Title: Infectious diseases and social distancing in nature

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Abstract: Spread of contagious pathogens critically depends on the number and types of contacts between infectious and susceptible hosts. Changes in social behavior by susceptible, exposed, or sick individuals thus have far-reaching downstream consequences for infectious disease spread. While 'social distancing' is a now too-familiar strategy to manage COVID-19, non-human animals also exhibit pathogen-induced changes in social interactions. Here, we synthesize the effects of infectious pathogens on social interactions in animals (including humans), review what is known about underlying mechanisms, and consider implications for evolution and epidemiology.

Word count (title, abstract, main text, references without title, figure legends): 6640

References: 90

One Sentence Summary: Infectious diseases change social network structure in animals, including passive and active behavioral changes by both sick and healthy group members.

Main Text:

Introduction

A crucial question to understand the spread of infectious diseases is how animal social networks change through time as uninfected, exposed, or sick individuals alter their behavior in response to contagious pathogens (*1–5*). Compartmental epidemiological models (e.g., Susceptible-Infected-Recovered models) often make simplifying assumptions that hosts participate equally in contacts, and contacts remain constant through time (*6*). Contact rates, however, clearly vary among individuals and over time, and network-based epidemiological models demonstrate that contact variation significantly affects disease dynamics (*7–10*). One key source of contact-rate heterogeneity lies in behavioral responses to pathogens by infected, contaminated, or susceptible individuals. While some parasites famously manipulate the behavior of their hosts to facilitate transmission to new hosts (reviewed in *11*), behavioral responses to infection in social animals are more often host-driven (*12*). Here, we review the diverse suite of host-mediated behavioral responses to pathogens, which include sickness behaviors (immune-mediated lethargy and social disinterest) by infected hosts, and avoidance or exclusion of potentially-infectious conspecifics by susceptible individuals, which both likely suppress population-level pathogen spread. Conversely, infected individuals may receive care from uninfected group members, facilitating transmission. Such social responses to infection are commonly observed in non-human animals; thus, considering the evolutionary and epidemiological implications of social distancing in nature could shed important light on our understanding of human outbreaks.

Pathogens change social cues, signals, and behaviors

Pathogens induce a wide array of changes in the behaviors of individuals they successfully colonize, and their uninfected group members. These changes arise at distinct stages across systems, beginning as early as initial host exposure to the pathogen (i.e., 'contamination') or as late as symptomatic stages of disease (Figure 1). Some externally transmitted pathogenic fungi in social insects elicit host behavioral changes as early as 15 minutes after exposure, when individuals are already potentially *infectious*, but not yet *infected*, which requires fungal spores to pierce the cuticle (*13*). For example, termites exposed to entomopathogenic fungal spores produce immediate vibratory alarm signals that trigger avoidance or hygienic responses in nestmates (*13*, *14*); the same pathogen induces self-removal and care responses in ants within hours of exposure (*3*, *15–17*), suggesting that social insects detect cues associated with the pathogen itself on the surface of the cuticle.

In other systems, changes in behavior are triggered by modifications in social cues and signals caused by infection itself or by challenges of the immune system with pathogenic compounds – either during the incubation period while the host is not yet infectious, or during the symptomatic disease phase (Figure 1). For example, virus-infected or immune-challenged mice produce specific olfactory cues (*18*); feces of protozoa-infected mandrills have a distinct smell (*19*); immune-challenged humans have more aversive body odor (*20*); and fungus-infected ant pupae produce chemical cues that trigger hygienic behaviors in adult ants, including destruction and disinfection of the cocoon (*21*). Visual cues can also be altered by infection: for example, Trinidadian guppies avoid conspecifics with characteristic dark spots caused by parasitic infection (*22*, *23*); and humans can identify immune-challenged individuals by examining facial photos (*24*). Infection or immune stimulation can also affect auditory cues, as is

the case for vampire bats challenged with immunogenic lipopolysaccharide (LPS), which reduce contact calling rates (*25*), and LPS-challenged men, who experience audible breathing changes (*26*).

In addition, innate immune responses to pathogens typically stimulate physiological (e.g. fever) and behavioral changes in infected host, including lethargy and reduced social interactions, particularly early in infection (*27–30*). These 'sickness behaviors' occur widely across host taxa and in response to diverse pathogens (*27–31*). Because the predominant physiological mediators of sickness behaviors are the pro-inflammatory cytokines that link the immune, endocrine, and nervous systems (*28*, *29*, *32*), the consequences of these behavioral changes for social interactions can be experimentally explored by injecting hosts with immunogenic substances like LPS or cytokines to induce sickness behaviors (*2*, *28*, *33*). Given how common they are across taxa, sickness behaviors could also serve as a relatively universal cue for recognizing infected conspecifics. Detecting sickness behavior may be easier when the observer is familiar with the baseline behavior of the sick individual. Hence, such recognition mechanisms could be more common in species that live in close-knit groups. However, the sensory and neural mechanisms responsible for the recognition of such indirect cues are still poorly known.

How individuals detect, recognize, and respond to disease-related cues -especially chemical - has received a lot attention (*18*, *19*) and changes in appearance, smell, vocalizations, or behavior are known to induce “social distancing” (i.e. reduction in potentially transmission-causing contacts) in both animal and human societies. However, natural selection can also lead to seemingly altruistic behaviors, such as helping infected conspecifics, which may instead increase disease transmission. Here, we focus on six pathogen-induced physiological or behavioral

changes in hosts that cause changes to social interactions in groups and can be driven by conspecifics or the potentially-infectious individual (Figure 2).

Passive self-isolation by potentially-infectious individuals

Passive self-isolation is a component of sickness behavior (*27–29*) that occurs when a sick individual directly or indirectly reduces contact with others while remaining within the group. It can occur directly when infected animals lose motivation to engage in physical social behaviors such as grooming or food sharing (*33*, *34*), a phenomenon termed social "disinterest." For instance, immune-challenged vampire bats reduce grooming of certain conspecifics (*33*), virus-infected bees share less food with nestmates (*34*), and humans challenged with bacterial endotoxin self-report feelings of social disconnectedness that may reduce contacts (*35*).

Passive self-isolation can also occur indirectly due to physiological responses to infection such as lethargy, which is challenging to tease apart from direct effects without measuring the motivation of the test subject. Passive isolation can happen, for instance, when sickness-induced lethargy reduces individuals' social investments in the biological marketplace, such as allogrooming or provisioning of food (*36*), which could reduce reciprocal services from, and contacts with, group members. Immune-challenge and resulting lethargy can also reduce social vocalizations, which as an incidental side-effect may make group members less inclined to interact with the sick individual (*25*). Lethargy can also alter patterns of movement and dispersal, which determine contact with other individuals (*2*, *5*). Thus, reduced movement could restrict the spread of directly-transmitted pathogens between clusters of individuals. However, such passive isolation likely does not evolve as an adaptation specifically for this purpose.

Active self-isolation by potentially-infectious individuals

Potentially-infectious human and non-human animals sometimes actively remove themselves from others, thereby preventing susceptible individuals from interacting with them. This differs from passive self-isolation, where susceptible group members can maintain interactions with lethargic infected individuals. For instance, although immune-challenged bats perform less grooming, they remain part of the group and still receive food donations from conspecifics ((*33*). In contrast, fungus-exposed ants spend more time outside the nest, and thus actively self-isolate, limiting encounters with susceptible nestmates (*3*, *37*, *38*, Figure 3). Self-isolation is a seemingly altruistic act hypothesized to evolve through kin selection, as evidenced by its widespread occurrence in eusocial insects, where high within-colony relatedness favored the evolution of numerous collective disease defenses termed "social immunity" (*3*, *37–39*). Active self-isolation appears to be a general response to apparent detection of impending death, not only from pathogens but also from CO_2-poisoning and toxins (*37*, *40*). However, the cues and mechanisms underlying initiation of self-isolation remain unknown.

Despite anecdotal observations, like a tuberculosis-infected badger leaving its group to die alone (*41*), systematic investigations of active self-isolation in animals outside eusocial insects are lacking. By contrast, infected humans are known to actively self-isolate, as evidenced by historical outbreaks (*42*). However, such self-isolation is often driven by governmental policy directives rather than personal initiative (*43*).

Avoidance of potentially-infectious conspecifics

In animals affected by contagious pathogens, selection should favor susceptible individuals who can detect and subsequently avoid potentially-infectious conspecifics (*44*). Indeed, avoidance of exposed or infected conspecifics occurs in diverse non-human animals including lobsters (*45*),

Trinidadian guppies (*22*, *23*), mandrills (*19*, *46*), and termites (*14*). Humans can avoid conspecifics based on facial cues or chemosensory cues (*20*, *24*) and awareness of infectious threats can exaggerate avoidance responses even without proximity to infected people (i.e. gathering information online; *47*). Avoiding infectious conspecifics requires (i) cues that differentiate potentially-infectious individuals from healthy group members, (ii) sensory systems to detect those cues, and (iii) neurological pathways that translate cues into behavioral changes. Importantly, pathogen-exposure and infection alter a suite of sensory cues that need not be pathogen-specific (generally "disgust-eliciting"; *48–50*) and could, therefore, result in rapid manifestation of avoidance behaviors in animal populations (*51*).

Exclusion of potentially-infectious individuals (enforced isolation)

Exclusion of infectious conspecifics, by aggression or other means, represents another direct way by which pathogens lead to social distancing. We distinguish exclusion from self-isolation in that exclusion is enforced by *uninfected* individuals. Aggressive exclusion of infected individuals is mostly documented in eusocial insects (*39*, *52*), such as virus-infected honeybees forcibly dragged out of the nest (*52*). Much like avoidance, active exclusion requires an ability to recognize infected individuals. In *Lasius neglectus* ants, destructive removal of infected broods is driven by changes in cuticular chemical composition that allow uninfected workers to detect otherwise asymptomatic fungal-infected broods and remove them (*21*). Enforced exclusion has not been experimentally demonstrated in mammals, though observational evidence exists (*53*) and enforced quarantine has occurred throughout human history and remains an important public health measure against pathogens like Ebola and SARS (*54*, *55*).

Increases in social contact through caregiving

Helping is one of the main aspects of human healthcare, whether from family, friends, or healthcare workers (*56*). However, such caregiving incurs increased infection risks for caregivers (*57*). The extent of caregiving in non-human mammals is still unclear, so far relying largely on opportunistic field observations (*56*). The clearest evidence for caregiving behaviors outside humans comes from antifungal grooming in eusocial insects: ants and termites routinely physically remove or chemically deactivate infectious fungal spores on contaminated nestmates, thereby decreasing the risk of infection for their nestmates, but increasing their own risk of low-level infection (*15*, *16*, *58*. Figure 3). Recognizing infected or exposed conspecifics is a precondition of caregiving. Such recognition could occur through detecting infection cues (see above), the pathogen itself in the case of external contamination, or active solicitation of help such as the vibratory alarm behavior termites use to elicit care (*13*).

Proactive social distancing among susceptible or asymptomatic individuals to slow spread

In the ongoing COVID-19 pandemic, most countries implemented generalized social distancing, requiring asymptomatic and uninfected individuals to minimize all contacts. This drastic measure proved effective in reducing transmission rates in affected communities (*43*). A similar strategy is employed by colonies of black garden ants: upon entry of fungus-contaminated nestmates, nurses and foragers increase their social distance from one another, reducing inter-group contact rates (*3*). This early colony-wide reaction likely reduces the risk of an epidemic by limiting inadvertent transmission from asymptomatic carriers (Figure 3).

Epidemiological consequences for directly-transmitted pathogens

The structure and dynamics of social contact networks fundamentally determine the fate of contagious pathogen outbreaks—how fast and far they spread and who becomes infected (*7–10*). Contact rates vary among individuals based on social structure, sex, age, among others, and shape individual and community level risks of transmission (*8*). Studies of human viruses such as influenza shed light on how individual-level behaviors, such as social withdrawal during infection, could inform public health responses (*5*). In the race to combat COVID-19, numerous studies examined the public health utility of unprecedented large-scale social distancing (reviewed in *43*). By studying pathogen-induced social network changes in non-human animals, we may learn about the efficacy of naturally-evolved social distancing rules that could inform the management of contagious pathogens in humans.

Passive and active self-isolation, avoidance, exclusion, and group-wide social distancing can profoundly affect the spread of contagious pathogens by reducing the degree of contact between susceptible and sick individuals and, hence, altering network-level contact heterogeneity (*1–3*, *5*, *59*, *60*, Figure 4). For instance, network centrality of wild vampire bats is reduced when their immune system is challenged, but this effect diminishes over time (*60*). Similarly, immune-challenged mice reduce connectivity to their group due to lethargy (*2*), and ant social networks undergo deep restructuring to prevent colony-wide spread of an infectious fungal threat (*3*, Figure 3). Unfortunately, most research on sickness behaviors has been done on lab models like mice, often in dyads to identify physiological mechanisms; this mechanistic focus prevents inquiry into epidemiological effects in larger populations and networks. Such larger-scale research is increasingly possible thanks to technological advances such as next-generation proximity loggers and automated tracking of RFID-tags or QR-code labels, which provide high-

resolution data on network structure and track how individuals and group properties change over time (*61*). A key future research goal is to understand how social effects of infections alter both the topology and overall transmission properties of contact networks.

Epidemiological studies of passive self-isolation in humans are mainly modeling-based (*62*) or from surveys of social contacts in the presence or absence of infection. For example, influenza-induced sickness behaviors reduce the number of social contacts and, hence, the virus's reproduction number by about one-quarter relative to expectations without sickness behavior (*5*). However, the effectiveness of passive self-isolation in suppressing transmission will depend on the extent to which behavioral changes align with the infectious period of a given pathogen (Figure 1). Further, sickness behaviors and their effect on social interactions are themselves confounded by other factors such as social stress, sex, and kin relationships (*12,* Figure 5). In humans, sociocultural factors can affect expression of sickness behavior. For instance, there are often economic or social motivations for persistent work attendance when sick, a phenomenon known as 'presenteeism' (*63*). There is also preliminary evidence that personality traits or cultural norms such as stoicism and familism affect sickness behavior differently based on demographic characteristics (*64*). Any epidemiological benefits of isolation and sickness behavior cannot accrue in sociocultural systems that stigmatize rest, recuperation, and isolation or do not provide individuals the means of safely engaging in these behaviors. The additional level of complexity contributed by environmental, biological, and cultural variation in the expression of isolation and sickness behaviors should be incorporated in future models of pathogen-induced behavioral changes and transmission (Figure 5).

Active self-isolation prevents conspecifics from interacting with infected individuals, while passive self-isolation may not have the same effect. Therefore, active self-isolation,

particularly when such behavior occurs early in the infectious period, should decrease transmission-causing contacts more effectively (Figure 4), as shown recently for ant-foragers that self-isolate when exposed to a fungus, greatly reducing their contacts with other colony members (*3,* Figure 3). The epidemiological effects of enforced exclusion should be similar, as it prevents all subsequent interactions with conspecifics. For instance, in *L. neglectus* ants, removal of infected broods reduced transmission by 95% (*21*). Measures that isolate infectious individuals are more effective when asymptomatic transmission is rare and lose efficiency as asymptomatic transmission increases (*65*). In the latter case, active isolation must be supplemented with other pro-active measures such as quarantine of contacts due to contact-tracing or generalized social distancing (*43*).

Avoidance behaviors by uninfected individuals reduce pathogen spread but require cues that may not align well with a pathogen's infectious period (Figure 1). Further, there can be substantial inter-individual variance in avoidance based on traits such as an individual's immune susceptibility or kinship to the sick conspecific (*12*, Figure 5). Theory suggests that risk-based evaluation of infectious conspecifics could have important epidemiological consequences and determine whether pathogens persist or disappear (*59*). Environmental cues like unsanitary conditions might also modulate avoidance behaviors (*66*) and could be incorporated into epidemiological models.

Caregiving inherently increases contact between helpers and infectious individuals but may accelerate recovery of sick individuals, reducing infectious period length. Their combined impact on pathogen transmission will depend on the nature of caregiving behavior (e.g., directly removing pathogens such as antifungal grooming in ants, versus mitigating harm to sick individuals), and how carefully caregivers mitigate their own risk. Healthcare workers are

among the most affected in recent pandemics, comprising 18.6% of MERS cases, 21% of SARS cases, and similarly high numbers for the COVID-19 pandemic (*57*). Because of their risky occupations, healthcare workers can become "superspreaders" (*9*), connecting patients, their families, and friends, and contributing disproportionately to overall spread than the average person. Some healthcare workers continue to work while symptomatic – despite acknowledging that this places patients at risk - due to structural concerns about staffing as well as cultural norms that support presenteeism (*67*). Thus, targeted infection control procedures for healthcare workers are imperative, as are policies that discourage presenteeism such as sufficient paid sick leave. Because evidence of helping behavior is rare outside humans and eusocial insects, we know little about its epidemiological effects in non-human animals. Social insects, however, highlight the complex balance between costs and benefits of care behavior; for example, ants with high disease susceptibility preferentially use safer care behaviors, such as antimicrobial spraying, over riskier behaviors such as grooming (*17*). In humans, lower susceptibility (i.e. no pre-existing conditions) or targeted vaccination might affect decision making about when and how intensively to care for the sick, and that care's impact on pathogen spread.

Evolutionary consequences for pathogens

Despite social distancing strategies, contagious pathogens persist in human and animal populations. Thus, social distancing behaviors and the capabilities of pathogens to counteract these behavioral defenses could result in evolutionary arms races and, hence, shape evolutionary trajectories of both hosts and pathogens (*12*, *68*).

Pathogens are predicted to evolve a virulence level (i.e. damage to host) that optimizes their overall growth rate within the population. Theory suggests that this growth rate for

contagious pathogens reflects a balance between within-host replication to generate infectious propagules (e.g., pathogen shedding), which typically underlies virulence, against the need to get those propagules to new hosts before the infectious individual dies or recovers (*69*, *70*). There is surprisingly little research on how pathogens evolve to optimize the trade-off between sufficient shedding by hosts, while reducing host symptoms that induce social distancing by infectious or susceptible hosts. Pathogens may evolve counter-adaptations that minimize host isolation, whether by mitigating symptoms (e.g., lethargy) that affect behavior of infectious hosts, or altering sickness cues available for detection. Inhibition of pro-inflammatory cytokines that drive passive self-isolation – including lethargy – might be a target for such counteradaptations by pathogens. Inhibition of cytokine responses is well described in bacterial and viral pathogens (*71*). Similarly, upregulation of anti-inflammatory cytokines could theoretically affect sickness behaviors and social contact rates (*72*).

All forms of social distancing, whether driven by infectious or susceptible hosts, should generally select for less-virulent pathogens with milder symptoms, or asymptomatic infectious periods (*69*, *70*), especially for pathogens whose transmission is weakly reliant on virulence (*72*). Further study is needed to determine whether avoidance behaviors favor pre-symptomatic infectious periods as pathogen counterstrategies. Conversely, helping behavior may increase transmission opportunities, potentially favoring increased pathogen virulence because high virulence no longer limits, and may even facilitate, transmission opportunities. An intriguing prediction is that pathogens might evolve to elicit helping behaviors (e.g., inducing signals of distress) to attract susceptible caregivers. Such pathogen manipulation occurs for other contact behaviors such as augmented aggression (reviewed in *11*), or increased acceptance of non-colony members in honeybees (*34*).

Evolutionary significance for the host

Social distancing can have substantial fitness costs for infected individuals, which may experience loss of social status, increased exposure to predators, decreased foraging efficiency, and reduced social support (*27*, *29*, *30*, *73*). Susceptible individuals can also incur costs such as reduced mating opportunities when they avoid or exclude infectious conspecifics (*49*), particularly if there are false-positive signals. Proactive general social distancing may compromise other collective functions such as food sharing or information flow (*3*). This raises questions about the evolutionary origin of and persistence of pathogen-induced social distancing in humans and non-human animals.

Social distancing by susceptible individuals (i.e., avoidance, exclusion of infectious individuals, and proactive distancing) should be favored whenever the benefits of avoiding infection outweigh costs of distancing, which include indirect effects of disrupting the social group. These mechanisms should therefore mostly evolve in loose social groups, where costs of forgoing social interactions are small (*74*, *75*), or in the face of virulent pathogens, where costs of contracting infection are high (*76*). Consistent with these predictions, highly social animals appear less likely to avoid sick peers, and low-virulence diseases such as sarcoptic mange in grey wolves do not elicit exclusion (*51*, *73*). Further, because the costs of contracting infection can even vary among individuals within a species, avoidance behaviors should be variable such that highly susceptible individuals show stronger avoidance responses, as occurs in Trinidadian guppies (*22*, Figure 5). In addition to variable costs, because the benefits of social interactions vary according to individuals' social roles and position, avoidance behaviors should depend on both individual risk (*51*) and social context. For instance, in humans, population-level differences in disgust perception and sensitivity (*77*) may be linked with differences in pathogen

threat (*78*). Social status and financial resources clearly affect individuals' ability to absorb costs of social distancing, and in humans, some costs of distancing may be lowered through virtual interactions (*51*). Further work is needed to clarify connections between individual social status, role, and – in humans – attitudes and practices and behavioral changes.

The evolution of social distancing enacted by potentially-infectious individuals themselves is a more complex question, since leaving the group incurs significantly higher costs for isolated individuals (who forgo the benefits from all kin or group members) than for remaining group members (who only experience a small decrease in group size). This asymmetry in costs may lead to conflicts of interest between infectious and susceptible group members, where concealing an infection may be beneficial to sick individuals if it allows them to maintain benefits of sociality (i.e. presenteeism in humans). This is supported by studies showing that social context alters expression of sickness behaviors (*79*): for instance, immune-challenged zebra finches express stronger behavioral sickness symptoms when housed alone than in a group (*80*). Other cues (e.g., olfactory or visual signs of infections) may be less plastic, harder to conceal, and potentially constitute more honest information for conspecifics.

Whether sickness behaviors are expressed as an inevitable side effect of infection or as an active, adaptive host response has been highly debated (*81*) given the difficulty in disentangling the behavioral and inflammatory components. Sickness behaviors are generally hypothesized to improve recovery by redirecting energy to costly immune responses (*27*). Direct tests of the adaptive benefits of sickness behavior are rare (but see *82, 83*). However, multiple studies find that sickness behavior and physiological responses to infection, such as fever, are not always correlated and can arise independently of one other (*30, 84*). This led to the hypothesis that passive social distancing mediated by sickness behavior, as well as active self-isolation, may

confer additional indirect benefits to infectious individuals beyond beneficial effects on recovery (*30*).

The most obvious social benefit of self-isolation lies is kin protection, as social distancing reduces the risk of transmitting pathogens to related group members, thereby increasing the indirect fitness of infected individuals (*85*). Kin selection should therefore favor the evolution of self-isolation within highly related groups, as likely occurred in many eusocial insects (*3*, *12*, *37*, *38*), which are characterized by unparalleled levels of relatedness among group members (*86*). In social insects, active self-isolation cannot be a mere side-effect of infection, as it often occurs after exposure but before the onset of infection (*3*, *38*) or even in the absence of an infectious organism as a response to other causes of mortality such as poisoning (*37*, *40*); instead, it appears to be a seemingly altruistic act that contributes to the colony's cooperative disease defenses (*39*). Interestingly, self-isolation in humans could have the opposite effect of self-isolation in other animals, as it might decrease contact with unrelated individuals outside the home, but increase contact with family members, thus putting kin at higher risk than non-kin.

Kin selection theory also predicts that caregiving should evolve among relatives, as increased kin survival may outweigh the risks associated with caring. This is supported by multiple studies of non-human animals: mandrills do not avoid grooming parasitized offspring and half-siblings (*46*); antifungal grooming is omnipresent in eusocial insects, greatly increasing the survival of exposed workers (*15*, *16*, *39*, *58*). Similarly, humans are more likely to receive aid from relatives than strangers across a range of conditions (reviewed in *87*). However, helping behavior can also evolve in groups with low relatedness provided the benefits of aiding a diseased group member outweigh potential costs to helpers. This may occur in close-knit groups

strongly reliant on cooperation for survival or host-pathogen systems with low transmission risk or intermediate pathogen virulence (*12, 73, 74*).

An alternative explanation for the evolution of caregiving is that it confers direct benefits to helpers. For example, in social insects, caring individuals gain protection against secondary infection with the same pathogen through a temporary boost of their immunity (*15*, *58*); similarly, in humans, being close enough to recognize an individual's ailment might prime the caregiver's immune system (*88*). Other benefits could accrue through reciprocity (i.e. delayed benefits) or reputation enhancement and subsequent reputation-dependent benefits from third parties; *87*).

Conclusions and future directions:

Social distancing behaviors have been studied extensively in humans and non-human animals. While these behaviors (especially sickness behaviors) are often studied using immuno-stimulants, far less research has been done with pathogens that have naturally co-evolved with their hosts. This is an important next step because the considerations outlined above suggest that the strength and nature of distancing behaviors may be a key element of host-parasite coevolution (*12*, *68*), which may favor changes in virulence, pre-symptomatic or asymptomatic periods, and pathogen-induced cues. We should use naturally co-evolved systems to examine how effectively sick individuals are isolated; the physiological, sensory, and neurological basis of any isolation; and its epidemiological effects. How do individuals sense their own (or others') illness or pathogen-exposure? When during the infection do cues arise and are some of them present before obvious signs are noticeable? To what extent is the timing of cues driven by host versus pathogen-mediated mechanisms? How does perception of cues influence decisions to change social dynamics and group structure? Understanding these mechanisms and their

consequences is crucial for then predicting how broadly hosts can use them in the face of diverse pathogens, and how and when pathogens may co-evolve to combat these mechanisms. While we largely discuss pathogen exposure and infection interchangeably, the fact that some species can respond to mere pathogen presence, while other behaviors are expressed only when individuals become visibly sick raises important questions about the extent to which the cues used for social distancing correlate with infectiousness (i.e. pathogen shedding). Specifically, what are the epidemiological effects of early versus late pathogen-induced social distancing, and at what stage do the benefits to host of preventing ongoing transmission outweigh costs of distancing?

Studies in eusocial insect societies have been especially productive, as they practice seemingly altruistic behaviors such as active self-isolation and caregiving, which decrease the risk of outbreaks through the colony (*3*, *37–39*). These organisms' social networks share many characteristics with human societies and have evolved properties to prevent pathogen transmission (*3*, *4*, *39***)**. As a result, their social distancing strategies may prove key to investigating the epidemiological effects of such behaviors and thus their potential public health utility. There are, however, important differences in interpreting how social network structures evolve in response to pathogenic threats. In eusocial insects, the behavioral repertoire known as "social immunity" most likely represents group-level adaptive behaviors that evolve in response to high relatedness in the group and result in collective properties (*39*, *89*). In comparison, pathogen-induced changes in social networks of other animals including humans (*2*, *5*, *60*) often do not have the same properties, such as high relatedness levels, and can create conflicts of interest that incentivize selfish behaviors.

Public health measures experienced during past and current pandemics have raised awareness for social distancing and epidemiological studies are actively evaluating their

effectiveness and required duration. Humans are by no means alone in using social distancing to mitigate risk of infection (*90*). The widespread occurrence of pathogen-induced changes to social behaviors across animals in diverse taxa represents a valuable opportunity to investigate underlying mechanisms, epidemiological consequences such as effectiveness and required duration, and host-parasite co-evolution. Non-human animals' social distancing strategies may be experimentally tractable, enabling manipulative experiments or multi-generation observations that are impossible with humans. These systems represent a valuable guide to understanding how contagious pathogens spread through social networks, how networks change in response to pathogens, and how these bidirectional feedbacks alter pathogen dynamics and evolution.

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Acknowledgments: We thank two anonymous reviewers for helpful comments. Figures were created with BioRender.com. **Funding:** N. Stroeymeyt was funded by an ERC Starting Grant DISEASE (No. 802628). **Author contributions:** all authors contributed equally. **Competing interests:** We have no competing interests.

Figures

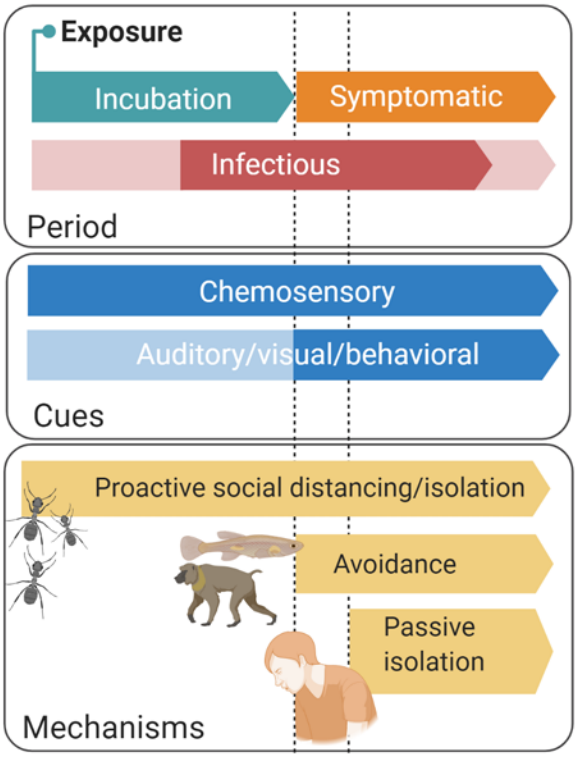

Figure 1: Behavioral changes in response to pathogens (yellow) and their potential cues (blue) can occur upon initial exposure, during the pre-symptomatic incubation period

(teal), or the symptomatic / clinical period (orange). The degree to which behavioral changes overlap a pathogen's infectious period (red) will determine their effectiveness at preventing spread. In ants, chemosensory recognition can occur immediately after exposure, triggering self-isolation and proactive social distancing. In other systems (e.g. guppies, black-spot disease), infectiousness and avoidance behavior are aligned with clinical signs, or, for parasites that do not cause obvious clinical signs, with changes in chemical cues (i.e., mandrills, protozoal parasites). Behavioral changes can also occur later in infection (i.e. Humans, influenza infections). Semi-transparent arrows indicate variability and uncertainty in timing across systems.

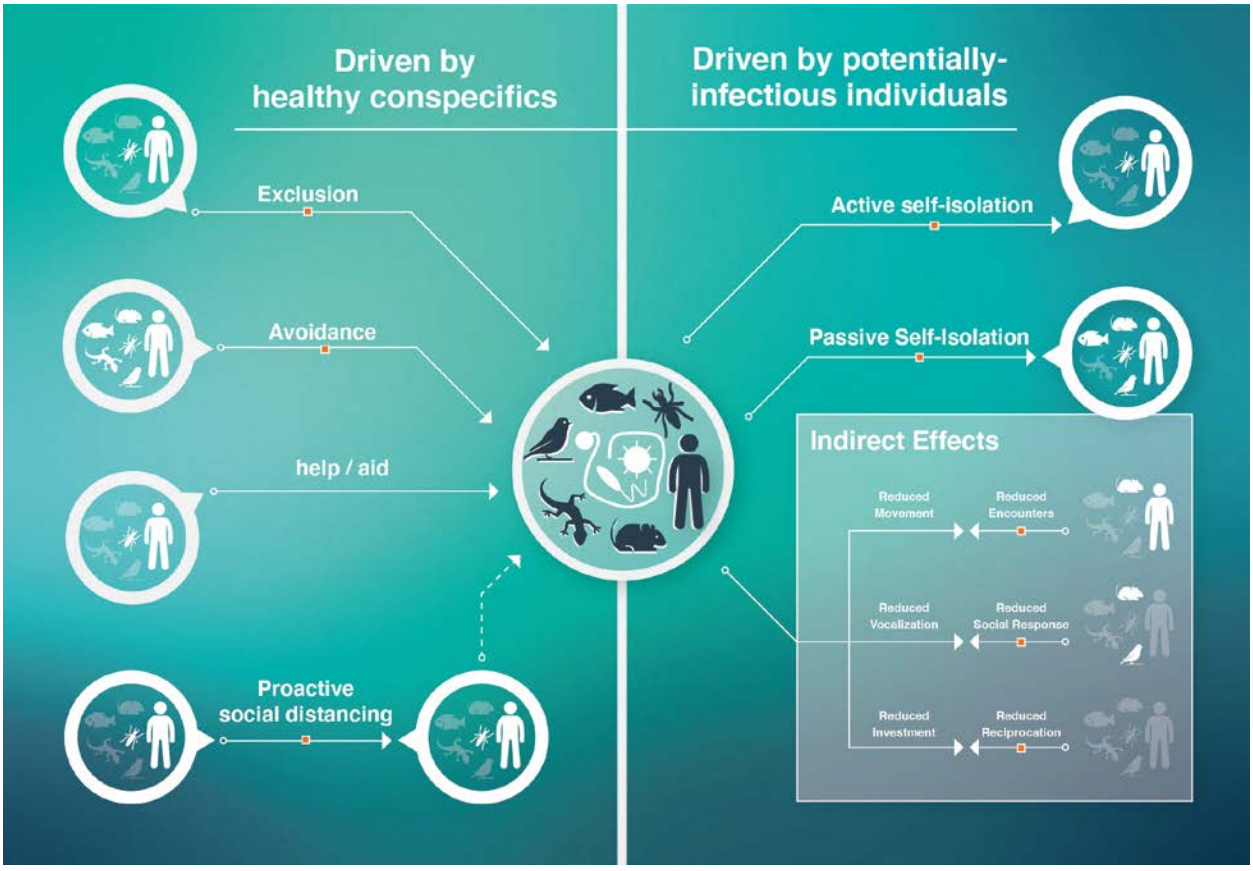

Figure 2: Effects of pathogen exposure on social behaviors can be driven by susceptible, or pathogen-affected individuals, and increase (help/aid) or decrease contact (see orange squares).

For individual-driven effects, we distinguish direct effects and indirect effects (grey area). Animals are highlighted based on available studies in respective systems in birds, non-human mammals (mouse symbol), humans, insects/other invertebrates (mostly eusocial insects; ant symbol), reptiles/amphibia (lizard symbol), and fish.

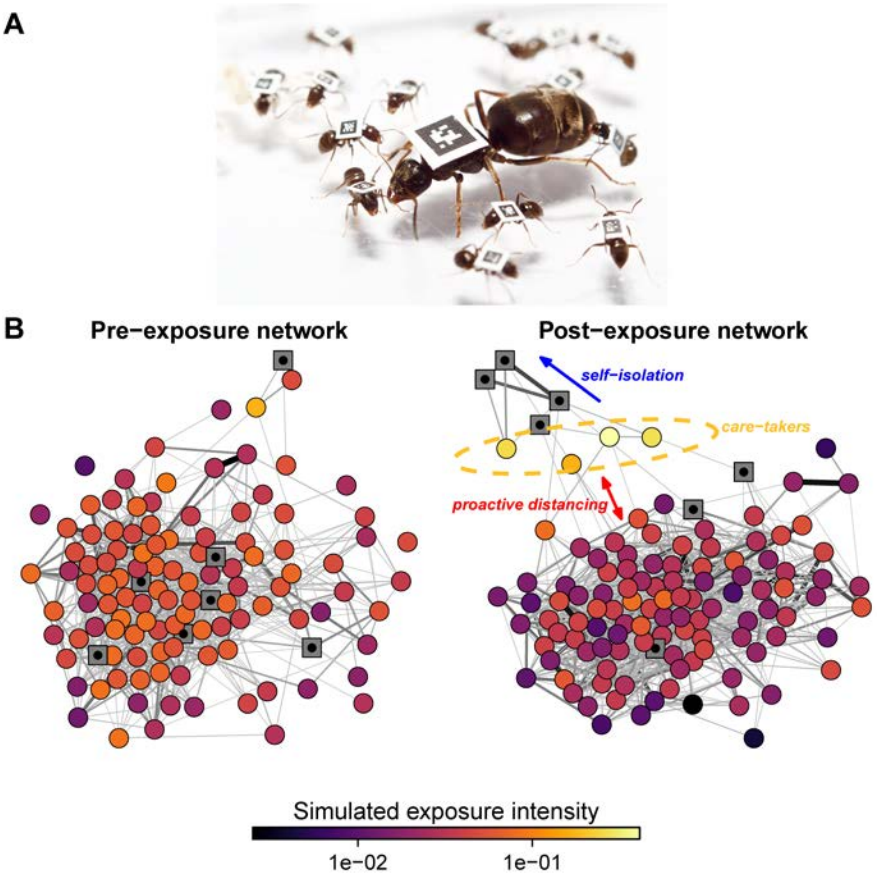

Figure 3: Network changes and epidemiological consequences of pathogen exposure in ants (case study). **A**. Common garden ant (*Lasius niger*) queen and workers marked with fiducial markers used for automatic detection of social interactions. **B.** Social interaction networks before and after exposure of some workers (grey dotted squares) to infectious fungal spores. Circles represent non-exposed individuals and circle colours represent the predicted intensity of

exposure to the pathogen based on epidemiological simulations run on each network (data from *(3)*).

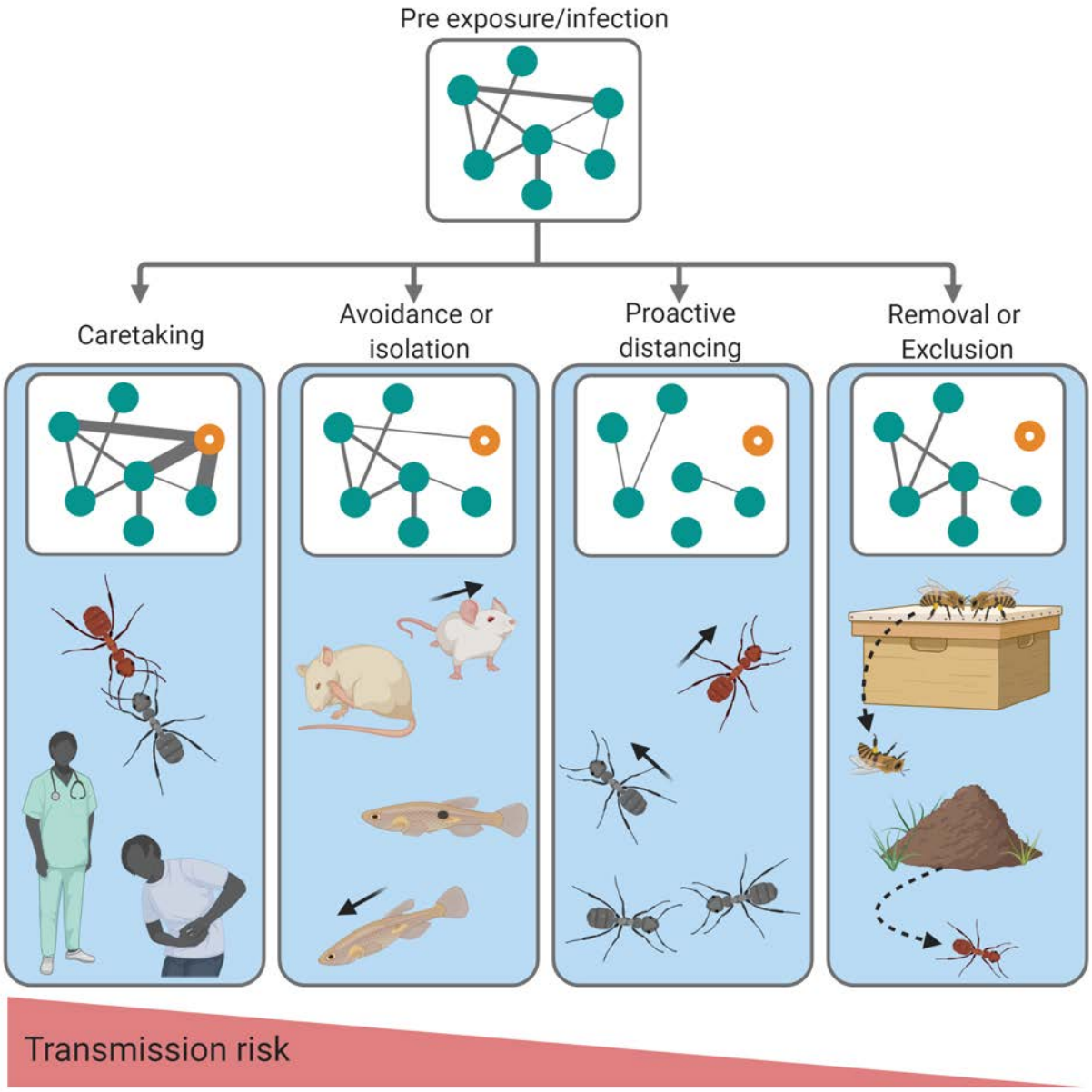

Figure 4: Social distancing mechanisms affect the number (connecting lines) and strengths (width) of network connections for susceptible (green circles) and exposed/infected (orange

circles) individuals. Mechanisms are ordered based on transmission risk from caretaking (high risk) to complete removal/exclusion (low risk).

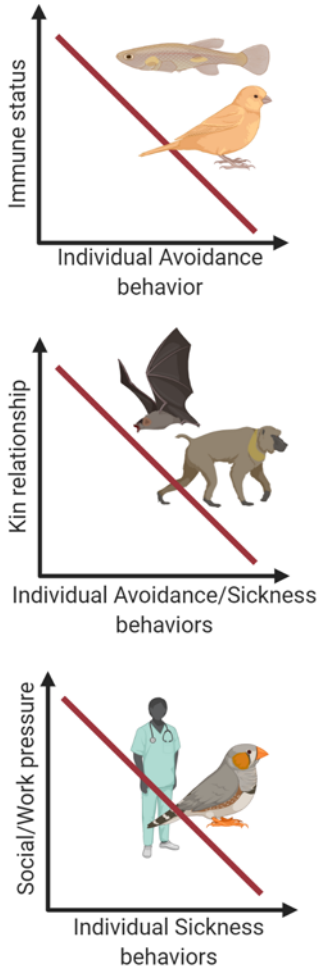

Figure 5: Individuals within a species can vary social distancing behaviors based on immune status, kinship, and social/work pressure. Icons show species for which these patterns have been shown to date.