amplified and sequenced the DNA present. The approach was standard: they needed just a tiny patch of skin to represent the life of the whole.

Measuring the biodiversity outside took the most work. Hanski chose to survey plants. Plants don't move, which makes them easy to count; it might also (although this is pure speculation) make them more likely to accumulate microbes as they settle out of the drifting snow of bacteria-laden air. Hanski and his crew of ten field assistants counted and identified every plant in each and every backyard. They did ecology in the way Hanski has done it throughout his entire career.

The idea was to test whether places with high biodiversity outdoors tended to have high microbial biodiversity indoors, which would in turn lower the inhabitants' risk of allergic diseases. In retrospect, it seems unlikely that Hanski and his colleagues would find a strong relationship between plant biodiversity, microbes, and allergies. If you are studying patches of grassland and butterflies, there are relatively few species in play. One can reasonably expect to understand the main factors that influence where they occur. But thousands of species live on the human body—most of which have not yet been named, much less well understood. The microbe communities found on different body parts of a particular person—say the tongue and the toe—are predictably different. The microbes of a tongue never remotely look like those of a toe. But why your tongue has species so different from my tongue has been impossible to explain. An individual body encounters tens of thousands or more bacteria in its lifetime. Just which ones stick and establish themselves might be mostly a matter of chance.

Yet, when Hanski and his colleagues looked at their data, they found a remarkably clear pattern. Higher native-plant diversity appeared to be associated with altered microbial composition on the participants' skin, which led in turn to lower risk of allergies.

One group of microbes, the gammaproteobacteria, seemed to be particularly strongly associated both with plant diversity and with allergies. Unbeknown to Hanski, more than 40 years earlier this same group of bacteria had been shown to wax and wane on human skin with variation among the seasons. Hanski and his colleagues found that the bacteria also vary in space. It didn't matter whether they considered allergies to cats, dogs, horses, birch pollen, timothy grass, or mugwort. In each case, individuals with more kinds of gammaproteobacteria on their bodies were less likely to have allergies.

No one had ever shown this before. No one seems ever to have looked. When I consulted my colleagues about the results, some were excited. Others were skeptical. Maybe the analysis wasn't quite right. Maybe Hanski focused too much on the gammaproteobacteria and not enough on other kinds of bacteria. But all agreed that, as they went forward with their research, they would be looking for similar effects. Can the wildness outside sneak all the way inside?

No one has offered a very compelling explanation of how the diversity of plants or life in general in backyards alters the composition of bacteria on human skin. It is too early to know the answer. But the bigger question is how the composition of bacteria on our skin (perhaps in concert with the diversity of plants and other organisms outside) influences our potential to develop allergies. Several options have emerged.

The biodiversity of the gammaproteobacteria and other bacteria might directly benefit us. We tend to think of the immune system as our body's attack dog. It is not. The primary role of the immune system is to distinguish deadly species

from good species and, some argue, good species from simply innocuous ones. The attacks are secondary—the easy part. In this way, the immune system is our sixth sense. It is our inner taxonomist. And this inner taxonomist needs to see a lot of species to learn to distinguish good from bad from innocuous. If it does not, it makes mistakes. It sees our body's own cells or pollen grains and judges them to be dangerous. In this model, the world around us needs to be diverse enough for our immune system to gain perspective.

Or maybe, as Hanski and his colleagues have suggested (and as the studies of dogs have suggested independently), the odds of having some beneficial bacteria species in a house increase with certain kinds of microbial diversity. The diversity of the gammaproteobacteria or other bacteria in this telling would be a kind of insurance policy.

Finally, a third possibility harks back to ancient wars. Bacteria and fungi compete. Fungi are everywhere in households and, in contrast to bacteria, seem more likely to cause allergies than to prevent them. Fungal diversity appears to be lower in houses where bacterial diversity is higher. Maybe more diverse household bacteria can fight off fungi, winning an invisible war on our behalf.

Hanski himself does not yet have enough perspective—nor data—to distinguish among explanations. Nor does anyone else. We wait.

Perhaps we need something like an ecological theory of disease. Such an ecological theory of disease would posit that we can get sick either because we are afflicted by the presence of bad species or by the absence of good species—or a good mix of species. Such a theory would be new to the medical world and to society in general. We are good at killing species around our houses and on our bodies, but far less practiced at cultivating them.

Yet, as much as the idea that some of the species around us are beneficial is foreign to doctors, it is old hat to ecologists. To ecologists such as Hanski, the interdependence of species is self-evident; the normal status of life is to be enmeshed in other life. Our conscious minds and progressive societies seem slow to realize this, but our subconscious immune systems may have known it all along.

As we wait for more understanding, we continue to simplify the world. We will become more urban and thus more likely to suffer from allergies and autoimmune diseases, at least if Hanski is right. And if he is right, there may also be a way forward, a way out of our sick and simple morass. Could we rewild the places around us, plant a richness of species in our backyards and so raise healthier children covered in more kinds of bacteria? As a country boy who is living now in the city, raising two children, I hope so. Whatever we do, we will be measured by our immune systems and our microbes, which in their function or dysfunction seem to record the richness of our lives.