This Week in Evolution

"Darwinian Agriculture" (2009?) author R. Ford Denison discusses recent papers on evolution.

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Mixed infections, for better or worse

If being infected is bad, is being infected by two different pathogens at once even worse? Not necessarily, as this week's paper shows. "**Quorum sensing and the social evolution of bacterial virulence**" was published in *Current Biology* by Kendra Rumbaugh and colleagues. Their results contradict an earlier prediction, although not the fundamental evolutionary principle behind that prediction.

The fundamental principle is that a multiply infected host is analogous to grazing land shared by several families, with no overall regulation. Garret Hardin used this example in his 1968 essay, "The Tragedy of the Commons." If the land is owned by only one family, they might limit the number of sheep to what the land can feed sustainably. If ten families share the land, however, each might reason that "one more sheep (ours) won't do much harm, relative to the ten already there, and we'll have another sheep." Together, they add ten more sheep, destroying the grass.

Similarly, if most hosts are infected by only one strain of bacteria, those strains that kill their host to quickly (before spreading to another host) will tend to die out. With mixed infections, there is no benefit to self-restraint, as the other strain may kill the host anyway. Based on this idea, George Williams and Randolph Nesse (in "The Dawn of Darwinian Medicine") predicted that "diseases that result from single infections of a host will be less virulent than those that normally arise from multiple infections from different sources." (The "normally" is what makes this an evolutionary argument. We need not assume that strains act differently when they are part of a mixed infection, but only that their behavior has been shaped by past natural selection. Natural selection is less likely to have favored restraint if most past infections were mixed.)

The prediction that mixed infections will be more severe assumes that "selfish" bacteria cause more damage to the host than those that "cooperate" with other bacteria in that host. This is true if cooperation equals restraint, but there are other kinds of cooperation.
In particular, some bacteria release "virulence factors", molecules that are expensive for an individual bacterial cell to produce but which benefit bacteria collectively (at the expense of the host) by breaking down defenses or releasing nutrients from host tissues. With one strain per host, a strain that doesn't produce virulence factors may die out. But what if hosts are often infected by two strains at once?

In that case, strains that do not produce virulence factors may outcompete those that do. This is because they can benefit from virulence factors produced by another strain in the same host, without paying the cost of producing virulence factors themselves.

To test this hypothesis, the researchers infected mice with one or two strains of pathogenic bacteria. With one strain at a time, strains that made virulence factors killed the mice faster, as expected. A mixed infection, however, was no more lethal than the no-virulence-factor strain alone. You might expect lethality intermediate between the two strains, but only if you ignore evolution.

The cost savings from not making virulence factors was enough that the low-virulence

mutant increased in frequency (e.g., from 1.3% initially to 32.4%) at the expense of the strain making virulence factor. The “cheater” that didn’t make virulence factor had higher fitness when rare, so increased in frequency. Once they became a larger fraction of the population, their relative fitness benefit decreased, because there were fewer bacteria making the virulence factor they need. This sort of frequency-dependent selection is common and not surprising, but it suggests that the 50:50 mixture probably didn’t evolve to 90% low-virulence cheaters. So maybe the fact that the 50:50 mixture was no more lethal than the low-virulence strain alone is surprising after all. Does making half as much virulence factor result in much less than half the virulence?

Posted by R. Ford Denison on March 3, 2009 04:46 PM | Permalink

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