Letters Response

Response to: Eliot and Gandon and Day: Revisiting virulence management

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Virulence management is the proposal to manipulate human activities in order to direct the evolution of parasites towards lower virulence. Our article [1] criticized proposals for virulence management on the grounds that current data do not support such proposals. We further suggested that models underlying many of those proposals are too distinct from biology to warrant such proposals.

It is important to distinguish virulence management from virulence evolution. The premise of virulence management is the promise of large and rapid evolutionary changes in virulence. By contrast, studies of virulence evolution can address virulence changes over any scale of time and magnitude. We had specifically challenged virulence management.

Our pessimism on current views of virulence management began from two lines of observation that are not challenged by either Gandon and Day's or Elliot's letters. First, the literature does not support the view that many infectious agents have evolved new levels of virulence in recent years, despite profound changes in intervention and cultural practices (e.g. use of vaccines, modern hygiene, medical treatment). Some of these changes should have selected large changes in virulence if the theory was correct. We hope that our article will encourage researchers to determine whether the general impression is true or that virulence might instead have changed over time (e.g. nutrition has also changed and could mask changes in virulence). Second, experiments to test predictions of the trade-off model have not been supportive or have resulted only in weak effects. These two lines of argument led us to doubt whether approaches based on present theories will be widely successful. We suggested some reasons why the theory might be problematic, chiefly that current models might not incorporate sufficient biology.

Virulence management proposals assume that high levels of virulence curtail parasite transmission, an assumption known as a trade-off. Explicit trade-off models usually assume that virulence is manifested as host mortality, and transmission stops only when the host dies. We think that virulence management based on this simple trade-off model is unlikely to succeed because the rapid and profound virulence evolution needed to justify virulence management requires extreme and unrealistic trade-off functions (i.e. that small changes in transmission cause large changes in host mortality). By contrast, long-term processes of virulence evolution can be explained without extreme trade-offs and is thus more likely to succeed. A more realistic view of trade-offs should include not only host mortality, but also the immune response, the time course of infection and perhaps tissue tropisms of infection. Recent papers that identify pitfalls of, or provide useful extensions to, the trade-off model take an important step in this direction [2–4]. A greater realism should benefit both bodies of theory, but is especially relevant to understanding the potential for virulence management.

Adding greater realism to the models could have its downsides. When studying two-species systems (here, a host and a parasite), researchers invariably discover that much of the system's behaviour is due to interactions, which are often highly specific to the host and to the parasite. If the outcome of an interaction is system-specific, generalized models might perform poorly in predicting the course of virulence evolution in the short term (relevant for virulence management), even if the underlying basic model for virulence evolution is correct and useful in the long term. For a powerful and satisfactory management of virulence, it might be necessary to construct system-specific models, which take the details into account and thus do not generalize. Just as we use specific drugs for different parasites, and even different variants of the same parasite, we might need different models to understand how to manage virulence in different infectious diseases. This view is not at variance with either letter; instead, it challenges many of the earlier proposals to manage virulence.

We share the view that more work is warranted to understand virulence evolution and virulence management, and we acknowledge that many studies of virulence evolution and some of virulence management have been appropriately cautious. We would be delighted to be wrong in our doubts, but we feel that at least some balance is needed in discussions of virulence management, because the evidence does not yet offer much promise.

We hope that our article inspires broader approaches to studying virulence evolution and management. There are demonstrated applications of evolutionary theory in medicine and biology that warrant considerable enthusiasm for extending theory to other problems. At the same time, we need to discuss where our efforts are best applied.

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References

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