What Might Cause Parasites To Become More Virulent

The traditional medical wisdom of the past 100 years has taught doctors that disease-causing pathogens evolve to become more benign over time. Otherwise, the theory goes, they will kill off their hosts—and thus themselves as well. But over the past decade, this comforting idea of a world growing toward greater cooperation and mutualism has been challenged by biologists who hold a different—and still controversial—view based on the application of Darwinian evolutionary theory to the study of human disease. Their much more unsettling prediction is that if a pathogen can be transmitted easily from one host to another, it will be less dependent on its current host and will likely become more virulent as it selfishly turns the host's resources to its own purposes. Now comes the first support for this heretical view from a study of a natural population—albeit one far removed from human medical practice.

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Evolutionists' friends. Fig wasps' habits make them good subjects for studying parasite virulence.

On page 1442, Allen Herre, a fellow at the Smithsonian Tropical Research Institute station on Barro Colorado Island in Panama, reports the results of a 10-year field study of the parasitic relationship between tiny wasps living in Panama's riverine fig trees and the even tinier nematodes (roundworms) that infest them. His conclusion: The easier it is for a species of nematode to find new host victims the more virulent that nematode appears to be, fitting the heretics' predictions to a "T." Paul Ewald, an evolutionary biologist at Amherst College in Massachusetts and a leading proponent of "Darwinian medicine," calls Herre's study "beautiful," adding that it's "more powerful than anything that's been done in the past." Even researchers who have criticized the Darwinian medicine view of virulence evolution as lacking an empirical foundation welcomed Herre's study. "This first demonstration of a range of virulences evolving in response to differences in transmission rates in the wild is quite important," says one of them, research fellow Andrew Read of the University of Edinburgh, Scotland.

And it may be important practically as well as theoretically. If the proponents of Darwinian medicine are correct, decreasing disease transmission rates can not only stop the spread of infectious human diseases, it can also decrease their virulence.

Herre's ability to perform his study depended on the unusual life cycle of the fig wasp. The female of the species lays all her eggs within a single fig. As a result, Herre was able to count all the progeny produced by an infected or uninfected female by looking inside a single fruit, thus quantifying the most evolutionarily relevant measure of virulence, its toll on a female's contribution to future generations. This elusive variable, while crucial to evolutionary theoreticians, can't be measured in most natural systems.

The females of the 11 wasp species studied by Herre have different egg-laying habits. Females from some are nearly always found laying eggs alone in their figs while in other species multiple females are nearly always found together. Though Herre originally collected these data for a study on sex ratio variation among the wasp species, he realized that their differences also provided the opportunity to study the effect of transmission rates on the virulence of the wasps' parasites. Herre then found that when multiple wasps were present in a fig, providing a nematode with ample opportunity to escape its original host and attack the offspring of another, the worms seemed to use their hosts more carelessly in that infected wasps produced significantly fewer offspring.

In addition, Herre found that all 11 nematode species he studied were members of a family dominated by species that form harmless associations with their hosts. Membership in such a benevolent clan suggests that the ancestor of the parasites was a much more benign nematode. Once again, contrary to conventional wisdom, rather than evolving to become benign, these nematode species appear to have done just the opposite, Herre says. He also points out that they apparently had plenty of time to become less virulent, if that's the way evolution was driving them.

His studies of DNA patterns in the fig and wasp species suggest they diverged in tandem over the aeons, indicating that they've been associated a long time, perhaps 40 million years. And around the world, wherever figs are found, so are both the wasps and nematodes, suggesting that the wasp-nematode relationship is similarly ancient. Says Herre, "In all likelihood, the first wasp entering the first fig millions of years ago was probably carrying a nematode. Yet we still have some nematodes that are very, very nasty."

While researchers have praised Herre's as the first study to test theories on the evolution of virulence in the field, Jim Bull and colleagues at the University of Texas at Austin are credited with doing the first and some say most rigorous test yet of the theory. In the laboratory, the Texas group infected the bacterium *Escherichia coli* with a bacterial virus. When the virus was not provided with new bacterial cells to infect, effectively tying its fate to its current victim's lineage, it quickly evolved to be more benign, producing fewer harmful toxins. When the same virus was supplied with more opportunities to infect new bacterial hosts, it once again became more virulent.

Though the Texas study has been the only one to actually manipulate transmission frequencies, even Bull concedes it has not held much sway with the medical community, as the study of bacteria and their viruses seems too far a cry from humans and human disease. "This whole area is still in its infancy," he says, and well-supported explanations for the evolution of human disease may be a long time coming.

And more evidence will certainly be needed to convince such critics of Darwinian medicine as theoretician Bruce Levin of Emory University. Levin takes issue with Darwinian medicine's fixation on evolution of virulence as an adaptive strategy by a pathogen. "I don't disagree with the fact that there's a positive relationship between ease of transmission and virulence," he says. "But I don't think transmission explains all or even most of virulence." In particular, he has suggested the possibility that virulence might actually be coincidental to a pathogen's well being.

Nevertheless, Bull suggests that Herre's study is an indication that the theory so far has pointed biologists in the right direction. "Evolutionary biologists don't often come up with a principle that can cleanly extend from something as bizarre as fig wasps to bacteria and bacteriophage," he says. I think that's the appeal of this new study. In the end we may discard the idea but for now we have to hammer away at it until we see what we get."

–Carol Kaesuk Yoon

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