Babies who share their homes with a dog are much less likely to grow up into adults with allergies than those who don't.

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MICROBIOME

Puppy power

Once anathema, it now seems that a 'dirty' environment can enrich a baby's microbiome and lessen her or his likelihood of developing everything from obesity to asthma. Again, it seems that we can rely on man's best friend to help us out.

BY SUJATA GUPTA

Two decades of research have made it clear that children who grow up with dogs have lower rates of asthma than those who do not. Many researchers attribute this finding to the hygiene hypothesis — the idea that exposure to a little dirt early in life can ward off allergic diseases that can appear later. Without firm data to show a link between owning a dog and improved immune health, however, the idea remained alluring, but unproven.

Perhaps mums who own dogs are healthier or more likely to breastfeed, says Anita Kozyrskyj, a paediatric epidemiologist at the University of Alberta in Edmonton, Canada. "It could be the lifestyle."

In 2013, Kozyrskyj set out to see if she could pinpoint what might be going on. Kozyrskyj's team evaluated the various microbes present in 24 faecal samples collected between 2008 and 2009 from 4-month-old infants enrolled in the Canadian Healthy Infant Longitudinal Development (CHILD) cohort study. Of the 24 babies, 15 lived in houses with at least 1 dog or cat[1].

The researchers discovered that infants living with pets had a higher diversity of microbes in their guts (as measured in their faeces) than infants without pets. A generation ago, Kozyrskyj's findings would have been cause for alarm. Microbes — synonymous at the time with germs — were thought to be best kept at bay. A family history of allergies may even have prompted physicians to advise expectant parents to give up the family pet.

But now, says Kozyrskyj, it's known that the immune system develops alongside the gut microbiome — the genetic material of the community of microorganisms that live in the gut. That means that if infants grow up with limited exposure to microbes, such as those present in dog fur or those tracked into the house on muddy paws, the child's immune system may deem those particles worthy of attack.

This lack of exposure to microbes is especially problematic in developed countries, where people spend most of their time indoors. Researchers are beginning to suspect that dogs present one way for people to safely sully a baby's environment.

It's premature, however, for doctors to start writing prescriptions for pooches. Kozyrskyj's study was too small to draw any firm conclusions. Rob Knight, a microbiologist and director of the Center for Microbiome Innovation at the University of California, San Diego, points to the gaps that remain to be filled. "What hasn't been done is the type of intervention study that would definitively prove that if you got a dog, it would improve your child's health," says Knight. "But there are a lot of different lines of evidence that point in that direction."

THE THEORY

In developed countries, the incidence of allergic and autoimmune diseases has been rising for decades. In 1989, David Strachan, an epidemiologist now at St. George's, University of London, found that children who grew up with more siblings had lower rates of hay fever than those with fewer[2]. Strachan, who introduced

the hygiene hypothesis, proposed that the rise in allergic diseases was the result of cleaner environments brought about, in part, by higher standards of personal cleanliness.

Many researchers have since confirmed that exposure to a little dirt — through siblings, growing up on a farm or living in a developing country — can be beneficial and even ward off disease. For instance, in 2015, capping decades of observations, researchers quantified the reduction in risk of asthma for children growing up with dogs[3]. The investigators combed through the records of more than one million children born in Sweden between 2001 and 2010. Of the 275,000 or so school-age children in the cohort, the researchers found that the children of dog-owning families had a 13% lower chance of developing asthma than their peers who grew up without a dog.

The idea that pets can enhance the microbiome makes even more sense when viewed in light of the old friends hypothesis, a refinement of the hygiene hypothesis. In this view, humans' co-evolution with livestock and animals has made us dependent on their microbes for our health and even survival. Losing contact with these 'old friends' might tip the delicate evolutionary balance.

Researchers suspect that our long association with canines means that human and dog microbiomes may have developed in tandem. The microbiome of a baby growing up without a dog (and of a puppy growing up without a human) is, in a sense, incomplete. "All of the people alive today probably had ancestors who lived in tribes that hunted with dogs," says Jack Gilbert, director of the Microbiome Center at the University of Chicago in Illinois.

DOGS AS CONDUITS

Sorting out how dog microbes benefit humans is tricky. With disease, a single exposure can transfer pathogenic bacteria between dog and human and make the recipient sick. The exchange of non-pathogenic bacteria over long periods of time is less clear cut. But such sharing could be more common than previously realized.

Knight and his team compared microbes from the skin, tongue and intestines of 159 people and 36 dogs in 60 families[4]. They found that skin microbiomes of people in families with a dog were more similar to each other than the microbiomes of members of dog-free families. The dogs, in other words, were serving as microbial transfer agents.

Meanwhile, Gilbert made a serendipitous discovery of his own while studying what happens to a family's microbiome after a move to a new home[5]. Gilbert and his team had recruited seven families, including three on the verge of moving, and started swabbing microbes from the participants' homes and bodies. Then, Gilbert recalls, "we walked into one of the homes and discovered three dogs." Gilbert knew that the dogs must also be influencing the microbial composition of the household, so he told his team to swab them, too. At another house, the researchers also roped in a cat.

When Gilbert mapped the movement of bacteria between all the mammals and objects in the home — the surfaces, humans, dogs and cats — he, like Knight, found that in the household with the dogs, the furry animals had a central role in moving microbes from person to person. (Gilbert also found that the occupants of a house harbour a unique microbial fingerprint that they carry over to a new residence.) But the health implications, if any, of that constant flow of microbes were murky.

A PROBLEM OF AGE

Whether dog-assisted microbial transfers cause lasting changes to humans' microbiomes is unclear. Knight collected data on his participants only once, and Gilbert's study tracked people for just six weeks. Perhaps the microbial transfer between dogs and people that Knight and Gilbert were seeing was transient. Knight says that he tried to conduct a follow-up study but too many participants had since divorced, or the family pet had died.

Research presented at the annual symposium of the Society for Animal Welfare Administrators last November has cast doubt on whether dogs' microbiomes affect those of adults. Twenty adults between the ages of 50 and 80 provided baseline blood, skin, saliva and stool samples, then temporarily cared for dogs from the local humane society. The volunteers were then re-tested at one-month intervals for three months. (Participants had the option to adopt the dogs at the end of the study).

Although the new dog carers saw a marked improvement in mood — they had lower levels of inflammatory cytokines that have been implicated in depression, dementia, diabetes, cancer and cardiovascular disease — the participants' microbiomes remained unchanged. "The dogs clearly impacted people's emotions and immune systems, but not through the microbiome," says study leader Charles Raison, a psychiatrist now at the University of Wisconsin–Madison.

"Dogs protect kids because the kids' microbiome is still forming."

To Raison, this finding suggests that there is a crucial window during which exposure to dogs (and other sources of dirt) matters. That conclusion squares with several other studies showing that the human gut microbiome is largely established during the first few years of life. "One of the interpretations is that dogs protect kids, especially in early childhood, because the kids' microbiome is still forming," Raison says. "In an old geezer, you're stuck with what you've got."

Back in Canada, Kozyrskyj expanded her pilot study from 24 to 746 infants, around half of whom were living in households with pets. Her team then compared the babies' microbial communities.

As before, Kozyrskyj found that microbial richness was higher in three-month-old infants with pets than in those without. What's more, the team was now able to show that babies from families with pets (70% of which were dogs) had higher levels of two types of Firmicutes microbes — *Ruminococcus* and *Oscillospira*, which have been associated with a lower risk of allergic disease and leanness, respectively. The team showed that an abundance of *Ruminococcus* reduced the risk of allergic disease.

"Pet exposure can reduce allergic disease and obesity" later in life, says Hein Min Tun, a veterinarian and microbial epidemiologist at the University of Alberta, who presented the team's findings at the International Human Microbiome Consortium in Houston, Texas, last November.

FUTURE DIRECTIONS

One endeavour that may yield some insight into the interplay between the microbiomes of humans and dogs is Knight's American Gut Project. In this citizen-science project, people pay to have their gut microbes analysed. For a little extra, the team will also sequence the microbes of the family pet, be it dog, snake or cockatoo. Knight has used the data from more than 10,000 humans and dozens of dogs to analyse hundreds of variables that affect the microbiome. The research is under review, but a key finding, he says, is that people with dogs seem to have more diverse microbiomes than those without, although other factors, such as antibiotic use and diet, seem to have a bigger role than dogs in making the microbiome more eclectic.

As sequencing gets cheaper, Knight hopes to translate those findings into medical treatments. For instance, he says, because overweight people tend to have heavier dogs, putting a dog on a diet could, in theory, transfer 'weight-loss' microbes to its owners.

Or, he says, it may become possible to isolate the beneficial dog microbes and create a drug that confers those benefits without having to own a dog. Knight muses on the possibilities. "Could you get the dog in a pill? Could you get the dog as a spray? Or maybe the dog could come as one of those air fresheners, one that wafts microbes as well as chemicals." Perhaps one day, having to breathe in the aroma of fresh dog will be a small price to pay for a healthier, leaner life. ■

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