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Evolution of Parasite Life History Traits: Myths and Reality

R. Poulin

Parasitism has evolved independently several times in many different animal lineages. Observations made on distantly related parasites have revealed a variety of adaptations to parasitism, including changes in physiology, morphology, and life history traits. These observations have led parasitologists to formulate general rules about the evolution of parasites, rules that define a common evolutionary path presumably followed by all parasitic organisms. Robert Poulin uses recent evidence to question the generality of these rules and to show that parasite evolution may take different roads. The selective pressures acting on parasites are diverse and may guide their evolution in any direction, just as they have shaped a wide variety of free-living organisms.

Parasites often look nothing like their closest free-living relatives, and have obviously undergone important evolutionary changes since switching to a parasitic way of life. Attachment to, and feeding on, the host and transmission to other hosts are problems faced by all parasites. The idea that these problems could have been solved in a similar manner by unrelated parasites is attractive. Indeed, a superficial survey of parasite groups reveals some similarities in general biology suggestive of convergent evolution toward some common ideal. Old parasitology textbooks[1,2] contain several examples of generalizations about parasite evolution based on these apparent similarities among distantly related parasites. The same arguments, although disguised, may be found in more recent texts and are tacitly accepted by many (if not most) parasitologists.

A re-examination of these general rules of parasite evolution is now overdue. Exceptions to the rules are usually ignored, although they might tell us a lot about how natural selection might act under special conditions. Information about parasite phylogeny is only beginning to be incorporated in tests of evolutionary hypotheses, and can produce surprising outcomes. There is also the recognition that host and environmental variables may have partially shaped the evolution of parasites, such that it proceeds differently in different systems. Some beliefs about parasite evolution have recently been shattered[3], but there still remain some widely accepted myths that do not bear up to close scrutiny. In particular, trends in the evolution of parasite body size and fecundity are ripe for a re-evaluation.

Two myths about parasite evolution

A widespread view about parasites is that they are evolutionarily retrogressive, and that, through time, they evolve toward reduced structural complexity and smaller body sizes[4,5]. By definition, parasites are smaller than their hosts: in order to attach to the host and feed on it without killing it rapidly, parasites must be at least one order of magnitude smaller than their hosts. The impression that parasites evolve toward smaller sizes comes from these entirely inappropriate comparisons between host and parasite body sizes. The proper comparisons to make in order to determine the direction of evolutionary changes in parasite body size would be between parasites and either their extinct free-living ancestors, or their closest extant free-living relatives.

A second, even more widely accepted, myth about parasites is that they all evolve toward extremely high fecundity. Explanations for this trend typically involve arguments about the need to compensate for massive losses of infective stages during transmission[6], or about automatic evolutionary responses to the high nutrient availability provided by the host[7–9]. Parasites are currently viewed as paradigm examples of high reproductive output. This is commonly illustrated by tables in which the high fecundity of selected parasite species is pitted against the low fecundity of some more or less closely related free-living species[10–12]. However, such comparisons say little about the evolution of fecundity: they only show that a subjective collection of parasites is on average, more fecund than a subjective group of free-living species. Phylogenetic relationships among parasites and their free-living counterparts must be

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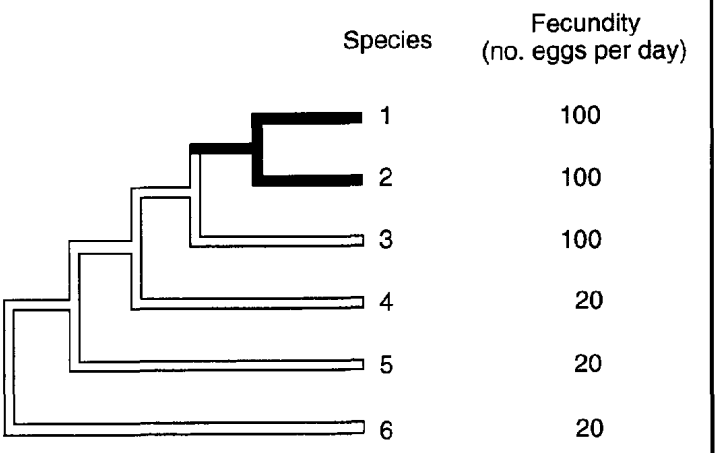
Box 1. Parasite phylogeny and adaptation

It is misleading to compare parasitic species with their free-living relatives without taking phylogenetic relationships into account. Consider the following hypothetical example (see Fig. right).



Species 1 and 2 are parasitic (indicated by black lines). If we ignore phylogeny and compare the average fecundity of parasite species with the average fecundity of free-living species, we conclude that parasites (average 100 eggs per day) have greater fecundity than free-living species (average 40 eggs per day). To test whether high fecundity may have been an adaptation to a parasitic way of life, however, the only appropriate comparison would be between the branch in which parasitism evolved (leading to species 1 and 2) and its free-living sister branch (leading to species 3). This latter comparison would yield no difference in fecundity between parasites and free-living species, and would lead to the conclusion that a switch to a parasitic way of life has not been followed by evolution toward greater fecundity. In the present example, the evolution of high fecundity has preceded the transition to parasitism, a fact only apparent from a phylogenetic reconstruction.

known to resolve the evolution of fecundity or any other trait (Box 1). As with the evolution of body size, actual trends can be much more variable than suggested in parasitology textbooks.

Evolution of parasite body size

Ideal groups for investigations of parasite evolutionary biology are those that include both free-living and parasitic species (Fig. 1). Among nematodes, for instance, species parasitic in invertebrates are roughly the same size as free-living species, whereas species parasitic in vertebrates attain much larger body sizes[13]. Similar patterns emerge from investigations of copepods[14] and isopods[15]. These observations clearly do not suggest that parasitism as a way of life leads to smaller body size through evolutionary time. However, this trend can only be tested by comparisons between parasitic lineages and their closest free-living relatives. In copepods, transitions from free-living to parasitic on invertebrates were consistently coupled with small but significant increases in body size, whereas switches from parasitic on invertebrates to parasitic on fish typically lead to much larger increases in body size[14]. On the other hand, in both isopods[15] and amphipods[16], transitions from free-living to parasitism (or other forms of obligate associations with hosts) were consistently associated with reductions in body size. There is therefore no universal rule guiding the direction of evolutionary changes in parasite body size.

In invertebrates, in general, body size is positively correlated with fecundity, both within and across species[17–19]. We may then expect natural selection to favour increases in body size of parasitic species if fecundity is a determinant of transmission success. Large body size may also help the parasite escape host defences[20]. Other selective pressures on parasites come from the host or the external environment, and may constrain the evolution of parasite body size. One such constraint may be the space available for parasite occupation in or on the host. The size of the free-living ancestor is the starting point of parasite evolution, and whether parasites evolve to be larger or smaller, or do not change in size, may depend on how much space is available at their site of attachment. Within species, there is some evidence of developmental plasticity in size, with individual parasites attaining a size proportional to the size of their host. Examples of this include copepods parasitic on fish[21] and isopods parasitic on other crustaceans[22]. Across species, after controlling for phylogenetic effects, positive associations are found between parasite size and host size in chewing lice infecting rodents and in pinworms infecting primates[23], but not in copepods parasitic on fish[14]. A positive relationship between parasite size and host size may also exist among taeniid cestodes parasitizing mammals[20]. Other host characteristics such as life span[23] may also determine how large parasites can grow. Parasite body size can depend on developmental sites within the host, too; among nematodes parasitizing mammals, taxa undergoing juvenile migrations through host tissues attain larger adult sizes than related taxa developing entirely within the gastrointestinal tract (A.F. Read and A. Skorping, pers. commun.). Finally, environmental variables such as temperature can influence parasite body size through developmental effects causing variability within species[24] or adaptive responses resulting in interspecific differences[14–16]. Thus, it seems that the direction of body-size evolution in parasites is more variable than commonly believed, and is influenced by too many variables to be described by a single general rule.

Evolution of parasite fecundity

While it is true that the total egg output of some parasitic helminths is astronomical, many other parasitic organisms have a lifetime fecundity that is well within the range of their free-living relatives. For example, females of many copepod species parasitic on invertebrates produce only a few dozen eggs in their lifetime; species parasitic on fish may produce a few hundred or a few thousand eggs[14]. Monogeneans ectoparasitic on fish typically produce a few hundred eggs during their entire life[25]. Ticks are also not more fecund than most free-living arachnids[26]. The generality of the idea that parasitism *per se* invariably leads to the evolution of high fecundity has therefore been greatly exaggerated.

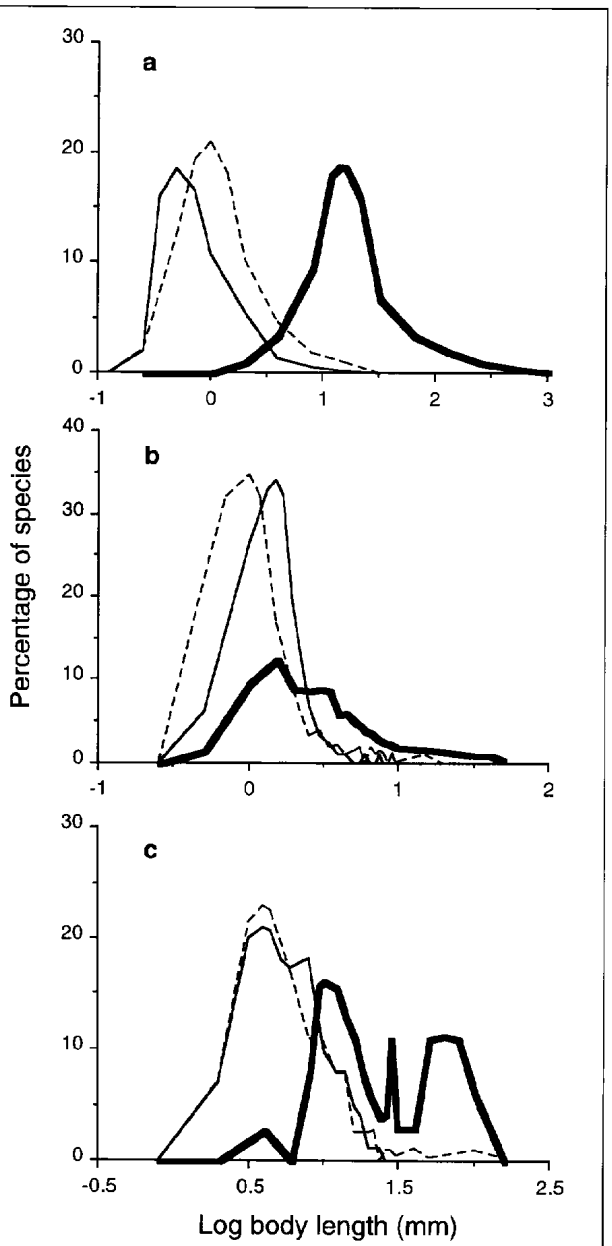


Fig. 1. Frequency distribution of body sizes in nematodes (n = 829 species) (a), copepods (n = 1038 species) (b), and isopods (n = 563 species) (c) (adapted from Refs 13, 14 and 15, respectively). Free-living species (broken curves), species parasitic in or on invertebrates (thin curves) and species parasitic in or on vertebrates (thick curves) are shown separately.

Comparisons among copepod lineages in which phylogenetic and body size effects were removed indicate that copepods parasitic on fish produce relatively more and smaller eggs than copepods parasitic on invertebrates[14]. Among schistosome species infecting mammals, fecundity ranges from quite low to very high, and correlates negatively with egg size[27]. Among intestinal nematodes of mammals, there is also a range of fecundities across species[28–30]; although nematode fecundity does not correlate negatively with egg size, it may correlate negatively with the thickness of the egg shell and the protection it gives to the larva[29,31]. Finally, among species of freshwater mussels (in the order Unionoidea) that have an obligatory parasitic stage on fish, fecundity is negatively related to the size of the infective larvae, or glochidia[32]. Trade-offs between egg numbers and offspring size are common throughout the animal kingdom, and represent a continuum of reproductive strategies that are the product of different selective pressures[33,34]. In free-living species, the partitioning of reproductive effort between egg number and egg size is influenced by several factors; environmental effects on juvenile survivorship appear to be fundamental[34]. For parasites, the expected probability of transmission may be the single most important determinant of whether selection will favour the production of many offspring that each have a minuscule chance of reaching a host, or whether it will favour investments in few offspring that will each have a high probability of success. The reproductive strategies of parasites are therefore no different from those of free-living organisms. Mode of transmission, host abundance and mobility, and environmental conditions may all affect the likelihood of a larva finding a host, and may push the evolution of reproductive strategies toward either 'many small eggs' or 'few large eggs'. Many parasites are indeed highly fecund. However, for each species (like the many cestodes or nematodes) that produce several hundred thousand or several million eggs, there are species that produce relatively few offspring that are better equipped to find a host. Monogeneans, for instance, produce relatively few eggs, but these can survive for long periods and only hatch when hosts are nearby, releasing larvae that are efficient at locating and attaching to the host[35,36]. At the many-small-eggs end of the spectrum, fecundity will eventually be limited by the minimal egg size that can lead to a viable larva: fecundity cannot increase at the expense of egg size past some point. At the few-large-eggs end, low fecundity may be compensated by short generation times that result in high reproductive potential anyway[20,29].

Fecundity of adult parasites is only one component of total reproductive output in many parasites. No discussion of fecundity would be complete without mentioning the ability of many helminth larvae to multiply asexually in their intermediate host. In species where larvae undergo extensive asexual multiplication, fecundity may take second place to other strategies or investments. This appears to be the case in taeniid cestodes, in which species displaying prolific asexual multiplication usually have low adult fecundity, and vice versa[20,37]. It may thus be that high fecundity, far from being the end point of parasite evolution, is only one of several strategies that may be adopted during the course of evolution.

Conclusions

Fossilized remains of parasites are not commonly recovered; therefore, parasite evolution can only be reconstructed through an analysis of relationships among living species. There have been only a handful of studies that have addressed the evolution of parasites using a phylogenetic approach. What they have taught us is that the evolution of organisms that have switched to a parasitic way of life does not follow strict rules, but may instead follow a variety of paths all leading to successful transmission. It is possible that some types of parasites follow the old rules, and that others do not. For example, ectoparasite body size may not be as constrained as that of endoparasites. Larval establishment rates may differ between ecto- and endoparasites, leading to different reproductive strategies. In addition,

ectoparasite fecundity may be constrained by limited resource availability and/or by pressures from the physical environment, factors that may be less important for endoparasites. In general, parasites as a whole are subject to pressures and constraints that do not differ greatly from those acting on free-living organisms, and consequently there is no reason to believe that their evolution should proceed differently and be forced down a single path. The recognition of this fact should help us to understand more clearly why parasites are what they are and do what they do, particularly those that do not fit the old myths.

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Letters

AGA/AGG Codon Usage in Parasites: Implications for Gene Expression in *Escherichia coli*

Our interest in schistosomal gene products as candidate vaccines has led us to examine the codon usage of this and other parasites. Amino acids such as methionine and tryptophan are encoded by unique codons, while others, such as arginine, may be encoded by one of six triplets Sequence analysis has revealed that codons are not necessarily used to the same extent where degeneracy exists. Codon bias may have profound effects on the expression of parasite genes in heterologous hosts with conflicting codon usage.

The usage of the codons AGA and AGG (arginine) by several eukaryotic parasite species is presented in Table 1. These codons are used preferentially in the species shown, and are found in particularly high frequencies in the human parasites *Plasmodium falciparum* and *Entamoeba histolytica*. The latter organism has a marked preference for AGA codons (85% of its arginine residues) In contrast, the codons AGA and AGG are the rarest in *Escherichia coli*[1] Approximately 60% of *E. coli* genes contain neither codon. Several other genes contain a single AGA/AGG codon, often within the first 25 codons of the gene Such codons may play a role in the regulation of gene expression[2].

Open reading frames containing AGA and AGG codons may experience slow translation in *E. coli* relative to genes containing the more common codon CGU[3]. This may be due to a rate-limiting interaction with scarcely available $tRNA^{AGA/AGG}$ (Ref. 4). Gene expression may be severely inhibited if several AGA/AGG codons are present[5], especially if these occur in tandem[4,6] or are present near the initiation codon[7]. These effects can be suppressed experimentally by moving the minor codon further away from the initiation codon, or by overproducing tRNA for the minor codon in the bacterial host. The effect may be explained by the minor codon modulator hypothesis; at slow growth rates the rate of translation of minor codons is reduced due to a lack of appropriate tRNA. If ribosomes stall at minor codons near to the initiation codon, a queue of ribosomes may form, blocking entry at the initiation site[7].

Tandemly repeated AGA/AGG codons may cause frameshifts[4] or early termination of expression[8]. These effects may be due to a lack of appropriate tRNA, as tRNA overproduction suppresses frameshifts experimentally[9]. However, repeated AGG can also have other effects, with the ability to slow down gene expression even if located in a non-translated region of the gene[10]. This may be because the AGGAGG sequence resembles the bacterial Shine-Dalgarno (SD) consensus sequence (AAGGAGGU) Competition between such sequences may delay the formation of functional SD–16S rRNA complex[10]

We suggest that appropriate steps should be taken to improve heterologous expression of AGA/AGG containing genes. Parasite genes expressed poorly in *E. coli* may have greatly enhanced expression upon co-transformation with a plasmid able to overproduce appropriate tRNA for the AGA/AGG codons, as demonstrated for other eukaryotic genes[11]. Alternatively, a yeast host in which the AGA and AGG codons are frequently used, may be a more suitable choice

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