



Commentary

Conflict between co-occurring parasites as a confounding factor in manipulation studies?

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In their review, [Thomas et al. \(2005\)](#) highlight that, in cases where multiple infections occur in the same intermediate host individual, parasitic manipulation may be the result of not just a single parasite, but may be the cumulative effect of infection by two or more manipulating parasites. Such parasites may be in conflict when they share the same intermediate host but have different final hosts: they may manipulate the host in different ways in order to effect their different transmission patterns. In this comment, we extend the argument of [Thomas et al. \(2005\)](#) by first considering inter-specific conflict between parasites with different transmission routes sharing the same host. We go on to discuss intra-specific conflict between the same parasites infecting the same host with respect to developmental stage and sexual reproduction.

1. Conflict within parasite species: a matter of transmission route

Competition between parasites within the same host leads to conflicts when co-occurring parasites have op-

posing interests in their use of the host to favour transmission. Such conflicts may be widespread in nature since there are many cases where hosts are infected by multiple parasites, of which many may be phylogenetically unrelated ([Petnay and Andrews, 1998](#)). Thus, there should be a high likelihood of finding a “manipulator” (P1) co-infecting a host with another parasite type (P2). If P1 has a complex life-cycle and manipulates the host to ensure its horizontal transmission (e.g. trophic transmission) and P2 has a more simple life-cycle involving one host only, a conflict situation arises. This conflict may be solved by avoidance or virulence sabotage ([Thomas et al., 2002](#)). [Thomas et al. \(2002\)](#) investigated this idea in the amphipod *Gammarus insensibilis*, which is infected by a manipulative trematode (P1) and a non-manipulative nematode (P2). While there were contradictions between their field and experimental data with regards to support for their “sabotage” hypothesis, they concluded that the selective pressure imposed by P1 on P2 may not be strong enough for sabotage to evolve. Indeed, the strength of selection pressure will determine the outcome of conflict between co-occurring parasites, and depends, for example, on the relative prevalences of the parasites, the strength of virulence, host-resistance to one or both parasites, and the mode of parasite transmission.

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The conflict of interest between two parasites will be particularly strong in cases where a manipulator shares its host with a vertically transmitted (VT) parasite. VT parasites are transmitted from mother to offspring via the eggs, in so-called transovarial transmission (Bandi et al., 2001). Their fitness is directly related to that of their hosts, since they rely on host reproduction for transmission, and therefore should not be virulent to their host (Fine, 1975). VT parasites may exhibit sex-specific virulence by altering host sex ratio to increase the proportion of the transmitting sex (Hurst, 1993; Bandi et al., 2001) but, everything else being equal, they are predicted to have either a positive or neutral effect on host fitness, and in particular, on host reproductive success (Ebert and Herre, 1996; Hurst et al., 1994; Dunn and Smith, 2001). Thus, where a host is also infected by a trophically transmitted parasite, there is conflict in transmission mode, and therefore with respect to virulence. In such cases, the co-occurrence of a manipulating parasite will exert a strong selective pressure on the VT parasite to counter-manipulate the host (i.e. sabotage, Thomas et al., 2002), to decrease the probability of predation. Note, however, that avoiding infecting intermediate hosts that are already infected by a manipulator (Lafferty et al., 2000) is not an option in this case, since the VT parasite is present in the host from birth, before infection by the manipulating parasite.

VT microbes are ubiquitous (Stouthamer et al., 1999; Zchori-Fein and Perlman, 2004; Terry et al., 2004), some are able to manipulate host behaviour (Varaldi et al., 2003), and some are known to share the same species or group of species as manipulators. For example, the freshwater amphipod *G. roeseli* is host to acanthocephala, a phylum of manipulating helminths, and VT microsporidia (Bauer et al., 2000; Haine et al., 2004). Where such parasites co-infect the same host, most studies concentrate on the host–parasite interactions of one, or the other, type of parasite and do not consider potential interactions between them. Indeed, coexistence of manipulating parasites and VT parasites may be an important confounding factor for descriptions of behavioural manipulation and in the study of adaptive significance, and since many VT infections are asymptomatic and require PCR-based detection, they may not be identified as co-occurring parasites in a particular host. The importance of such interactions has been clearly overlooked and is illustrated by

a recent study: Oliver et al. (2003) found that VT bacterial endosymbionts confer resistance to their aphid host against a virulent co-occurring parasitoid.

2. Conflict within parasite species: a matter of developmental stage and sex?

In addition to conflict between parasite species, there is potential for conflict to occur between individuals of the same parasite species. Conflict may arise, e.g., where two parasites of different maturation stages simultaneously infect a single individual host. If a parasite at the infective stage co-occurs with an immature, non-infective, parasite there is conflict: the immature parasite requires further time to develop before transmission to the final host, while the infective parasite requires transmission to the final host in order to continue its development in the next stage of its life-cycle. There are a number of examples showing that transmissible and non-transmissible stages differ in their effect on intermediate host behavioural changes, both in trematodes (e.g. Levri and Lively, 1996; McCarthy et al., 2000) and acanthocephalans (Bethel and Holmes, 1974). Generally, the immature stage does not change host behaviour (or induces few changes), while the infective stage does. However, the effect on host behaviour when the two developmental stages co-occur in a single host has not been determined. The two most simple resolutions of conflict in this case would be either repression of behavioural manipulation by non-infective stages (because of the strong selective pressure imposed on the non-transmissible stage to maintain the intermediate host alive until maturation), or maintenance of the behavioural changes by the transmissible stage despite the presence of the immature stage. A recent result on *Acanthocephalus dirus* infecting an aquatic isopod is in favour of the later hypothesis (Sparkes et al., 2004), but some preliminary observations in *Pomphorhynchus* acanthocephalans (M.J. Perrot-Minnot, personal communication) showed no behavioural change when some infective and non-infective stages co-occur, suggesting that a “sabotage” of behavioural changes by non-transmissible stage might occur.

Intraspecific conflict may also arise as a result of parasite sex ratio. The argument is similar to that used for explaining the sex ratio of malaria parasites (Jovani,

2002; Gardner et al., 2003). If a manipulating parasite reproduces sexually, it is imperative that both sexes are present in the final host, for continuation of the life-cycle. It is potentially beneficial for one parasite to share an intermediate host with a con-specific of the opposite, rather than the same, sex. For trophically transmitted parasites, this is conditional on sex determination occurring during development in the intermediate rather than the final host, but reproduction occurring vice versa. The selective pressure would be particularly strong where intermediate hosts have a generally low intensity of infection (i.e. only a few parasites are able to share the same individual host). Ensuring co-infection with a con-specific of the opposite sex may be achieved in different ways. First, many parasites are not able to choose their host (i.e. choosing between a potential host that is already infected or uninfected) since infection often results from ingestion of parasite eggs. In such cases, environmental sex determination (ESD) may be selected (Charnov and Bull, 1977), an evolutionary pathway beyond the scope of this paper. Second, where parasite sex determination is not plastic, killing a con-specific, or avoiding co-infecting a host with a con-specific, of the same sex, could occur. A third possible strategy for a parasite to ensure reproduction in the final host could be to delay manipulation of the intermediate host until it is co-infected by an individual of the opposite sex. In this case, behavioural changes induced in singly infected hosts (or hosts infected with two parasites of the same sex) should be lower than in hosts infected by two parasites of different sexes. However, a study of two acanthocephalan species revealed that a single parasite is capable of inducing as much behavioural change in its intermediate host as two or more co-infecting parasites (Cézilly et al., 2000); parasite sex was not taken into account in this study, and this hypothesis requires further investigation. While these alternatives are speculative, it may be an interesting avenue of research to compare the sex ratio of manipulating parasites singly and multiply infecting intermediate host species, and to compare the degree of behavioural changes according to parasite sex ratio in the intermediate host.

3. Concluding remarks

We propose that infections involving conflicting parasites may be a common source of confounding

data in interpreting parasitic manipulation. A variety of conflicts may occur between parasite species, but also within species, conflicts that can (at least potentially) lead to modifications in behavioural changes induced by manipulative parasites. Such interactions may at least explain some of the variation generally observed in behavioural changes associated with infections by manipulating parasites (e.g. Thomas et al., 2002).

References

- Bandi, C., Dunn, A.M., Hurst, G.D.D., Rigaud, T., 2001. Hereditary symbiosis, sex specific virulence and reproductive parasitism. *Trends Parasitol.* 17, 88–94.
- Bauer, A., Trouvé, S., Grégoire, A., Bollache, L., Cézilly, F., 2000. Differential influence of *Pomphorhynchus laevis* (Acanthocephala) on the behaviour of native and invader gammarid species. *Int. J. Parasitol.* 30, 1453–1457.
- Bethel, W.M., Holmes, J.C., 1974. Correlation of development of altered evasive behavior in *Gammarus lacustris* (Amphipoda) harboring cystacanths of *Polymorphus paradoxus* (Acanthocephala) with the infectivity to the definitive host. *J. Parasitol.* 60, 272–274.
- Cézilly, F., Grégoire, A., Bertin, A., 2000. Conflict between co-occurring manipulative parasites? An experimental study of the joint influence of two acanthocephalan parasites on the behaviour of *Gammarus pulex*. *Parasitology* 120, 625–630.
- Charnov, E.L., Bull, J.J., 1977. When is sex environmentally determined? *Nature* 266, 828–830.
- Dunn, A.M., Smith, J.E., 2001. Microsporidian life cycles and diversity: the relationship between virulence and transmission. *Microbes Infect.* 3, 381–388.
- Ebert, D., Herre, E.A., 1996. The evolution of parasitic diseases. *Parasitol. Today* 12, 96–101.
- Fine, P.E.M., 1975. Vectors and vertical transmission: an epidemiologic perspective. *Ann. NY Acad. Sci.* 266, 173–194.
- Gardner, A., Reece, S.E., West, S.A., 2003. Even more extreme fertility insurance and the sex ratios of protozoan blood parasites. *J. Theoret. Biol.* 223, 515–521.
- Haine, E.R., Brondani, E., Hume, K.D., Perrot-Minnot, M.J., Gailard, M., Rigaud, T., 2004. Coexistence of three microsporidia parasites in populations of the freshwater amphipod *Gammarus roeseli*: evidence for vertical transmission and positive effect on reproduction. *Int. J. Parasitol.* 34, 1137–1146.
- Hurst, G.D.D., Purvis, E.L., Sloggett, J.J., Majerus, M.E.N., 1994. The effect of male-killing *Rickettsia* on the demography of female *Adalia bipunctat* L. (2-spot ladybird). *Heredity* 73, 309–316.
- Hurst, L.D., 1993. The incidences, mechanisms and evolution of cytoplasmic sex ratio distorters in animals. *Biol. Rev.* 68, 121–193.
- Jovani, R., 2002. Malaria transmission, sex ratio and erythrocytes with two gametocytes. *Trends Parasitol.* 18, 537–539.
- Lafferty, K.D., Thomas, F., Poulin, R., 2000. Evolution of host phenotype manipulation by parasites and its consequences. In: Poulin, R., Morand, S., Skorpung, A. (Eds.), *Evolutionary Biology of*

- Host–Parasite Relationships: Theory Meets Reality. Elsevier, Amsterdam, pp. 117–127.
- Levri, E.P., Lively, C.M., 1996. The effects of size, reproductive condition, and parasitism on foraging behaviour in a freshwater snail *Potamopyrgus antipodarum*. *Anim. Behav.* 51, 891–901.
- McCarthy, H.O., Fitzpatrick, S., Irwin, S.W.B., 2000. A transmissible trematode affects the direction and rhythm of movement in a marine gastropod. *Anim. Behav.* 59, 1161–1166.
- Oliver, K.M., Russell, J.A., Moran, N.A., Hunter, M.S., 2003. Facultative bacterial symbionts in aphids confer resistance to parasitic wasps. *Proc. Natl. Acad. Sci. U.S.A.* 100, 1803–1807.
- Petnay, T.N., Andrews, R.H., 1998. Multiparasite communities in animals and humans: frequency, structure and pathogenic significance. *Int. J. Parasitol.* 28, 377–393.
- Sparkes, T.C., Wright, V.M., Renwick, D.T., Weil, K.A., Talkington, J.A., Milhalov, M., 2004. Intra-specific host sharing in the manipulative parasite *Acanthocephalus dirus*: does conflict occur over host modification? *Parasitology* 129, 335–340.
- Stouthamer, R., Breeuwer, J.A.J., Hurst, G.D.D., 1999. *Wolbachia pipientis*: microbial manipulator of arthropod reproduction. *Annu. Rev. Microbiol.* 53, 71–102.
- Terry, R.S., Smith, J.E., Sharpe, R.G., Rigaud, T., Littlewood, D.T.J., Ironside, J.E., Rollinson, D., Bouchon, D., MacNeil, C., Dick, J.T.A., Dunn, A.M., 2004. Widespread vertical transmission and associated host sex ratio distortion within the eukaryotic phylum Microspora. *Proc. R. Soc. London B* 271, 1783–1789.
- Thomas, F., Fauchier, J., Lafferty, K.D., 2002. Conflict of interest between a nematode and a trematode in an amphipod host: test of the “sabotage” hypothesis. *Behav. Ecol. Sociobiol.* 51, 296–301.
- Thomas, F., Adamo, S., Moore, J., 2005. Parasitic manipulation: where are we and where should we go? *Behav. Process.* 68, 185–199.
- Varaldi, J., Fouillet, P., Ravallec, M., Lopez-Ferber, M., Boulétreau, M., Fleury, F., 1930. Infectious behaviour in a parasitoid. *Science* 302.
- Zchori-Fein, E., Perlman, S.J., 2001. Distribution of the bacterial symbiont *Cardinium* in arthropods. *Mol. Ecol.* 13, 2009–2016.