PARASITES

Kitty carriers

A pathogen spread by domestic cats threatens the health of humans and livestock. Could a solution as simple as taking better care of cats help to combat the infection?

BY SARAH DEWEERDT

The parasite *Toxoplasma gondii* is one of the most successful in the world. Its primary host is the cat, but the organism has managed to colonize nearly every ecosystem on the planet, even those that lack native species of cats. It has been found in creatures ranging from mice and muskrats to manatees — as well as humans.

Toxoplasmosis, the infection caused by *T. gondii*, can have serious consequences in humans. If a woman contracts toxoplasmosis during pregnancy, it can cause miscarriage, stillbirth or neurological problems in her child. And the parasite is the most common cause of infectious retinal disease. In Brazil, for example, where *T. gondii* strains are more virulent than those found in Europe and North America, almost one-fifth of human infections result in lasting vision damage¹.

The parasite can affect livestock too. Toxoplasmosis is one of the leading causes of miscarriage in domestic sheep and goats, placing a heavy economic toll on farmers. *T. gondii* is also implicated in a large number of deaths of southern sea otters (*Enhydra lutris nereis*) since the early 2000s off the coast of California².

It's possible that the risk to people could increase. Highly virulent strains that can cause severe illness and even death in healthy adults have been

Cats that catch their own dinner are the likely source of the toxoplasmosis parasite in the environment.

identified in the jungle ecosystems of French Guiana — areas that are separated from densely populated regions only by a porous and fragile ecological barrier³. For these reasons, scientists are trying to understand why *T. gondii* is so widespread and how it moves through today's environment.

T. gondii invades and lives inside the cells of other organisms. The single-celled protozoan owes some of its success to its unique biology — namely, its ability to establish and transmit infections through an unusually wide array of host species and to persist in these animals for years. But its prevalence is, in the most part, down to an aspect of history: the symbiosis between people and domestic cats that began around 10,000 years ago helped the parasite to become astonishingly abundant and widespread. Understanding this history illuminates the nature of the global spread of toxoplasmosis — as well as giving some clues about how to manage the infection. It turns out that the solution may involve not just science, but also compassion.

PATIENCE REWARDED

T. gondii has two major biological advantages: patience and flexibility. “*Toxoplasma* has this extraordinary lifestyle which is basically based on waiting,” says Jonathan Howard, an immunologist who studies the parasite at the Gulbenkian

Institute of Science in Oeiras, Portugal.

The sexual phase of its life cycle can take place only in the gut of a member of the cat family, and lasts a few days. At the end of this process, the parasite's oocysts, fertilized eggs enrobed in a tough, environmentally-resistant coating, are shed in cat faeces and can remain dormant, but viable in soil or water for more than a year.

When the oocysts are ingested by other mammals or birds, the parasite divides rapidly and then, after a week or so, forms tissue cysts in the animal's brain or muscles. There, the parasite can live for years waiting to be eaten by a cat to start the whole process again.

Although it can reproduce sexually only in cats, *T. gondii* can also reproduce asexually and establish a chronic infection in almost any mammal or bird species. “We have not yet found a warm-blooded vertebrate that is not susceptible to infection,” says Michael Grigg, a parasitologist at the National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland.

By contrast, most related species, such as the malaria-causing parasite *Plasmodium*, have a much more limited range of secondary hosts. What's more, *T. gondii* tissue cysts can form new infections when one secondary host eats another — when a fox eats a hare, for example, or when a person eats a sheep. Other similar parasites cannot move between secondary hosts in this way.

John Boothroyd, who investigates the biology of *T. gondii* at Stanford University School of Medicine in California, suspects that the fact that cats tend not to be picky about their

Egyptian mummy of a cat.

TOP: AMBRE HALLER/GETTY; BOTTOM: CM DIXON/PRINT COLLECTOR/GETTY

prey helps to explain *T. gondii*'s wide range of secondary hosts. "When they come out of the back end of a cat, they don't know whether the best way back in is through a sparrow or a crow or a mouse or a rat," Boothroyd says. So evolution has favoured a parasite that can establish itself almost anywhere.

GOING GLOBAL

As a species, *T. gondii* is thought to be about 11 million years old, although a genetic analysis published last December traces the origin of the strains now in circulation to South America about 1.5 million years ago⁴. From there, these strains would have moved into North America, then crossed the Bering Strait land bridge to colonize Asia, Europe and Africa.

This means that *T. gondii* had a global reach long before people domesticated cats, and even before modern humans evolved some 200,000 years ago. "It's likely that humans have been infected with *Toxoplasma* forever," says Howard. Early humans could have picked up the infection from oocysts shed by any number of African cat species, or by eating meat from infected game animals.

But there's no question that the domestication of the cat in Egypt and Mesopotamia, around the same time as the development of agriculture there, represented a big change for *T. gondii* — and an opportunity. "What happened 10,000 years ago was something really quite spectacular, which is that its definitive host became incredibly abundant," Howard says.

As predators sitting atop the food chain, cats are among the rarest animals in an ecosystem.

Most species of cat are also solitary. But with the advent of agriculture, *T. gondii*'s definitive host and multiple secondary hosts found themselves living together in close proximity.

This probably marked the beginning of widespread human infection, says Alan Sher, a parasitologist at the NIAID. And as domestic cats spread around the world, *T. gondii* went with them. The parasite population that now circulates in Europe and North America is dominated by a few strains that arose about 10,000 years ago. Some say that this lack of diversity is the signature of a parasite that has become adapted to a specific host — domestic cats.

"This is not dissimilar from what we've done with the rest of the landscape," says Benjamin Rosenthal, a parasitologist at the US Department of Agriculture (USDA) in Beltsville, Maryland. Especially over the past 500 years of colonialism and globalization, human activities have resulted in the homogenization of landscapes, with the same crops and weeds growing everywhere. "Our parasites may fall into that same pattern for similar reasons," he says.

VACCINE VEXATION

Domestic cats are by far the most numerous felines in the world. And a single cat can shed up to a billion oocysts in its faeces during the initial infection. Although these oocysts are produced only during the brief sexual phase of the parasite's life cycle, their hardiness means that there is always a large number in the environment.

In the past, it has been difficult to know whether people became infected with the parasite mainly through direct contact with these oocysts or by eating undercooked or cured meat from infected livestock. But researchers at the USDA have identified a molecule that is specifically produced by the parasite in its oocyst form, enabling them to identify the source of some infections⁵. A few studies using this technique suggest that it is the oocysts that are responsible for most human infections, says USDA scientist Jitender Dubey.

Oocysts are the source of infection for some vulnerable wildlife species, too. At first, researchers were puzzled to find toxoplasmosis in sea otters, because the marine mammals rarely come ashore and do not consume warm-blooded prey. But it turns out that oocysts washed into the sea from rivers and streams can remain viable in the bodies of cold-blooded creatures such as mussels and snails. Sea otters pick up the parasite from these favourite prey species.

If oocysts are the main problem, the question becomes: what is the best way to address it? One possibility is vaccination of the species that are vulnerable to infection. A vaccine is available for sheep and goats that can prevent miscarriage owing to toxoplasmosis, says Elisabeth Innes, an

immunologist at Moredun Research Institute near Edinburgh, UK, and one of the vaccine's developers. Her team has shown that the vaccine can also reduce the number of tissue cysts in food animals, potentially making the food supply safer⁶.

But it's a live vaccine, which not only reduces its shelf life but can also raise safety concerns, making it unattractive for human trials. Innes and other scientists are working on alternatives, but figuring out how to induce the sort of immune response necessary to fight off an intracellular parasite has been tough.

Another idea is to cut the oocysts off at the source by developing a vaccine for cats. "That's the one that I think would have the biggest impact," Innes says. Researchers in the United States have developed an experimental version of such a vaccine⁷. But it involved growing a weakened mutant strain of the parasite in mice, then feeding the brains of infected mice to cats — a strategy that would prove hard to scale up.

Some scientists worry that even if a vaccine for cats was available, it might be a tough sell for cat owners because *T. gondii* poses little health risk to cats themselves. And vaccinating pet cats might not even solve the problem. Pets that are well cared for — even if they have access to the outdoors — have very low rates of infection⁸. Feral cats left to fend for themselves are the likely source of most oocysts in the environment. The common public-health warning that pregnant women should avoid cleaning cat litter boxes is a helpful precaution, but may not be sufficient, says Patricia Conrad, an animal-health researcher at the University of California, Davis. People are more likely to encounter the parasite when gardening, while playing in a sand box (a common source of exposure for children) or through bodies of water such as puddles or ponds.

But a study by Conrad's team suggests an opportunity⁹. When feral cats are fed by humans, they eat less wild prey that may be infected with *T. gondii*, and their risk of becoming infected with, and transmitting, the parasite declines significantly. One solution to the toxoplasmosis problem may not be scientific at all, but ethical. As Conrad puts it: "We have shown that the more you care for your cats, the better." If only all health problems benefited from such a virtuous circle. ■

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