

Parasite variation: immunological and ecological significance

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Preface

All organisms vary genetically and, hence, phenotypically. This variation is the stuff of evolution. This variation also affects where organisms live and what they can do to each other and to their environment. In these respects, micro- and macro-parasites are no different than any other organisms. The only special condition is that a significant part of their habitat is other organisms. Parasite variation which alters the interaction with the host environment should be of particular anthropocentric interest and significance. Variation that brings about reduced host fitness means disease and increased host mortality; variation that increases host fitness is a means by which we can effect parasite control.

Yet, with a few notable exceptions, parasitologists have not had a glorious history of taking account of virtually any aspect of parasite variation. Much parasitology is based on a single, long-term laboratory isolate maintained in a host (= environment) in which it does not naturally occur. This is true even for many of the protozoa, where there is overwhelming evidence of substantial genetic variation. It is hugely unlikely that this variation has no implications for our understanding of pathogenesis, infection and transmission. A paradox for sociologists of science is why it is that parasitologists typically ignore phenotypic variation in traits that matter, while geneticists have a long and noble history of investigating some of the least important traits imaginable (e.g. number of bristles on a *Drosophila* leg).

Parasites of vertebrates have to contend with the acquired immune response, an adaptive, dynamic and potentially deadly host defence. Given the huge selection pressure this must impose on parasites,

determining how parasites deal with immunity is to not only understand a remarkable aspect of biology, but also something of practical significance. Yet, here it is hard not to feel that the forest is being lost for the trees. We have an ever more exquisite understanding of the molecular control of antigenic variation in some taxa (e.g. trypanosomes) and are racing towards the same goal in others (e.g. *Plasmodium*). Conventional wisdom posits that antigenic variation has evolved for immune evasion, but there is no direct evidence to show that antigenic variation actually increases parasite transmission. It may be difficult to understand why else it exists, and the fact that so much genome is given over to it certainly argues that it must have some important fitness consequences. But we should not accept something just because we lack the imagination to consider alternatives. Moreover, if the idea is right, it ought to be able to explain why, for instance, an antigen repertoire is not larger or smaller. Further, we should not overlook challenging data: the free-living ciliate *Paramecium* has antigenic variation too, yet they never encounter a vertebrate immune system.

Parasite variation may also be responsible for variation in disease severity. Despite the many studies trying to find host genes associated with the outcome of parasite disease, we know of only one which has attempted to estimate just how important host genetic variation really is (Mackinnon *et al.* 2000). In that case, it explained about 10% of the variance in disease severity, even though the study concerned malaria parasites, one of the textbook situations where host genes are supposed to be important. Measured environmental variables accounted for perhaps another

20% of the variation, but what explains the remaining variation? Surely it is time to measure the contribution of parasite variation to disease severity?

The papers in this volume are the result of a meeting that considered parasite variation with a particular focus on its environmental significance. The full range of parasites were represented, and were considered from an empirical, theoretical (and even anecdotal) view. It is clear that there is substantial variation within and between genotypes of parasitic protozoa, but that the actual effect of this in infections is still unclear. It is also abundantly clear that helminths vary in very many important ways, if one bothers to look. What does all this variation mean?

A recurring theme of the talks, and the papers in this volume, is the difficulty of obtaining relevant experimental data about the ecological and immunological significance of parasite variation. Endoparasite variation is hard to work with, even where appropriate animal models exist. Many of the phenotypes are ephemeral, and many depend on the precise environment in which the parasites are present. And while numerous laboratories have worked on a diversity of rodent hosts, because they can be readily obtained, almost all work with a single parasite strain. Part of this is surely habit, but it is difficult to escape the feeling that focusing on parasite variation is to open a can of worms. If we allow that host variation, parasite variation, the environment *and* the two-way and the three-way interactions are all important determinants of disease and epidemiology, we need vast numbers of experimental treatments to make

progress. Nonetheless, ignoring complexities is not the way to understand them.

The meeting took place in London at the Linnean Society of London only yards from the building where Darwin and Wallace presented their joint paper on the significance of biological variation. We thank the Society for their outstanding hospitality, particularly their enthusiastic distribution of wine. The meeting took place three days after the 11th September terrorists attacks. The resulting chaos prevented Dennis Minchella (Purdue University, IN, USA) from presenting the Wellcome Trust lecture. We are grateful nevertheless for his contribution to this volume. Two of the talks given on the day do not appear in this volume: Andrew Read filled Prof. Minchella's programme slot with a talk about virulence variation in malaria parasites, and Chris Newbold gave a stimulating view of antigenic variation in *Plasmodium*. We are grateful to all the contributors for their contributions to the meeting and this volume, and to Les Chappell and John Lewis for gentle and not so gentle nudges at usually appropriate times. We are grateful to the Wellcome Trust and Cambridge University Press for financial support for the meeting.

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