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Sexual transmission of beneficial microbes

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Beneficial sexually transmitted infections (STIs) are an understudied phenomenon with important implications for the evolution of cooperation and host reproductive behavior. Challenging the prevailing expectation that sexual transmission leads to pathogenesis, these symbionts provide new opportunities to examine how STIs might influence sexual selection and the evolution of promiscuity.

Introduction

STIs are taxonomically widespread and are expected to favor reproductive behaviors that reduce the probability of acquiring the infection [1]. Evidence is accumulating, however, that sexual transmission is also a viable transmission pathway for beneficial symbionts (Box 1). This discovery has important implications for our expectations for how hosts and their symbionts should evolve, as sexual transmission is intimately connected to mate choice and has counterintuitive effects on the evolution of virulence.

The prevailing view that STIs should be pathogenic is rooted in theory predicting that horizontal transmission between unrelated individuals leads to higher virulence, whereas vertical transmission from parent to offspring favors mutualisms [2]. STIs, however, are typically less virulent than their non-sexually transmitted counterparts because hosts must be in reproductive condition and appear asymptomatic to potential mates [1]. Furthermore, all of the known cases of beneficial STIs (Box 1) exhibit mixed-mode transmission [2], meaning that they are transmitted both horizontally and vertically. Theory and empirical studies have shown that virulence declines as the relative amount of vertical transmission increases because of the increased dependency of the symbiont on host reproduction for transmission [2]. Sexual transmission might facilitate vertical transmission by introducing the symbiont directly into the reproductive tract, reducing the need to migrate between tissue types to reach the ovaries. Whether higher levels of vertical transmission are observed in beneficial STIs compared with pathogenic ones remains to be studied.

Many beneficial symbionts, however, are not vertically transmitted, requiring other explanations for how mutualisms evolve. An alternative mechanism that has been proposed is symbiont choice [3], which requires that hosts can screen out non-cooperative symbionts. Symbiont choice can occur, for example, when hosts create environmental conditions that are too costly for non-cooperators to tolerate [3]. The antibiotic properties of male seminal fluid and the various physical and physiological defenses within the female reproductive tract, including the essential community of bacteria (e.g., *Lactobacillus*) that produce bacteriocins, hydrogen peroxide, lactic acid, and other antimicrobial compounds [4], could potentially mediate symbiont choice in STIs.

Beneficial STIs and sexual selection

A longstanding hypothesis in behavioral ecology is that parasitic symbionts influence mate choice decisions, with many studies showing that various sensory modalities are employed to discriminate between infected and uninfected individuals. Despite the large fitness advantage of acquiring beneficial STIs (Box 1), no studies to date have examined whether individuals with beneficial infections are preferred as mates. Unlike pathogenic STIs, sexual selection should favor the advertisement of beneficial infections [5] and signaler–receiver systems evolve more readily because the reproductive interests of the hosts and the symbionts are aligned in favor of transmission.

Mate choice for beneficial symbionts is compatible with existing theory proposing that direct or indirect benefits can result in the evolution of a preference. Symbionts can confer direct benefits when transmission increases the survival and fecundity of choosy individuals, while indirect benefits ('good metagenomes') can be obtained if vertical transmission increases the fitness of offspring. Genetic compatibility between symbiont and host genomes could similarly affect mate choice in an analogous fashion to when fitness depends on choosing the most genetically compatible mate rather than one superior genotype. The fitness effects of beneficial symbionts, however, would be realized immediately in newly infected hosts and, if vertical transmission occurs, in offspring as well. Because the costs and benefits of symbiotic associations can depend on the environmental context [6], we expect phenotypic plasticity in mate choice behavior and/or population differences in the strength of the preference across environmental gradients in the host's range.

Beneficial infections could influence mate choice in at least two ways. First, beneficial symbionts provide many critical physiological functions for their hosts; thus, individuals with preferences for high-condition mates might be more likely to acquire the infection as a result. Alternatively, symbionts modify host sexual behavior and participate in the production of sexually selected signals by metabolizing host substrates. Mate choice in fruit flies, individual recognition in mice, and plumage coloration in birds are a few empirical examples where microbes modify a signal or cue produced by the host [7]. Microbes also

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Box 1. Beneficial sexually transmitted microbes

Aphids

Acyrthosiphon pisum (Figure I) hosts three facultative symbionts that increase resistance to parasitoids and tolerance to heat stress and improve fecundity on alternative host plants. Two of these can be sexually transmitted from males to females and then vertically transmitted to offspring [12]. Sexual transmission allows ecologically beneficial traits to be transferred between lineages of aphids and influences symbiont evolution by providing the opportunity for recombination.

Mosquitoes

Asasia are acetic acid bacteria that colonize the gut, testes, and surface of developing eggs of *Anopheles* mosquitoes and other insects. Damaini *et al.* [13] used recombinant strains of fluorescently labeled *Asaia* to show that they can be sexually transmitted and passed to offspring. Mosquito larvae without *Asasia* have a 2–4-day delay in development time, suggesting a nutritional role for these bacteria.

Humans

GB virus C (GBV-C) is a sexually transmitted lymphotropic RNA virus that is associated with a 59% reduction in the mortality rate of HIV patients [14]. GBV-C attenuates HIV by reducing its ability to bind, enter, and replicate within T cells, stimulating the innate (interferon) and cellular (cytokine) immune responses, and reducing $CD4^+$ T cell apoptosis [14]. Vertical transmission of GVB-C also reduces the likelihood that infants acquire HIV from infected mothers [14].

Fungi

Beneficial mycoviruses increase thermal tolerance and host growth rates and secrete toxins ('killer yeasts') that kill competing fungi [15]. Mycoviruses lack an extracellular phase and thus are dependent on their host's survival for transmission, favoring mutualistic interactions [15]. Propagation of mycoviruses occurs during mitosis and anastomosis (hyphael fusion required for sex) with other fungi, the success of which can depend on the strain of the virus and the host [15]. Host–symbiont interactions thus can mediate sexual compatibility between fungi.

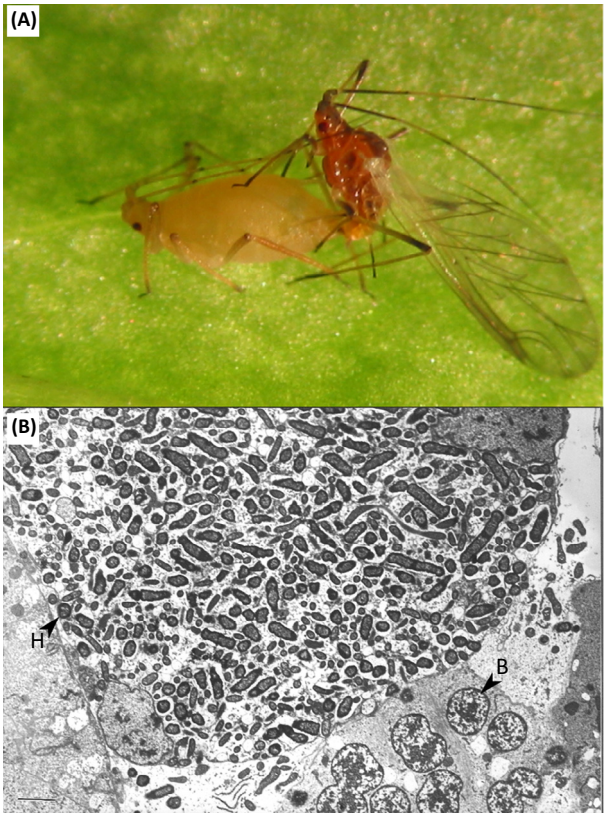

Figure I. **(A)** A male pea aphid mounts a female, which can result in the sexual transmission of **(B)** *Hamiltonella defensa* (H), a bacterium that confers protection against parasitoids. *Buchnera* (B), a nutritional symbiont with strict vertical transmission, is also indicated. Photograph credit: N. Moran.

influence the physical milieu of the female reproductive tract [4]; thus, it is possible that STIs could affect post-copulatory sexual selection by altering sperm survival or motility.

Beneficial STIs and promiscuity

Lombardo [5] first proposed that beneficial STIs could promote the evolution of multiple mating if copulating repeatedly with the same partner or with multiple partners increased the likelihood of acquiring the symbiont. STI prevalence among human populations is associated with higher levels of promiscuity [8], confirming the expected association between sexual behavior and infection rates. Promiscuity also impacts the overall community composition of the vaginal microbiome, increasing diversity in polygamous lizards [9], primates [10], and mice [11]. Mating multiply thus appears to lead to a greater sampling of the available microbial diversity within populations.

Because microbial communities comprise pathogens, commensals, and beneficial symbionts, the evolution of promiscuity in response to STIs will depend on the costs and benefits of each type of infection and their relative frequencies in the population, in conjunction with the other ecological and evolutionary factors that determine how many mates an individual has. Empirical studies assessing the impact of changes in the microbial community on the host and models evaluating the optimal mating rate when multiple types of symbiont are present are needed. Differences between the host and the symbiont in the optimal mating rate, for example, could provide an opportunity to study how conflicts of interest between hosts and symbionts influence the evolution of cooperation [6].

Concluding remarks and future directions

Lockhart *et al.*'s [1] seminal review stimulated research into the ecology and evolution of STIs by drawing attention to their ubiquity in nature. Whether beneficial STIs have not received similar attention because they have been overlooked or because they are rare can be answered only by discerning how the multitude of symbionts are transmitted (Box 2). That beneficial STIs include viruses, bacteria, and hosts that span distant taxonomic groups (Box 1) suggest that they are widely distributed in the tree of life. With the growing interest in understanding the evolution of microbial symbioses and the rapid advances in techniques for surveying their diversity and assessing their function, we expect that more beneficial STIs will be discovered and their effects on host reproductive physiology and behavior elucidated. We predict that theoretical

Box 2. Transmission pathways for STIs

STIs often infect the host as free-floating passengers in the seminal fluid, but they can also hitchhike by binding to the spermatozoal cell surface (Figure IA). Remarkably, intraspermatozoal infection by a bacterium has recently been reported, challenging the common view that reductions in cytoplasm during spermiogenesis eliminate bacterial symbionts (Figure IB,C). Hitchhiking might allow symbionts to bypass the defensive barriers of the female reproductive tract and facilitate vertical transmission by simplifying the often complex migration to the egg. In *Hamitonella defensa* (Box 1) and many other mutualists, the loci involved in infecting host cells and evading host defenses are homologous with their parasitic relatives [6]. This observation has led to new questions regarding how hosts facilitate mutualistic interactions while discriminating against pathogens.

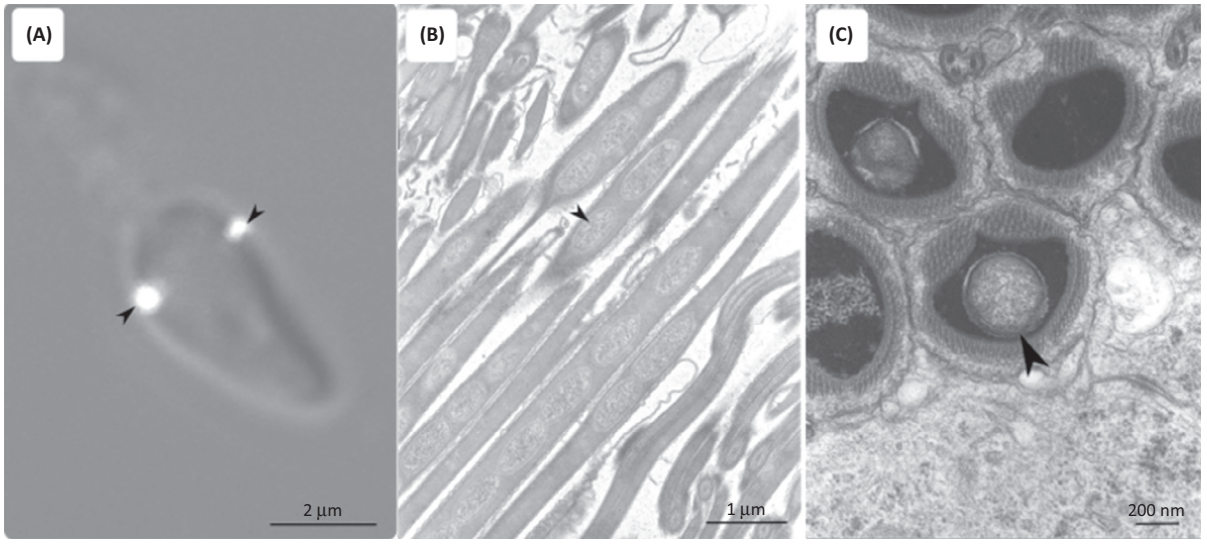

Figure I. **(A)** Human papillomavirus hitchhikes by binding to the cell surface of a human spermatozoon. **(B,C)** Intraspermatozoal infection of the leafhopper *Nephotettix cincticeps* by *Rickettsia*, which is transported to the sperm storage organ and then vertically transmitted to offspring. Reproduced, with permission, from (A) K. Ribbeck and (B,C) K. Watanabe.

and empirical studies of sexually transmitted beneficial microbes will open new research frontiers that integrate behavioral and microbial ecology.

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