

The epidemiology and evolution of parasite transmission through cannibalism

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Abstract. Cannibalism is a widespread behavior, and evidence is abundant for transmission from infected victims to susceptible cannibals in many parasite–host systems. Current theory suggests that cannibalism generally impedes disease spread, because each victim is usually consumed by a single cannibal. Thus, cannibalism merely transfers pathogens from one individual to another without spreading infections to additional hosts. This assumes that cannibalism is the only mode of transmission and that the host population is homogenous. However, host developmental stages are a key determinant of both cannibal–victim and host–pathogen interactions. We suggest that multiple modes of pathogen transmission can interact through host stage structure. We show theoretically that cannibalism can enhance disease spread by consistently transferring infections from low quality to high quality hosts that are more infectious via horizontal transmission. We review empirical evidence for the generality of key conditions required for this process, and analyze the implications for the evolution of transmission through cannibalism. More generally, our theory promotes the consideration of multiple transmission pathways when studying parasite–host systems, and advances a useful intuition for assessing whether or not such pathways may be mutually augmentative.

Key words: *disease ecology; ecological epidemiology; infectious diseases; population heterogeneity; predation; stage structure; trophic transmission.*

INTRODUCTION

Significant advances in epidemiology have been made by recognizing the rich biological detail that underlies the transmission of infectious diseases among animals, and particularly the importance of host trait variation and behavior (Anderson and May 1992, Dwyer et al. 1997, Lloyd-Smith et al. 2005, Bansal et al. 2007, Civitello et al. 2013, Disney and Dearing 2013). The idea that disease can spread through cannibalism has often been assumed in evolutionary and applied ecology. A classic, motivating case is the transmission of Kuru disease via ritual cannibalism in humans (Lindenbaum 2008). Indeed, evidence is abundant for parasite transmission from infected victims to susceptible cannibals in many host–parasite systems (Rudolf and Antonovics 2007). However, due to the difficulty of conducting experimental studies, it is not yet clear how this interaction scales up to the population level and whether it results in disease spread. Cannibalism can affect the prevalence of horizontally transmitted diseases through three parallel processes (Fig. 1):

(1) cannibalism is a density-dependent factor that suppresses populations of susceptibles (Claessen et al. 2004), therefore impeding disease spread (Kermack and McKendrick 1927, Anderson and May 1992); (2) cannibalism reduces disease prevalence by removing infected individuals from the population; and (3) cannibalism is a pathogen-transferring process, in which infections move from infected victims to susceptible cannibals. The first two processes are common with predation (see Packer et al. 2003), but the third is unique to cannibalism in transferring the infection within the host population.

Current theory considers pathogen transmission via cannibalism only in homogenous host populations, and holds that cannibalism does not spread parasites among hosts that do not engage in “group cannibalism,” because at most cannibalism can transfer an infection from one individual (the victim, who is killed) to another (the cannibal, who survives), with no net increase in the total number of infected individuals (Rudolf and Antonovics 2007). Thus, theory suggests that cannibalism cannot be the sole transmission mechanism for a pathogen. Indeed, most parasites that were reported to infect via cannibalism also employed additional modes of transmission (Rudolf and Antonovics 2007).

We ask, therefore, what is the role of cannibalism among hosts in the spread of common parasites that employ both cannibalistic and non-cannibalistic,

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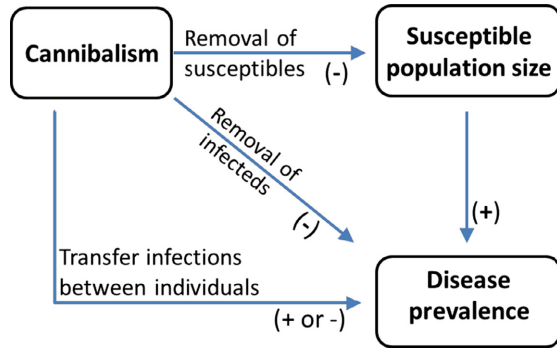


FIG 1. Decomposition of the effect of cannibalism on disease spread and prevalence into three fundamental processes: (1) cannibalism removes susceptibles and suppresses populations of susceptibles, thereby indirectly reducing the opportunities for pathogen spread; (2) cannibalism removes infected individuals from the population, directly reducing prevalence; and (3) cannibalism can transfer infections from infected victims to their cannibals.

horizontal modes of transmission (in Sadeh and Rosenheim [in press], we consider cannibalism and vertically transmitted pathogens)? More broadly, might the existence of multiple modes of transmission open the door to interactions between them that could produce important epidemiological effects? To answer these questions we introduce stage structure in the host population, a universal phenomenon that is tightly correlated with age and size structure. Host stages markedly alter infection biology (DeAngelis et al. 1993, Sait et al. 1994, Parker et al. 2003, Yee and Lacey 2003, Johnson et al. 2006, Harrison and Hoover 2012). Stage and size disparities are also key determinants in the outcome of cannibalistic interactions (Park et al. 1968, Polis 1981, Hopper et al. 1996, Boots 1998, Persson et al. 2003, Sadeh et al. 2009). The idea that host size structure might allow cannibalism to enhance pathogen spread has been suggested by Pizzatto and Shine (2011) for the spread of lungworms (*Rhabdias pseudosphaerocephala*) among cane toads (*Rhinella marina*);

may transfer disease between stages that differ in their non-cannibalistic infection biology. As a result of this interaction, depending on the specific biological differences between typical cannibals and typical victims, cannibalism may either impede or enhance parasite spread.

To ground the basic premises of our theory in empirical reality, we conducted a literature review of parasite–host systems where transmission through cannibalism has been demonstrated (Appendix S1). We adapted the literature review published in (Rudolf and Antonovics 2007), examined each paper, and then added literature published between 2007–2014. We noted for each system what modes of transmission are known other than cannibalism, and what kind of host population structure is known to be relevant for cannibalism. Since later developmental stages are often less susceptible to contracting infections, but are better survivors than earlier stages, we argue that they may commonly represent a higher quality host that is colonized by pathogens through cannibalism.

THEORY

Rudolf and Antonovics (2007) showed that parasites that are transmitted via cannibalism typically employ additional modes of transmission as well. Therefore, we begin with a modest extension to their model by adding a second mode of non-cannibalistic parasite transmission, modeled simply as direct horizontal transmission. Model 1 assumes a homogenous host population, where the cannibalistic transfer of infection between individuals (Fig. 1) is irrelevant. Model 1 is therefore used to conduct a detailed analysis of the negative effects of cannibalism on pathogen spread, and to analyze the evolution of cannibalistic transmission as a pathogen trait. In Model 2, we incorporate stage structure in the host population to account for the effect of pathogen transfer between individuals through cannibalism, as well as common stage-specific phenomena in disease biology. See Appendix S2 for notation used in both models.

Model 1: homogenous host population

$$\begin{aligned}
 \dot{S} &= \underbrace{bN}_{\text{births}} - \underbrace{dS}_{\text{background mortality}} - \underbrace{a_s NS}_{\text{cannibalism of susceptibles}} + \underbrace{cN(a_s + a_i I)}_{\text{added births by cannibals}} - \underbrace{\tau a_i SI}_{\text{cannibalistic transmission}} - \underbrace{\beta IS}_{\text{direct transmission}} \\
 \dot{I} &= \underbrace{\tau a_i SI}_{\text{cannibalistic transmission}} - \underbrace{\beta IS}_{\text{direct transmission}} - \underbrace{(d + \nu)I}_{\text{background mortality + virulence}} - \underbrace{a_i NI}_{\text{cannibalism of infecteds}}
 \end{aligned}
 \tag{1}$$

apparently, cannibalism transfers pathogens from young toads, which suffer high mortality rates, to larger toads, which are better survivors. This phenomenon may be more general. Broadly stated, our hypothesis is that population stage structure enables the cannibalistic and non-cannibalistic modes of transmission to interact: cannibalism

The model describes the rates of change over time of susceptibles (\dot{S}) and infecteds (\dot{I}) in an otherwise homogenous population ($N = S + I$). We assume that infected individuals are never cured of the infection. Both susceptibles and infecteds give birth to susceptible individuals (the parasite is not transmitted vertically) at a rate of b

offspring per individual per unit time. Both susceptibles and infecteds die from background causes at a rate of d individuals per capita per unit time. Infecteds also die from the disease (virulence) at rate v individuals per capita per unit time. Cannibalism occurs at a rate of a_s attacks on susceptible victims, and a rate of a_i attacks on infected victims (per potential cannibal per unit time), assuming a type I functional response for simplicity. Importantly, the model assumes that all members of the population are both potential cannibals and potential victims, and that each victim is consumed by a single cannibal. The nutritional gain to cannibals from consuming conspecifics is modeled by converting the consumed victims into additional births, while discounting for imperfect metabolic efficiency, c ($0 < c < 1$). For analytical tractability and consistency with the model of Rudolf and Antonovics (2007), we allow the host population to be regulated only by cannibalism, and indirectly by the infection.

Parasites are transmitted via two pathways: through the consumption of infected victims by susceptible cannibals (cannibalistic transmission), and through non-cannibalistic direct transmission (e.g., via social contact or short-lived, local environmental contamination). In each cannibalistic event involving a susceptible cannibal and an infected victim, the probability that the cannibal contracts the disease is τ . For simplicity, we model the direct, non-cannibalistic transmission using the standard mass action assumption. The rate of direct transmission is β per infectious individual per available susceptible per unit time. For simplicity, we assume that pathogen virulence affects host mortality (v) only, but not reproduction. Similar results are obtained when also incorporating reduced reproduction in infected hosts (results not shown).

By deriving the basic reproductive number, defined as the number of progeny infections produced in a susceptible population by a single introduced infected host, we find that the threshold susceptible-only host population size required for the pathogen to invade is $S^* > (d + v) / (\beta - a_i[1 - \tau])$. Thus, for given mortality rates ($d + v$), only sufficiently high direct transmission rates (β) enable the pathogen to invade. To the extent that cannibalistic transmission (τ) is imperfect, cannibalism on infected individuals (a_i) inhibits the pathogen's invasion, since each cannibalistic event at best merely replaces one infected individual with another. Note that if $\tau = 1$, then the invasion criterion is independent of a_i . So, cannibalism of infected individuals at best has no effect on pathogen invasion. We can also calculate from Eq. 1 the infection-free population size $S^* = (b - d) / (a_s[1 - c])$. Thus, cannibalism on susceptibles (a_s) reduces the size of the host population (in the absence of infection) toward or below the threshold required for pathogen invasion.

To characterize the influence of cannibalism on the prevalence of the infection in the population (number of infecteds/total population size) given that it has invaded, we solved the model numerically for varying cannibalistic attack rates, using Matlab's ode45 solver. Without cannibalistic transmission ($\tau = 0$), low cannibalism rates are

sufficient to exclude the disease. However, even with perfect cannibalistic transmission ($\tau = 1$), the effect of increasing cannibalism rates on disease prevalence is strongly negative (Fig. 2A). The threshold rate of cannibalism that suffices to exclude the disease (see derivation in Appendix S3) increases with both cannibalistic and non-cannibalistic

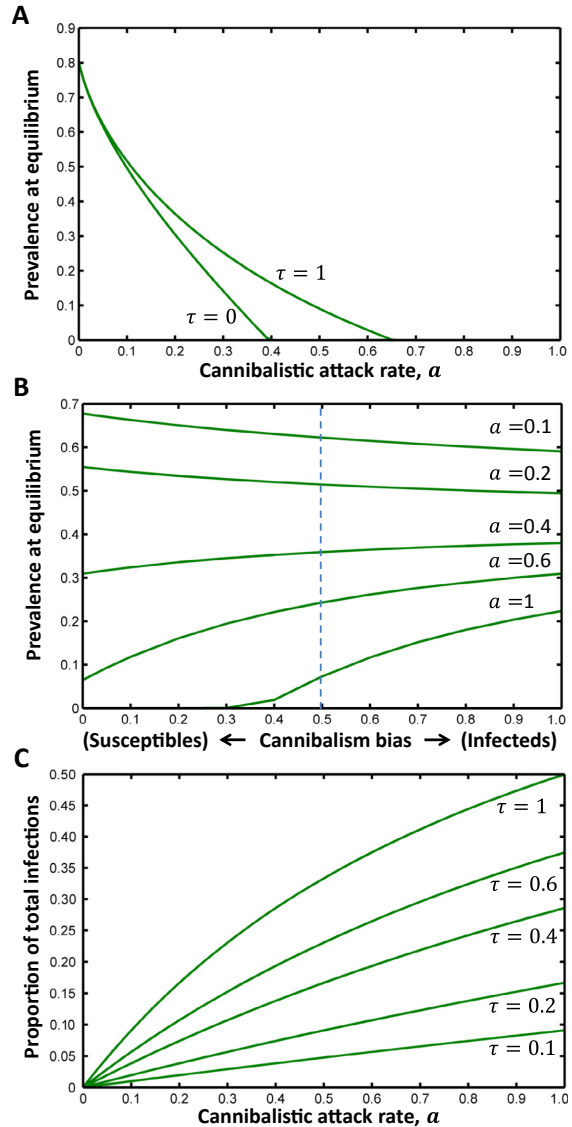


FIG 2. Model 1: homogenous host population. (A) Disease prevalence at equilibrium as a function of cannibalistic attack rate without cannibalistic transmission ($\tau = 0$) and with perfect cannibalistic transmission ($\tau = 1$). Parameter values: $b = 2$; $d = 0.8$; $v = 1.5$; $\beta = 1$; $c = 0.2$. (B) Prevalence at equilibrium as a function of cannibalistic bias toward susceptibles or toward infecteds at different overall cannibalism rates ($a_s + a_i = a$). The dashed line represents unbiased cannibalism ($a_s = a_i = 1/2 a$). At the left end of the axis, cannibalism is directed only at susceptibles, while at the right end cannibalism is directed only at infecteds. Parameter values are similar to those in panel A, with $\tau = 0.9$. (C) The proportion of total infections at equilibrium that result directly from cannibalism of infecteds, under different probabilities of transmission per cannibalistic event. Parameter values: $b = 5$; $d = v = 0.1$; $\beta = 1$; $c = 0.2$.

transmission rates. However, cannibalism reduces disease prevalence in this model regardless of the magnitude of any of these transmission rates.

Cannibalism rates on infecteds and on susceptibles may vary relative to each other across different pathogen-host systems in both directions. Often, infecteds are more easily subdued and cannibalized than healthy animals (e.g., Dhandapani et al. 1993, Williams and Hernandez 2006), while in some cases cannibals might avoid infected conspecifics (e.g., Boots 1998). In Appendix S3, we analyze the relative contributions of cannibalism toward infecteds and toward susceptibles to the exclusion of the parasite from the host population. We show that disease exclusion is more sensitive to cannibalism on infecteds than on susceptibles when the probability of cannibalistic transmission is sufficiently low [namely, if $\tau < 1 - (1 - c)(d + v)/(b - d)$], because many infections are then lost upon cannibalism without transmission. On the other hand, low birth rate and high mortality rates increase the relative importance of cannibalism on susceptibles for disease exclusion, because it is more likely to push the population below the threshold size. Thus, highly virulent, population-regulating pathogens tend to be more vulnerable to selective cannibalism toward susceptibles. We also solved Model 1 numerically to illustrate the effects of cannibalistic bias, toward susceptibles or toward infecteds, on disease prevalence (Fig. 2B). Regardless of the direction or the magnitude of bias, increasing cannibalism rate reduces disease prevalence. Since the parameter values represent a regulatory, virulent pathogen ($v > b - d$), cannibalism reduces prevalence more strongly when biased toward susceptibles. Negative effects of predation on disease spread have been similarly predicted by Packer et al. (2003).

Pathogen evolution

Although cannibalism in the host is detrimental to pathogen spread, it favors the evolution of greater cannibalistic transmission efficiency (τ) in the pathogen, either by strengthening selection for this trait or by weakening selection against it (Appendix S4). That is because cannibalistic transmission allows the parasite to survive events of cannibalism that would otherwise lead to its death. To complement this result, Fig. 2C demonstrates that the proportion of infections at equilibrium that occur directly as a result of cannibalistic transmission can be substantial, and increasing with cannibalism rate.

Model 2: stage-structured host population

We extend Model 1 to include simple stage-structure in the host

$$\begin{aligned} \dot{S}_1 &= b \cdot e^{-\alpha N} N_2 - m_s S_1 - d_1 S_1 - a N_2 S_1 + c a N_2 N_1 \\ &\quad - (\beta_1 I_1 + \beta_2 I_2) S_1 \\ \dot{S}_2 &= m_s S_1 - d_2 S_2 - (\beta_1 I_1 + \beta_2 I_2) \frac{1}{\gamma_2} S_2 - \tau a S_2 I_1 \\ \dot{I}_1 &= (\beta_1 I_1 + \beta_2 I_2) S_1 - m_i I_1 - (d_1 + v_1) I_1 - a N_2 I_1 \\ \dot{I}_2 &= (\beta_1 I_1 + \beta_2 I_2) \frac{1}{\gamma_2} S_2 + m_i I_1 + \tau a S_2 I_1 - (d_2 + v_2) I_2. \end{aligned} \tag{2}$$

The host population consists of small, pre-reproductive juveniles and large, reproductive adults (subscripts 1 and 2, respectively), each of which may be susceptible (S_1, S_2), or infected (I_1, I_2). While this approach to modeling stage structure trades biological realism for tractability, it is a good first approximation of stage-structured systems. Here, background death (d), virulence (v), and direct transmission (β) rates are defined as in Model 1, but each may vary between juveniles and adults. The rate of juvenile maturation to adults, m , may vary between susceptible and infected juveniles (m_s and m_i , respectively). Infected juveniles are assumed to retain their infection status after becoming adults. To prevent uncontrolled population growth when cannibalism is weak, we set the per-capita rate of new births as an exponentially decreasing function of population density with decay parameter α (analyses not presented here confirm that this added component does not alter the results qualitatively). Any susceptible individual, regardless of its stage, is exposed to a shared, directly transmitted infection force of $\beta_1 I_1 + \beta_2 I_2$, generated by all the infected individuals of both stages. We also introduce the degree of adult resistance to direct infection, γ_2 , relative to juveniles, taking values from close to 0 (adults are more susceptible than juveniles to direct, non-cannibalistic transmission) to infinity (adults are entirely resistant to direct transmission). $\gamma_2 = 1$ indicates that adults and juveniles are similarly susceptible to direct transmission.

Cannibalism is typically expressed as large individuals attacking smaller and less developed conspecifics (Appendix S1). To capture this tendency simply, we assume that only adults express cannibalism and that they cannibalize only juveniles. As in Model 1, we assume that each victim of cannibalism is consumed by a single cannibal. For simplicity, we assume that attacks are equally likely on susceptible and on infected juveniles, and occur at a single rate, $a_s = a_i = a$. Thus, in this model, an individual of any stage can be converted from susceptible to infected status by contracting the infection through direct contact, but cannibalism can only transfer infections from infected juvenile victims to susceptible adult cannibals. The only other way an infected juvenile can become an infected adult is by maturing. Fig. 3 presents the pathways of infection in this model graphically. Note that in the absence of cannibalism, Model 1 is a special case of Model 2, in the limit that $\alpha = 0$ and $m_s \rightarrow \infty$.

In nature, the biology of pathogen infection is generally also stage-dependent, which our modeling approach allows us to incorporate. Thus, we proceed to explore the effects of widespread biological phenomena that are associated with the development of organisms:

1. Adults (or later developmental stages in general) are often larger than juveniles, sometimes by a few orders of magnitude. Parasites generally convert host resources (biomass) into infectious propagules. With increasing host body size, parasite reproduction often

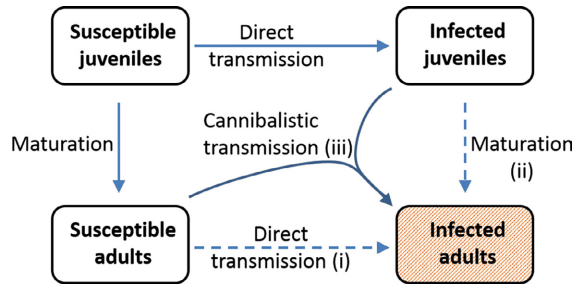


FIG 3. Transitions between infection states and developmental stages in Model 2. Cannibalistic transmission occurs when a susceptible adult consumes an infected juvenile, and thereby contracts the infection. Juveniles maintain their infection status through maturation. Note that there are three pathways to becoming an infected adult: direct transmission to the adult (i), carrying the infection through maturation (ii), and contracting the infection via cannibalism (iii). Adults (golden/shaded box) can be more beneficial hosts than juveniles for pathogen production by being more infectious or by surviving longer. Both delayed maturation of infected juveniles and developmental resistance of adults to direct transmission restrict these pathways to infecting the beneficial host stage (dashed arrows).

increases (Parker et al. 2003, Johnson et al. 2006). For example, entomopathogenic nematodes were found to produce more and larger infectious stages in larger larvae of two different insect species, while the number of propagules per unit host biomass varied little (Boff et al. 2000). Therefore, adults may be more infectious via direct transmission than juveniles. In many cases adults are also more infectious because they are more mobile than juveniles (for example, in insects only adults have wings). This can be incorporated into the model by setting stage-specific transmission rates, $\beta_1 < \beta_2$.

- Juveniles generally tend to suffer greater mortality than adults, especially when diseased (Boff et al. 2000, Yee and Lacey 2003, Begon et al. 2006, Kelehear et al. 2009). This may be due to compromised abilities to escape predators, to forage and compete over resources, or due to lethal interference of the pathogen with host development. This can be incorporated by setting stage-specific virulence, $v_1 > v_2$.
- In many organisms, susceptibility to infection pressure decreases with development, a phenomenon called developmental resistance (Feng et al. 1985, Sait et al. 1994, Briggs and Godfray 1995, Boff et al. 2000, Haislip et al. 2011, Harrison and Hoover 2012). That juveniles are often more susceptible to contracting infections than adults can be incorporated by setting $\gamma_2 \gg 1$. The prevalence of examples of adult stages acquiring infections through cannibalism (Appendix S1) indicates that developmental resistance does not usually compromise this infection pathway. The reason may be that the ability of pathogens to overwhelm their host's immune system and cause systemic infection is positively dose dependent, typically resembling a sigmoidal dose-response function

(Schmid-Hempel 2011). When cannibalizing an infected conspecific, the pathogen dose that is delivered is many orders of magnitude greater than that obtained through ingesting contaminated food or water, or through topical exposure (e.g., Goertz and Hoch 2008).

- Morbidity in infected juveniles often results in retarded development and substantially reduced growth and maturation rates compared to healthy juveniles (e.g., DeAngelis et al. 1993, Sait et al. 1994, Kelehear et al. 2009). This can be incorporated by setting disease-dependent maturation rates, $m_s > m_i$,

Fig. 3 illustrates how these common developmental phenomena affect pathogen epidemiology. Either of the first two phenomena (i.e., more infectious adults, greater juvenile mortality) is sufficient to make the adult stage a more profitable host for the pathogen to exploit than the juvenile stage, because they increase the total number of infectious propagules produced during the host's lifetime. The third phenomenon (developmental resistance) effectively inhibits the direct transmission pathway (Fig. 3i) of infections to the higher-quality adult stage. Similarly, the fourth phenomenon (retarded development of infected juveniles) reduces the rate at which infections reach the adult host via maturation of infected juveniles (Fig. 3ii). This elevates the importance of cannibalistic transfer (Fig. 3iii) as a pathway of the pathogen to the superior adult stage.

To explore the effect of cannibalism on pathogen prevalence at equilibrium, we solved Model 2 numerically under different scenarios using Matlab's ode45 solver. Our starting point is where parameter values are similar for adults and for juveniles. In this case, the model invariably results in a negative effect of cannibalism on disease prevalence, reaffirming this key result from Model 1. This reflects the absence of any biological difference between the two stages; therefore the transfer of infection from juveniles to adults through cannibalism does not matter epidemiologically, just like in a homogenous host population. In Fig. 4, we present the effects of either higher juvenile virulence (Fig. 4A) or more infectious adults (Fig. 4B) combined with developmental resistance and retarded development. In both cases, cannibalistic transmission becomes the primary pathway to infect adult hosts, from which further spread through direct transmission is amplified. In both cases, cannibalism can strongly enhance pathogen spread. When the adult stage is not sufficiently superior to the juvenile stage as a habitat for pathogen reproduction, the positive effect of cannibalism disappears. While these strongly positive effects require the combination of three conditions, each of these conditions is widely satisfied, and therefore their combination is likely prevalent. A sensitivity analysis (Appendix S5) shows that slowing maturation rates in infected juveniles are in fact not necessary to generate a positive effect of cannibalism, but intensify this effect. In addition, only modest developmental resistance is required to generate

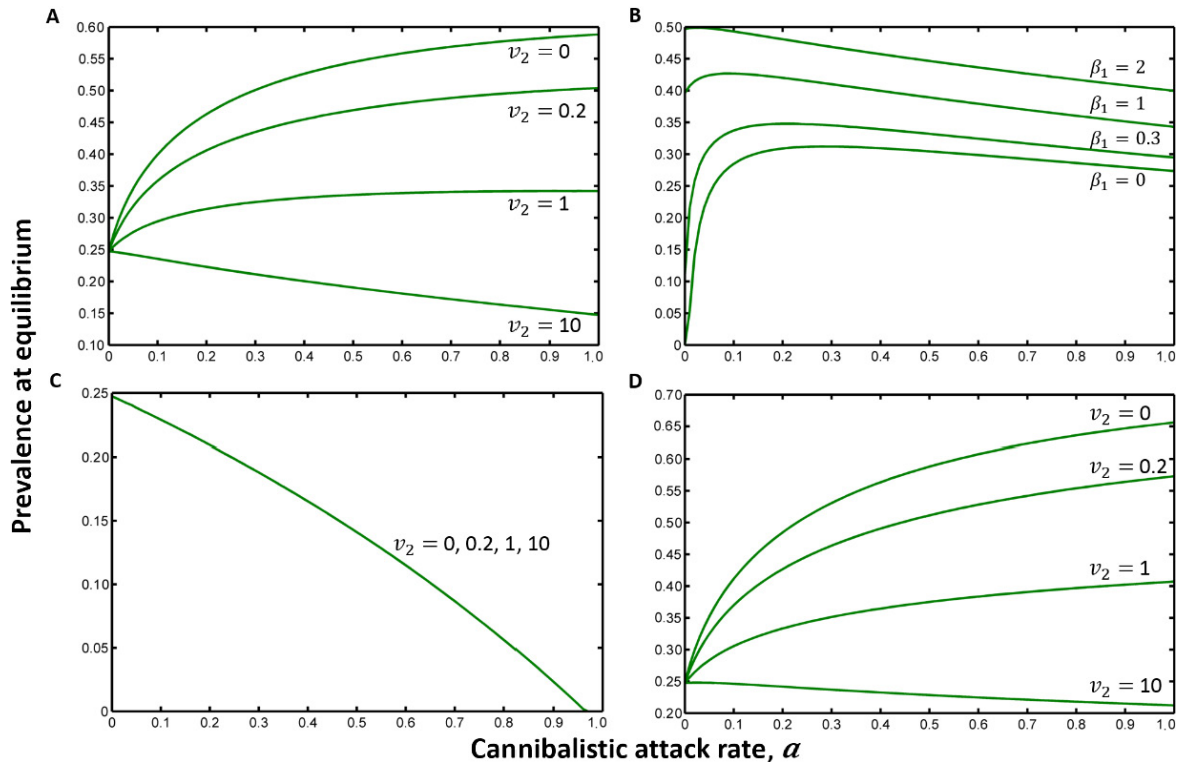


FIG 4. Model 2: stage-structured host population. Disease prevalence at equilibrium as a function of cannibalistic attack rate ($a_s = a_i = a$). (a) Varying relative virulence in adults. Top curve demonstrates a positive effect of cannibalism on pathogen prevalence when infected adults do not suffer any added mortality due to the infection, whereas, in the juveniles, virulence is high. As virulence in the adults approaches that in the juveniles, the effect of cannibalism on pathogen prevalence becomes similar to that in Model 1. Parameter values: $b = 10$; $\alpha = 0.05$; $d_1 = d_2 = 0.5$; $m_s = 1$; $m_i = 0$; $\beta_1 = \beta_2 = 4$; $\gamma_2 = 10^{20}$; $v_1 = 10$; $\tau = 0.9$; $c = 0.2$. (B) A hump-shaped effect of cannibalism on prevalence occurs when infected juveniles are not infectious via direct transmission whereas the adults are infectious. As infectivity of the juveniles approaches that of the adults, the effect of cannibalism on prevalence becomes similar to that in Model 1. Parameter values are similar to those in panel A except $v_1 = v_2 = 3$. (C) Eliminating pathogen transfer during cannibalistic events by setting $\tau = 0$. Parameter values are otherwise identical to those in panel A. (D) Eliminating the demographic effects of cannibalism while retaining pathogen transfer by setting $c = 1$. Parameter values are otherwise identical to those in panel A.

a positive effect of cannibalism. Furthermore, in cases where the juvenile stages are essentially noninfectious but the adults are infectious, cannibalism becomes necessary to allow disease invasion even without developmental resistance. That is because the absence of cannibalism breaks the lifecycle of pathogens that infect juveniles, making the juvenile a dead-end host. Finally, our assumption of a uniform attack rate, a , among hosts is highly conservative. In reality, cannibals often tend to be the healthy and more vigorous, while the victims tend to be those that are sick, weak and easily subdued (Dhandapani et al. 1993, Williams and Hernandez 2006). This increases the frequency of the type of cannibalistic events that allows pathogen transfer, and reduces the frequencies of cannibalistic events in which pathogen transfer to a susceptible host cannot occur (i.e., cannibalism of susceptible victims or cannibalism by an already infected cannibal).

Density dependence in stage-structured populations can, in some models, lead to complex demographic feedbacks. For example, asymmetrical density-dependent

regulation of juvenile maturation and adult reproduction can in some cases lead to overcompensatory demographic responses to mortality (De Roos et al. 2007). These demographic responses, in turn, can also affect disease spread in complex ways that are beyond the scope and modeling approach used in this paper. However, to demonstrate that the positive effect of cannibalism on disease spread results only from cannibalistic pathogen transfer and not from any demographic effects of cannibalism, we removed cannibalistic transmission from juveniles to adults ($\tau = 0$), while retaining all the demographic effects of cannibalism. In this case, the positive effect of cannibalism on disease spread disappears (Fig. 4C). Alternatively, if we assume that each victim of cannibalism is immediately replaced with a new, susceptible juvenile ($c = 1$), we can eliminate the demographic effects of cannibalism while maintaining the pathogen transfer effect (upon “cannibalistic” encounter, the adult may simply contract the infection with probability τ , but does not kill the juvenile). In this case, cannibalism still carries the strong positive effect on disease spread (Fig. 4D).

These analyses indicate that the positive effect of cannibalism is driven in our model only by the consistent transfer of infections toward more developed hosts.

DISCUSSION

The role of cannibalism in the epidemiology of common parasites that can be transmitted both via cannibalism and via non-cannibalistic horizontal transmission is threefold (Fig. 1): (1) cannibalism suppresses populations of susceptibles, thus reducing the opportunity for infectious pathogens to spread; (2) cannibalism removes infecteds from the population, thus directly reducing the prevalence of the disease; and (3) cannibalism transfers infections from infected victims to susceptible cannibals. While the effect of cannibalism on pathogen spread can be negative (Fig. 2A) due to the operation of the first two processes, we have argued that the third process may lead to a prevailing net positive effect on pathogen spread in structured host populations (Fig. 4). This adds to the spreading mechanism identified by Rudolf and Antonovics (2007), “group cannibalism,” in which multiple susceptible cannibals share each infected victim. However, whereas group cannibalism may be uncommon (Rudolf and Antonovics 2007), population structure is universal. In addition, a complementary study (Sadeh and Rosenheim, *in press*) shows that when combined with vertical transmission, cannibalism amplifies disease spread without the need for population structure.

Our work advances a simple intuition that may be useful in the study of many parasite–host systems in which the parasite can be transmitted through cannibalism. First, it is essential to consider how cannibalism maps onto population structure: who are the typical cannibals, and who are the typical victims of cannibalism? Once these questions are answered, differences among these groups in biological traits that are relevant for disease spread will determine the effect of cannibalistic infection transfer. If cannibalism tends to transfer infections to sufficiently superior hosts, then it can enhance spread in the population at large. A compatible process has been suggested by Pizzatto and Shine (2011) for the spread of lungworms in cane toad populations in Australia. While confined to their natal pools during the tropical dry season, the larger metamorphs cannibalize smaller conspecifics. Infected toads are more likely to be cannibalized because of their compromised locomotion. Cannibalistic, larger metamorphs are more likely to survive interspecific predation, infection and other mortality risks, and therefore recruit disproportionately to the adult population. Thus, cannibalism transfers lungworms “from a “doomed” host to a “safe” host” (Pizzatto and Shine 2011).

The spreading mechanism that our model emphasizes is directly analogous to the common trophic transmission of parasites with complex life cycles through interspecific predation, where each prey is also often consumed by a single predator. It has been suggested that in these

systems, trophic transmission was favored evolutionarily as a result of the risk of mortality of the parasite due to the predation of its host (Lafferty 1999), the opportunity for transferring into a higher-quality host of larger body size (Parker et al. 2003), and the possibly greater probability of infecting a definitive host by encysting in its prey (the intermediate host) rather than by environmental transmission between definitive hosts (Choisy et al. 2003). The evolution of transmission through cannibalism may be driven by similar benefits. Cannibalism can provide opportunities for a parasite to transfer to a host of higher quality. Moreover, even if all hosts are of similar quality (as in a hypothetical homogenous population) and cannibalism functions just as a strong source of host mortality, cannibalistic transfer still allows the parasites of the victims of cannibalism to persist, and is therefore expected to be selected for more strongly as cannibalism rates increase (Appendix S4). Thus, cannibalism remains an important transmission mechanism that may account for many of the cases of infection (Fig. 2C).

On the other hand, the obligatory trophic transmission of parasites with complex life cycles across host species involves serious ecological risks of failure. Moreover, it often requires physiological adaptations to the dramatically different internal environments of phylogenetically distant intermediate and definitive hosts (e.g., from ectotherm snails to endotherm birds). In contrast, transmission through cannibalism may carry much lower costs. Parasite evolution of transmissibility through cannibalism may still be constrained by tradeoffs with alternative modes of transmission. For example, cannibalistic transmission may require propagules specifically differentiated to survive in the digestive tract of the cannibal, or to migrate from the gut to the target tissue, while horizontal transmission may require a different set of traits in the infectious propagule, such as surviving in the external environment. Nevertheless, for any given trade-off, sufficiently high cannibalism rates in the host are expected to maintain positive selection for cannibalistic transmission.

Stage structure is a universal phenomenon and an important source of functional variation (Miller and Rudolf 2011). While stage and size are very commonly correlated with roles of cannibalistic interactions (Appendix S1), other forms of population structure may also be relevant. For example, many populations are behaviorally structured due to personalities (Sih et al. 2012). Aggressive behavioral types can be expected to include a disproportionately high share of cannibals (e.g., Pruitt et al. 2008). Aggressiveness, in turn, may also be correlated with certain activity or dispersive tendencies (Kortet and Hedrick 2007, Pruitt et al. 2008), social dominance (Kortet et al. 2010), immune function (Kortet et al. 2010, Réale et al. 2010), or other behavioral or physiological traits that affect the production, duration or range of spread of infectious propagules by the cannibals.

Our modeling approach allowed us to elucidate the effect of consistent pathogen transfer toward more

developed and higher quality hosts. We suspect that additional mechanisms may exist that are not captured in our model, by which cannibalism can enhance the spread of horizontally transmitted diseases. For example, Holt and Roy (2007) considered interspecific predation on the host in an SIR model, where some of the infected hosts are cured from the disease and are thereafter immune to reinfection for the rest of their lives. In their model, predation can enhance disease prevalence, because the predatory removal of immune hosts makes room for greater birth of new susceptibles who are vulnerable to infection. This mechanism could presumably also operate with cannibalism, especially if immune individuals that have fought off an infection are weaker and more likely to be cannibalized than susceptibles. Similarly, physiologically structured and biomass models (e.g., Persson et al. 2003, De Roos et al. 2007) should be useful for further increasing the biological realism of theory and advancing our understanding of demographic and resource-dependent mechanisms through which cannibalism may influence disease spread. For example, stage-specific mortality due to cannibalism can lead to an overcompensatory increase in the host population size that may, in turn, create more opportunity for disease spread.

More broadly, our work demonstrates the importance of evaluating possible interactions between multiple modes of transmission. It has been shown that taking into consideration only one of multiple modes of transmission may result in mis-estimation of epidemiological quantities such as the basic reproductive number and epidemic growth rate (Cook et al. 2007, Tien and Earn 2010), which can seriously compromise the efficacy of control strategies. The qualitatively different results between our homogenous and stage-structured models are a particularly striking example for a transmission pathway whose positive interactive effect with another pathway can overturn its negative effect in isolation. Therefore, we suggest that known modes of transmission should be incorporated into epidemiological models jointly before any of them is considered to be unimportant.

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