

Comparative biology and disease ecology

Diseases transmitted during human sexual activity have received considerable attention from the scientific community. In contrast, sexually-transmitted diseases (STDs) of non-human hosts have been largely ignored or treated as rare curiosities, despite some well-documented cases of economic or conservation importance¹. But there is now a compelling case for more attention. A recent, monumental paper by Lockhart, Thrall and Antonovics² provides a wealth of evidence that STDs are extremely widespread. Furthermore, STDs differ consistently from what Lockhart *et al.* term 'other infectious diseases' (OIDs) in their ecology and disease severity. These differences are broadly as expected from theory, but Lockhart *et al.*'s discussion illustrates the complementary views offered by models of population dynamics and of adaptive evolution. Altogether, these recent analyses illustrate the potential of comparative analyses in the study of infectious disease agents.

From an extensive literature survey, Lockhart *et al.* document over 200 diseases from 27 host orders for which there is evidence of sexual transmission (for three-quarters of the diseases the evidence for this mode of transmission was either strong or unequivocal). The only taxa which seem to escape relatively unscathed are those with external fertilization. The parasites responsible show similar taxonomic breadth, with viruses, bacteria, nematodes and protozoans being particularly well represented. This review contains some fascinating natural history gems; our favourite is a (possibly) sexually-transmitted viral parasite of an order of nematodes parasitizing invertebrates. As Lockhart *et al.* point out, one factor common to almost all documented non-human STDs is that they involve infections with possible economic implications. As a consequence, the frequency of STDs is surely greatly underestimated: there are no good reasons to suspect that most animal species will harbour fewer STDs than humans (29 STDs in this review, which excludes those transmitted through oral or anal sex).

A key ecological difference between STDs and OIDs lies in their dynamics of transmission^{3,4}. OIDs (for instance, those spread through air, such as measles) can be reasonably well modelled by assuming that their transmission depends upon host density. In contrast, the transmission of STDs is more likely to depend upon the number of sexual contacts that individuals have, which may bear little relation

to density (except in very unusual night clubs⁵). Instead, the frequency of infected individuals in the host population is critical. From this difference, Lockhart *et al.* make a series of simple predictions about the disease phenotypes likely to evolve. For example, where host sex is confined to a short season in each year, and where within each such season an infected individual has limited opportunities to mate, sexually-transmitted parasites will be selected to cause long-lasting, persistent infections (decreased mortality) with long incubation periods, relative to OIDs. Even if STDs can't induce hosts to mate with more individuals, they should minimize their effects on sexual interest and attractiveness (decreasing virulence). Further simple predictions made from similar considerations can be found in Table 1.

These predictions were then tested by a comparative analysis of how STDs and OIDs differ in disease ecology. Much of the raw data were collected by parasitologists without the express aim of providing material for ecologists with an inclination to comparative analyses; consequently, data concerning some interesting variables (for instance whether infection by STDs affects host sexual activity differently from OIDs) are often absent or not very reliable. While these absences affected the power of some analyses, Lockhart *et al.* attempted to compensate for variation in the quality of data by restricting their analyses to relatively well-characterized diseases of mammalian hosts, and by varying the statistical weight of data based on assessments of its reliability. Their analyses also attempt to correct for phylogenetic non-independence by pairing each STD with an OID caused by a taxonomically similar parasite.

The resulting analyses reveal strong evidence for associations between mode of transmission and the diseases that they cause in their hosts: a selection of their predictions and the results of a suite of analyses are given in Table 1. In general, STDs, relative to OIDs, can be characterized as being less severe, and endemic rather than epidemic. An indication that the two classes of diseases really do have appreciably different ecologies is provided by the ability of a discriminant function to correctly classify almost all diseases based on characteristics of the disease such as length of infectious period, host range and the length of asymptomatic periods. The clear difference in virulence between STDs and OIDs can be taken as further support for the idea that selection pressures associated with different modes of

transmission are responsible for observed variation in virulence⁴⁻⁸.

In their paper, however, Lockhart *et al.* also consider an important alternative explanation derived from the ecological wing of evolutionary ecology. The idea is that 'ecological assembly rules' might predominate, such that the dynamical stability of particular host-pathogen interactions is the principle cause of the biological differences between OIDs and STDs. Ecological differences between species using different modes of transmission would occur if particular biological characteristics of the pathogen (e.g. rapidly killing their hosts) resulted in unstable host-pathogen dynamics in one transmission mode, but not the other. This idea is analogous to explanations of the characteristics of taxa inhabiting islands being based upon how the characteristics of taxa inhabiting the mainland affect their probability of successfully colonizing the islands, rather than resulting from micro-evolutionary change following colonization.

They assess the statistical support for the two ideas by constructing two different path analytic models, which specify differing causal relationships among the sets of variables measured. In both cases, the data fit the models reasonably well, although restriction of the analyses to those diseases that currently use sexual transmission as their main route suggests that variation in disease ecology may be best thought of as a pre-adaptation to evolving sexual transmission, so that ecological assembly rules might be the critical determinant. But given the patchiness of the data available for this analysis, it is unsurprising that no firm conclusions can be drawn about the direction of particular pathways. In reality, both processes are probably going on. Currently, the literature on evolution of virulence is largely concerned with optimizing selection, and at the very least, models based on the idea of ecological assembly rules might provide a profitable null hypothesis against which to test more complex hypotheses involving selection. The best test would probably involve long-term study of a single host-parasite system under artificial selection.

The effects of STDs upon the evolution of host mating behaviour has been an area for occasional speculation among evolutionary ecologists⁹⁻¹¹. Given the dependence of STD dynamics on the frequency of host sexual contacts, one might suggest that STD virulence and the frequency of mating with different partners would be subject to coevolution (something for which it has been claimed that there is evidence for HIV in humans⁵). Unfortunately, quantitative data on mating behaviour are scarce. However, the authors have for

Table 1. Associations between transmission mode (STD: sexually transmitted disease; OI: other infectious disease) and some characteristics of disease ecology^a

Disease characteristic	Prediction	Statistical support		
		Means analysis	PCA ^b	Path analysis ^c
Mortality/severity	OID>STD	Yes	Yes	Yes
Length of infection	STD>OID	Yes	Yes	Yes
Localization of infection	OID>STD	Yes	Yes	Yes
Host immunity	OID>STD	Yes	Yes	Yes (indirect)
Host range	OID>STD	Yes	Yes	Yes
Sterility	STD>OID	No	Yes	Yes?

^aAdapted from Ref. 2.

^bPCA, Principal Components Analysis.

^cResults presented for path analysis refer to a model postulating a causal effect of transmission mode.

some time worked on a system which provides support for these ideas. Another smut diseases of flowering plants are transmitted by pollinators and are therefore plant STDs; although the presence of pollinators as vectors adds some complexity, they have recently attracted attention as a model system for the study of epidemiology and ecology¹². In an analysis of plant hosts of these diseases¹³, it was found that host species that undergo more outcrossing and had larger floral displays (both likely correlates of the extent of multiple mating) harboured more smut diseases.

Lockhart *et al.*'s work is important for several reasons. It demonstrates beyond any doubt the ubiquity of STDs, and suggests that any biologist interested in mating behaviour and parasite-mediated selection should consider the role that STDs have played in structuring the system that they work with. Second, their

analyses provide striking support for the idea that the characteristics of diseases are inextricably linked with their ecology. Finally, their work should serve as an example of the scope possible for comparative analyses of disease; even in the face of data of varying quality, collected for reasons quite unconnected with the purpose of the analysis, it is possible to uncover unsuspected patterns.

Acknowledgements

We are grateful to A. Buckling, M. Mackinnon and P. Thrall for comments, and to NERC and BBSRC, respectively, for research fellowships.

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The breath of life – did increased oxygen levels trigger the Cambrian Explosion?

A literal reading of the fossil record would suggest that something uniquely strange went on during the first 10 million years of metazoan evolution. Metazoan animal life as we know it did not appear until the Cambrian, 544 million years ago^{1,2} (apart from the enigmatic 560–590 million year old Ediacaran fauna). But just 10 million years later the metazoans had achieved their maximum Cambrian diversity: well-preserved fossil representatives of two thirds of all known phyla are present in rocks about 533 million years old. A flurry of recent research agrees with Darwin's suggestion³ that the absence of fossil evidence of the metazoans before the Cambrian Explosion is not evidence

that the metazoans were absent. The Cambrian Explosion may not record the origin and explosive radiation of metazoan phyla, but instead it may record an extraordinary period when most of the known phyla simultaneously acquired both the large size and hard skeletons required for fossilization. Several recent independent studies provide molecular clocks that date the origin of the metazoans to at least 400 million years before the Cambrian. Developmental arguments suggest that there may have been a long period of cryptic evolution when metazoans resembled modern planktonic larvae (which do not fossilize). Finally, recent analysis of the ancient atmosphere⁴ may have provided a reason

why so many phyla first appear in the fossil record simultaneously. The Cambrian Explosion may have been triggered when rising oxygen (O₂) concentrations passed a threshold that permitted the development of large size and hard skeletal structures.

The origin of the metazoans has been put firmly back into the middle of the proterozoic era, at about 1000 million years ago, by two independent molecular clock estimates of the times of divergence of the major animal groups. Doolittle and co-workers⁵ use amino acid sequences from 57 different proteins, and Wray and co-workers⁶ use DNA sequences from seven genes to provide molecular clocks calibrated against the vertebrate fossil record (reviewed in the previous issue of *TREE* by Michael Bell⁷). The amino acid clock suggests a divergence time for the two main metazoan groups (Deuterostomes and Protostomes) of about 675 million years ago, while the DNA sequence clock suggests that this split had already occurred