



VEN ON A BLUSTERY winter's afternoon, Mount Lofty flaunts its splendour as a bushland oasis, one of the last vestiges of the original forests and woodlands that once dotted the Adelaide Plains. Walking the winding nature trails here, you encounter a multitude of native trees, shrubs, climbing plants, reeds and grasses, two-thirds of which harbour fruit, seeds or insects that attract birds, or nectar that brings butterflies. Meandering down the narrow tracks from the summit, you feel invigorated by the scenery, the silence, the smell of wet earth after a light shower. To a city dweller, the air itself

And it's not an illusion. Every time you enter wild spaces replete with biodiversity and breathe the air, microbes wafting through the ecosystem land on your skin, enter your lungs and gut and become part of you. They join the many billions already living in your microbiome – the community of symbiotic micro-organisms inside each human being.

seems therapeutic.

Scientists have long known about these minuscule, mutually beneficial helpers in our bodies. But thanks to technological developments in molecular imaging, computer speed and rapid genetic sequencing, they have in recent years been astounded to realise how crucial and widespread the role played by our microbiome is in everything from nutrition to disease resistance and even mental health.

The latest surprise is the discovery by researchers in Adelaide that the more diverse the microbes living in the soils around us, and the more you are exposed to them, the healthier you become. It's a discovery that could change our cities, and make us healthier, on a global scale.

And it all comes down to humble earth.



Reference soil

Soil from wilderness areas, or ecologically restored sites, holds a cornucopia of complexity. 'Oligotrophic' species dominate, which thrive in low-nutrient ecosystems and are key players in decomposition and nutrient recycling.



HE HUMAN BODY is made up of an estimated 37 trillion individual cells, from skin and liver cells to brain and gut cells. But the microbes – micro-organisms such as bacteria, viruses, protozoa and fungi – living in, and on, our bodies are thought to be more than double that, numbering about 100 trillion. While most of us might not give much thought to these tiny interlopers, they are beneficial – even essential – to our survival, many doing things our bodies can't.

Our microbiome is an enormous, invisible ecosystem that acts like a giant shadow organ, helping us digest plant matter, manufacture vitamins, regulate our immune system, form new blood vessels, coordinate hormone activity, store fat and modulate brain signals. In fact, its role is now considered so crucial that some leading researchers have argued that animals and plants are not autonomous entities but holobionts – dynamic biomolecular networks of different tiny species working in a symbiotic relationship for mutual benefit.

Some 70 per cent of microbes in the human body occur in the gastrointestinal tract – the mouth, oesophagus, stomach and intestines, which together make up the organ system that takes in food, digests it to extract and absorb energy and nutrients, and expels the remainder as waste. Study after study during the past 20 years has identified a marked difference in the gastrointestinal microbes of people living in rural surroundings compared with those living in cities.

Country dwellers have more diverse microbiomes; in city folk the diversity is much less. A lack of microbe diversity is also seen in people who suffer inflammatory diseases, such as asthma and food allergies, which plague city dwellers and the incidence of which has soared in highly urbanised populations.

"There's a whole host of benefits we derive from living in healthy environments," says Dr Philip (Phil) Weinstein, a University of Adelaide biological sciences professor with

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qualifications in both public health and ecology. "One of them is the ecosystem we're exposed to – the rich diversity of microbes in the soil, in the air, in the food we eat and the animals we interact with.

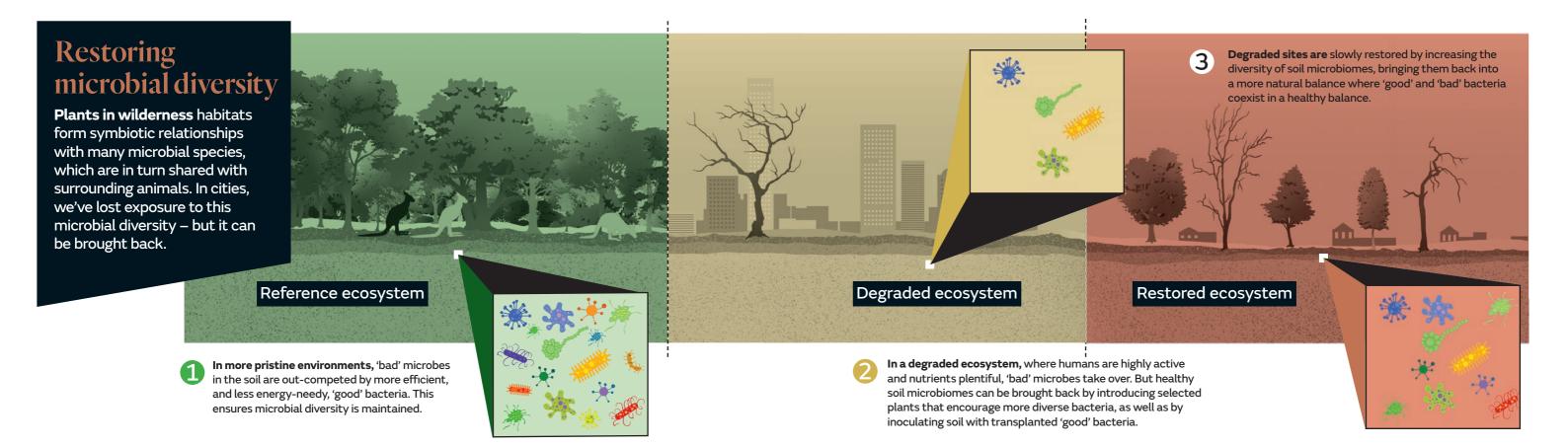
"For most of our history as a species, we've had exposure to that, and that's what we've evolved with and are adapted to live in – as well as eating high-fibre foods and running around all day. But the movement of people into cities has basically cut us off from that environment. And all of those diseases of the urbanised Western lifestyle – like cardiovascular disease, diabetes, obesity, asthma – have increased dramatically."

Researchers now know there's a connection. But the focus of health professionals has been on diet and exercise alone. Little attention has been paid to the role ecosystems around us can play in improving our health, particularly gut microbiome health.

Although we can't reverse urbanisation and return to the savannahs of Africa where humans evolved, we can bring those ecosystem benefits back to our cities. And that's exactly what Phil and his colleague Dr Martin Breed are trying to do.

The duo run the Healthy Urban Microbiome Initiative (HUMI), which has been exploring how adding microbial diversity to urban environments might improve ▶

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the health of people by boosting the population of good bacteria in their microbiomes.

"There are more species of bacteria, fungi and other microbes out there than anything else – all this incredible and mostly unknown diversity, which performs all sorts of different functions for not just us but the natural world," Martin says. "Plants form symbiotic relationships with many different microbial species, which provide the resources they need to grow. In healthy soil in the wild, in a quarter of a gram of soil, you often find 2000-5000 species – which is phenomenal.

"But when you look at degraded environments, like those in cities or crop pastures, there's usually a very different suite of microbes, far lower in diversity. And often what's there is an abundance of opportunistic species that can tolerate degraded environments, but are not all that good for plants, animals or for us."

Martin began his scientific career restoring ecosystems of degraded land when, while working in Sweden, he came to appreciate how a range of new techniques in genomics – the interdisciplinary field of biology that explores the structure, function and evolution of an organism's complete DNA – might help explain why some restored ecosystems thrive and some don't.

He suspected soil microbes played a part but needed evidence. Back in Australia, Martin, PhD student Craig Liddicoat and others collected soil samples from 200 sites across the country. Some were from patches of degraded land and some from wilderness areas rich in biodiversity. The team analysed genes in the soil



▲ Martin Breed assesses soil composition at a Mount Lofty wilderness site. He can tell much about the health of a soil from its appearance.

microbiomes to compare them and found consistent patterns in the proportions of opportunistic versus stable bacteria.

Degraded landscapes were dominated by what's known as 'copiotrophic' bacteria, including opportunistic species of *Bacillus*, *Clostridium*, *Enterobacter*, *Legionella* and *Pseudomonas*. These tend to thrive in nutrient-rich environments, such as sewage lagoons, and are similar to many bacterial species that cause disease in humans.

In the more natural locations these were also present, but in much smaller numbers. More abundant at these sites were 'oligotrophic' species, which thrive in lower nutrient ecosystems and are involved in decomposition and nutrient recycling. An example is *Bradyrhizobium*, which helps plants extract nitrogen from the soil.

What Martin and his colleagues were seeing was evolution in action. Where humans were active and nutrients were plentiful, copiotrophs took over. In more pristine environments, the copiotrophs were out-competed by more efficient, less energy-needy oligotrophs.

Could they restore the soil microbiomes at degraded sites, bringing them back into a more natural balance by encouraging the 'good' bacteria and discouraging the 'bad'? Martin's team decided to find out. At various degraded sites, carefully selected plants were cultivated to encourage more diverse bacteria, and then monitored to see if changes occurred to the soil microbiome. "There was dramatic change," Martin says.

The microbial communities in the degraded sites were returning to a biodiverse state after just 6–10 years. "This was a huge surprise, because we didn't know microbe communities could return so rapidly."

This process, known as "microbiome rewilding", attracted the interest of Phil Weinstein. The biodiversity of soil microbiomes outside cities might not only help explain why country folk tend to have healthier immune systems, but also offer a pathway to bringing those health gains to city dwellers.

"Among the benefits we've lost from our past is regular exposure to antigens, like those in microbes and allergens like pollen," Phil says. "The diversity of earlier ecosystems trained our immune systems, but that training is no longer happening as much. Kids growing up on a farm are exposed to more pollens and microbes, and that trains their immune systems,

so they do better. But city kids aren't, so their immune systems are bored. So, when a pollen grain comes along, there's an asthma attack, because their immune systems go into overload."

Phil says it's partly cultural. Since 1864 when French chemist and biologist Louis Pasteur established modern germ theory, proving in the laboratory that microorganisms cause disease, we have been at war with microbes. Sanitation, personal hygiene, vaccines, pasteurisation and antibiotics have laid waste to a plethora of infectious diseases, and even driven some pathogens, such as smallpox, to functional extinction.

This has been good for humanity. But we've gone overboard, Phil says: "The majority of urban populations now live in an environment that's safe from those environmental pathogens like cholera and typhoid. But we've still got a cholera mindset, and that's a mismatch."

Adelaide, an experiment is underway to see whether introducing a more biodiverse plant ecosystem can improve the soil microbiome in an urban setting. In 2015 the school completed the conversion of two ovals into Portrush Forest – an outdoor learning environment with native vegetation, wetlands, vegetable gardens, an orchard and an assortment of nature walks with fallen logs, cubby houses and sandpits.

The sprawling school grounds cover three suburban blocks, and Portrush Forest takes up a third of its north-eastern corner.

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Christian Cando-Dumancela filters soil samples to separate microorganisms, then ferments the extracts to grow the bacteria to sequence their genes.

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At 11 sites around the school, petri dishes are open to the air, protected by upturned milk crates. Six are in less diverse areas – the edge of a grass oval, a basketball court, a grassy area next to a playground slide, inside school buildings – while five are in the heart of the urban forest. Every morning and afternoon, a battalion of students acts as volunteer scientists to collect the petri dishes, inscribing the date and location of each collected sample and placing them in the school's freezer. At the end of each week, the HUMI team collects the samples and analyses the genetic data back at its labs.

When I visit, the experiment has been underway for only a month. But James Loader, one of Martin Breed's students, says data are already showing a boost in the diversity of soil microbes in Portrush Forest.

Another approach involves collecting microbes from wilderness areas and using them to inoculate degraded sites. At the University of Adelaide's Ecophysiology Lab, research assistant Christian Cando-Dumancela shows me soil samples from other locations the HUMI team has been analysing. Each is in a plastic centrifuge test tube with a conical base.

He holds up three samples: one from degraded agricultural land, which is filled with pale, sand-like soil; one from grassland parks where there are no bushes or trees, which is a deeper brown in which soil particles clump together; and one from a wilderness site. The latter holds a cornucopia of complexity, including plant and animal residues at various stages of decomposition, rootstalks, a smattering of plant litter and plenty of humus full of microbes.

Christian filters the soil to separate the bacteria from other micro-organisms. He then ferments the extracts to grow the bacteria and ultimately sequence their genes, which means he can catalogue the species found.

"We know we can bring degraded soils back to health by enriching the soil microbiome, but that can take 6–10 years," Martin says, holding up the vial with

rich wilderness soil. "So we wondered can we speed that up? Can we inoculate diverse bacteria in urban soils to regenerate it and bring back biodiversity and accelerate the complexity of soil microbiome?" Martin looks at Christian and they both beam excitedly. "No-one has connected highly interventional microbial ecology aimed at improving the health of soils and the health of people who interact with those soils," Christian says. "We have. And we think we have a way of speeding that process up."

But can heathy soils alone make people healthier? The HUMI team has evidence suggesting microbiome rewilding can achieve this. In a recent seven-week experiment, led by Craig Liddicoat, juvenile lab mice were kept in wire-top cages next to an adjoining container of living soil. Occasionally small fans blew a gentle breeze over the soil and into the cages.

One group was next to high-biodiversity wilderness soils, one next to grassland soils, and one next to a clean container with no soil (to mimic an urban setting). Mouse droppings were analysed throughout the process, and their guts sampled at the end of the study. The mice began with similar gut microbiomes and exhibited a normal range of anxious behaviour when exposed to standard experimental maze-navigating activity.

"The two groups exposed to soil were getting only a dusting of soil per mouse, per week," Christian explains. "For the 'wilderness' mice, their poo showed their gut microbiome slowly changed to match that of the high-biodiversity soils."

The researchers noticed two incredible things. The 'wilderness' mice showed a progressive reduction of anxiety behaviours and a rising abundance of bacterial communities in their guts that produce a compound called butyrate. This is known from both human and mice studies to be associated with a balanced immune system, protection from metabolic disorders and reduced rates of anxiety and depression. "And this," Christian adds, "was from just normal, passive exposure to soil dust in the air."

By contrast, the no-soil 'urban' group showed the most anxiety, while the mice exposed to low-biodiversity soils showed a mix of anxious and non-anxious behaviour in the maze. "It was unequivocal," Martin says. "Between 60 and 80 per cent of the variation in anxiety behaviour in the mice could only be explained



by the abundance of these butyrate-producing bacteria colonising the gut of the mice. It closed the loop for us between biodiversity exposure and improved mental health – at least in mice."

HIS IS THE heartland of the research we're trying to do," Phil Weinstein says, leaning forward, his eyes lighting up as he further articulates the purpose of his work. "We know immune-related disorders like allergies, auto-immune and chronic inflammatory diseases are rising in cities, where most of the world's population now lives. And we know microbial diversity in the gut has immune-boosting power and health benefits. What kind of measures can we take to encourage microbial diversity in environmental microbiomes?

"There are probably already healthy ecosystem microbes in urban landscapes, but they're being overwhelmed by these degradation specialists. We just need to help bring those good microbial communities back into dominance. We don't understand all the mechanisms [for why diverse gut microbiomes are heathier], but we know if you put a biodiverse environment back in an urban space and expose people to it, you will cut out a part of the disease burden."

Their approach captured the interest of the United Nations Environment Programme (UNEP) thanks to Phil's colleague, Dr Chris Skelly, a public health specialist in Britain.

In November 2018, UNEP signed a partnership with HUMI to apply their approach to 20 cities across 20 countries, in collaboration with the World Health Organization.

Professor Andrew Lowe, who coordinates agricultural research initiatives at the University of Adelaide and has collaborated with the HUMI team, is excited by the possibilities. He says that even though 90 per cent of the natural vegetation around the Adelaide Plains was cleared for farming or urban development, the remaining 10 per cent – at Mount Lofty, for example – provide vital ecosystem services such as habitat for bees and other pollinators, water filtration, carbon sequestration, nutrient cycling and nitrogen fixation. These just need to be expanded into urban areas again.

"The good news is we can return these natural soil microbiomes relatively quickly with a complex set of biodiversity plantings in urban environments," Andrew says. "You don't need large areas. Once you put the right mix back, the natural microbiome returns because microbes are highly dispersive, and when they settle in a suitable habitat, they form large colonies and do very well. Even if you do soil inoculations of positive microbes, you still need the plants in those systems for those microbes to survive in the first place."

It's an attractive vision: plant diverse species of trees, shrubs, herbs and grasses in open spaces – such as parks, along train lines, electricity corridors and the edges of highways – that not only make cities greener on the outside, but make us healthier on the inside. And maybe bring a little piece of Mount Lofty into every suburb.

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