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Lost in transmission..?

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Introduction

Parasites and pathogens (hereafter referred to collectively as parasites) can have devastating consequences for the individuals they infect, with Ebola and Zika being (at the time of writing) only the most recent examples in a very long list. When we think of the plethora of infectious diseases affecting humans, livestock, wildlife and all plant life, it is easy to be overwhelmed by the sheer taxonomic and life-history diversity of the parasites involved. However, despite this diversity, all infectious agents have one fundamental and essential aspect in common – they all require transmission to pass from one host to another. Indeed, transmission can be thought of as a scaling process, linking the occurrence of infection at the individual host level to the spread of that infection through the host population, or even the wider host community. However, by being a linking function between scales, transmission is notoriously hard to measure; almost always impossible to observe directly, and hence must generally be inferred from observing changes in patterns at either the individual or population levels. Despite this, it is of fundamental importance for disease management. Hence, we need clear conceptual and theoretical frameworks to understand it, coupled with appropriate technical and statistical methodologies to quantify it.

Given the clear importance of transmission in driving infection emergence and spread, the British Ecological Society's "Parasites & Pathogens" Special Interest Group (<http://tinyurl.com/BESP-and-P>) organised a retreat in Gregynog Hall in mid-Wales (www.gregynog.org) in September 2015 to discuss this important but complex topic. The retreat brought together individuals from a diverse range of backgrounds, with different interests and skills, working on a diverse range of host-parasite systems, and tasked them with defining, with respect to transmission, i) where the state of the art currently stood, ii) what the key gaps in knowledge were, and iii) what steps might be taken to move the field forward to fill such gaps. Thirty-four people attended, from universities both across the UK, and elsewhere (USA, Canada, Australia). Deliberately, no discussion topics were set at the start; however the initial discussions were framed following Keynote talks by two 'facilitators': Janis Antonovics (University of Virginia) and Joanne Webster (Royal Veterinary College), and the contents of those talks are summarised in their respective introductory papers ([1] and [2]). Those keynote talks raised a number of challenges and open questions that promoted debate and discussion and helped to define the areas taken forward for further exploration. The various participants then self-assembled into sub-groups to discuss these different aspects of transmission in full over the next three days. The papers in this issue [1-15] largely represent the outcome of this process, with a few solicited to expand on areas not wholly covered at the retreat. While the list of topics represented within this issue may not be a completely exhaustive list of key topics in transmission, we believe

that the broad profile of attendees has ensured that we have captured the majority of key challenges facing researchers in this field. We hope, therefore, that the volume will represent a substantial resource for future research.

Overview of papers and emerging topics

Despite the diversity of perspectives, skills and interests of the participants, recurring themes emerged. One important theme was that, despite standard formulations in epidemiological models, 'transmission' is not a single process, but comprises several discrete steps, and that more explicit consideration of each of these steps may provide important insight into the host, parasite and environmental factors affecting the overall transmission process [1-3, 6, 11, 12, 15]. For example, McCallum et al [11] explicitly considers interaction of the various steps involved in successful transmission from the initial infection load in an infected 'donor' host, to the dose arriving and establishing within a 'recipient' susceptible host, and proposes a general transmission framework potentially applicable to any host-parasite system. A key point to emerge from that paper, and also raised by many of the other authors [2-4, 9, 10, 12], is that there may be important nonlinearities and heterogeneities acting at the different stages of the overall transmission process, that can alter the magnitude and functional form of transmission. Previous work has discussed the importance of nonlinearities, with respect to the contact structure between infectious and susceptible hosts [e.g., see references in 11]. However, these studies have typically been restricted to directly transmitted microparasitic infections, with much less consideration of factors driving nonlinearities in (for example) contact between free-living infective stages in the environment and susceptible hosts. Furthermore, as this issue highlights, the contact process is just one step in the overall transmission process, and there is a need to more explicitly consider nonlinearities and heterogeneities at the other stages too (e.g., variation in pathogen load and stage of infection in the infectious hosts, release and survival of infective stages in the environment, susceptibility and subsequent establishment of the infecting pathogen load in the recipient host). An additional point relating to this, again raised by several of the authors [1, 3, 7, 11, 13, 14], is how hard it can be to estimate transmission rates in the field. However, considering each step explicitly may help the quantification process, enabling different techniques to be used to estimate the different components, and provide clarification about which specific aspects need further investigation [11].

Another key topic to emerge concerned the recognition that most parasites naturally circulate within communities comprising multiple host species [2, 5, 8, 11, 13-15]. These multi-host communities often form the natural reservoir for parasites of human concern, and are a source for many emerging and re-emerging diseases (e.g., as was the case for the recent Ebola outbreak in west Africa). As such, understanding the pathways and routes of transmission within and between multiple host species is of major importance, but also a major challenge. The paper by Webster and colleagues [2] provides a clear overview of the problems inherent in attempting to understand such community-level transmission dynamics, but also provides hope by outlining a number of approaches which have been, or could be, used to quantify or infer rates of cross-species transmission. Similar suggestions are also raised by some of the other papers in this issue, both in multi-host [14] and single host [7] contexts. In addition, related to the ecological transmission dynamics of parasites within multi-host communities, is the evolutionary issue of whether parasites

should evolve to be host generalists or specialists, and several papers addressed different aspects of this question [2, 5, 8, 13]. A key point emerging from these papers is the importance of host-specific traits and characteristics (e.g., body size, abundance, competence) in shaping the evolution of specialism or generalism, and that even apparently insignificant host species can be important in determining parasite transmission and fitness within multi-host communities.

A final broad topic covered by several of these papers was the importance of the environment in shaping parasite transmission [1, 4, 6, 13]. This reflects the recognition across many of the discussions that ‘transmission’ emerges from an interaction between host, parasite and environmental components, and so it is hard to interpret observed patterns of transmission without explicitly acknowledging the environment that the transmission is occurring within. This is becoming increasingly important as we consider transmission within an increasingly changing environment, be that in terms of climate, habitat composition, host availability and community composition, or other environmental stressors such as pollutants [3, 4, 6]. In particular, as emphasised by Cable and colleagues [6] (but also picked up on by the various other papers on this topic), parasites typically show a remarkable ability to respond to environmental changes, either through plasticity or the capability for rapid genetic responses, emphasising the need to urgently evaluate likely changes in risks of disease emergence and transmission as the environment changes.

Overall many of the papers raised challenges and logistic or operational constraints that need to be overcome as we move forwards. As already mentioned, one of the biggest challenges is quantifying transmission rates in the field [1, 3, 7], and this is particularly challenging in multi-host communities [2, 14]. Perhaps related to this is the growing recognition that many parasites actually have multiple routes and modes of transmission acting simultaneously [1-3, 11]. This greatly complicates not only the epidemiology and evolution of the parasite species in question, but also our ability to observe, and ultimately control it; quantifying transmission rates when the route is known is hard enough, let alone if we cannot or have not identified all possible routes that a parasite may take. Finally, several papers raised current use (and misuse) of terminology as being a stumbling block to improved conceptual and practical understanding of transmission. Confusion exists regarding the definition of phrases like ‘transmission mode’, ‘transmission route’ and ‘transmission pathway’, which can only obscure attempts to define and understand the underlying transmission process [1, 3]. This issue of consistent terminology is exemplified in the paper by Wilson and colleagues [15] which asks the question ‘What is a vector?’. The resulting discussion and summary table listing seven distinct definitions, reflects what happens when an apparently simple question is posed to a group of academics locked away in a house in mid-Wales. Perhaps the discussion could be summarised by re-phrasing Supreme Court Justice Potter Stewart as ‘I may not be able to define [vector transmission], but I know it when I see it’. Nevertheless, the discussion did settle on a limited set of working definitions – and importantly it highlighted the factors and issues likely to be important, or indeed unimportant, when considering broader aspects of transmission.

Conclusions and thoughts for progress

Despite the challenges raised in this special issue, many authors also provided grounds for optimism. Several authors highlighted recent advances, both in technologies that allow extensive data on the spatial and temporal dynamics of parasite genotypes to be generated, and in statistical techniques

(e.g., hierarchical Bayesian modelling) that can allow deeper insight into transmission pathways and rates than previously possible [2, 6, 14]. In addition, there were suggestions that transmission might not always be as complicated as feared. Although many of the discussions centred around deconstructing transmission into its component parts, it is perhaps reassuring that some papers that formally explored more explicit models of transmission concluded that in certain cases the standard formulation is fine. For example, Fofana and Hurford [7] showed that several different ways of explicitly modelling host movement did not differ in fundamental conclusions (i.e., threshold densities for persistence) from standard mass action assumptions, although spread of infection was affected. Similarly McCallum and colleagues [11] showed that combining several different nonlinear functions relating pathogen load at one stage to the next in the transmission process, resulted in only two functional forms of the overall transmission process (approximately linear or a step-function). Hence, while standard transmission theory is, both by necessity and desire, a simplification of reality, there are clearly circumstances where it is appropriate to subsume much of the complexity. Nevertheless there will always be exceptions and nuances that are not captured by current theories and concepts, and it is hoped that the papers presented in this issue provide a guide for how those aspects can be further explored in the future.

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