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Applied Darwinian medicine: Artificial selection for less-harmful parasites

The short generation time of many pathogens causes serious medical problems, such as the evolution of resistance. However, this causal force can be used against pathogens, potentially inhibiting or preventing the spread of some diseases in humans.

More or less virulent strains of infectious diseases can be produced *in vitro* (e.g. [2]) and infectious agents can be engineered to depend on a cofactor such as an enzyme in order to survive. (Providing a population of pathogens large amounts of a cofactor leads to selection for strains that do not have the burden of retaining the cellular machinery for the production of that cofactor. Selection can therefore do the work that might otherwise be difficult or impossible with current alternative technology.) A virulent, cofactor-dependent strain can then be released, along with the cofactor, into natural populations, such that it outcompetes the natural strain, driving down the frequency of the natural strain, at which point the cofactor can be removed and we are left with much lower rates of any strain than prior to the intervention. In principle, such a strain could even be introduced into individual hosts along with continuous doses of the cofactor; after the cofactor-dependent strain spread at the expense of the original pathogen, the cofactor could cease to be administered, leading to the death of the cofactor-dependent strains.

Ito et al. [1] produced a genetically-altered mosquito that is incapable of passing malaria to people. However, absent a selective advantage, such mosquitoes, if released into the wild, would not necessarily become the dominant strain. But, again in principle, such a mosquito could also be selected through careful artificial selection to be able to feed on a substance wild-type mosquitoes cannot, and that substance could be provided by people in regions with high prevalence of malaria. Mosquitoes reproduce sexually: by releasing malaria-safe

males and providing them with a selective advantage (e.g. keeping them especially well-fed), the anti-malarial gene could rapidly spread through the population. (To speed the process of replacing harmful mosquitos with harmless mosquitos, the provisioning substance could include a poison that especially affects non-engineered mosquitos.)

We might produce and provision new strains of mosquitoes and cockroaches that fear people and would spread at the expense of current strains, leaving us with less harmful and more controllable parasites and pests. We could then decide to live with or exterminate these relatively harmless populations. Artificial selection turned wolves into poodles. Now, combining what we know about the evolution of virulence, sexual selection, and genetic engineering, we might do the same for a wide variety of human pathogens.

References

- [1] Felton L, Dougherty K. Studies on virulence: II. The increase in virulence in vitro of a strain of Pneumococcus. *J Exp Med* 1924;39:137–54.
- [2] Ito J, Ghosh A, Moreira LA, Wimmer EA, Jacobs-Lorena M. Transgenic anopheline mosquitoes impaired in transmission of a malaria parasite. *Nature* 2002;417:452–5.

Robert Kurzban
University of Pennsylvania,
Department of Psychology, Philadelphia,
PA, United States

Marc Egeth
The Children's Hospital of Philadelphia,
Department of Radiology,
3400 Civic Centre Boulevard, Philadelphia,
PA 19104, United States.
Tel.: +1 215 519 2577.
E-mail address: marcege@yahoo.com