CHAPTER TWENTY-FOUR

Social Insects as Models in Epidemiology: Establishing the Foundation for an Interdisciplinary Approach to Disease and Sociality

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SOCIAL INSECTS have an abundance and diversity that, with the exception of beetles, is unrivaled among animal taxa. Two groups, the ants and termites, are ecologically dominant in tropical rainforests (Hölldobler and Wilson 1990; More than 12,000 species of ants and 2,650 species of termites have been identified so far (Bolton et al. 2006), and their local diversity and abundance can be extraordinary. The amazing diversity of ants is exemplified by Floren and Linsenmair’s (2000) discovery of 239 species on just 19 individual trees in Borneo, with as many as 61 species found on a single tree. In the Southern Cameroon, densities of 10,000 termites per square meter have been recorded (Eggleton et al. 1996). The soil and ground litter of tropical forests is the environment of adaptation and diversification of these two groups (Hölldobler and Wilson 1990; Eggleton 2000; Moreau et al. 2006). These environments are also inhabited by what is potentially an equally or even more diverse community of microbes that can be abundant and pathogenic.

Together with the diversification of the angiosperms and the litter of tropical angiosperm forests (Moreau et al. 2006), adapting to the disease risks inherent in soil, litter, and decaying wood environments exploited so well by ants and termites very likely constituted a major event in the diversification of ants and termites. Indeed, Bulmer and Crozier (2004, 2005) described
selection on immune genes associated with the transition from grass feeding to decayed wood feeding in Australian termites. Bees and wasps are also diverse and ecologically significant social insect clades whose colonies are impacted by arthropod, fungal, bacterial and viral parasites (cf. Bailey and Ball 1991; Rose, Harris, and Clare 1999). What role did sociality play in the evolution of disease resistance? Did the high density of individuals in social insect colonies render them more susceptible to infection through enhanced pathogen transmission? Or did group living offer new, cooperative mechanisms to lower disease risk? How can we begin to approach these and other questions of historical significance in social insect evolution?

We believe that concepts from human epidemiology have heuristic value for insect sociobiology and ecological immunology. Concepts derived from epidemiological theory can be tailored to questions that might at first appear to be outside the domain of studies of human disease dynamics. Extending the application of these theories beyond human disease to a novel system that might appear to hold little in common, presents a significant opportunity to deepen the understanding of the underlying principles of infectious disease spread. Human infectious disease epidemiology is based on a set of standard, disease-related statistical measures (cf. Nelson, Williams, and Graham 2001). Implicit in these measures is the underlying factor of exposure to disease. Human epidemiologists have generally assumed that the probability of exposure in a population is uniform for particular sets of susceptible individuals at a given time. The probability of exposure is integrated within the probability of becoming infected, developing the signs and symptoms of a disease, infecting others, and then either recovering or dying.

Exposure to disease is also a significant factor in evolutionary sociobiology. In group-living animals, especially those with complex social organization, probabilities governing the exposure of individuals to disease within a society can show strong variance (Andersson 1997). Behavior plays a critically important role in infection control: the removal, quarantine, or exile of infected individuals can greatly reduce the exposure of a society's population once disease is present (Clancy 1996). Additionally, behaviors such as decreasing activity after infection, avoiding infected individuals, nursing infected group members, soliciting care, and other social processes of infection control greatly impact the probability of exposure to infectious disease. All facets of social behavior directly impact the exposure and transmission risks of infectious diseases within a population, and therefore greatly influence the selective pressures on individuals that live in societies.
Just as exposure is implicit in principle epidemiological concepts, so is the concept of resistance to disease. Resistance can be defined narrowly as protection arising solely from immunity in the molecular and cellular sense, but when integrating the perspectives of epidemiology, immunology, evolutionary ecology, and insect sociobiology a more encompassing concept would offer greater applicability, allowing us to consider an array of defense mechanisms extending beyond purely physiological adaptations to social characteristics that protect against disease. Owens and Wilson (1999) proposed that immunocompetence be defined as "a measure of the ability of an organism to minimize the fitness cost of an infection *via any means* [emphasis added], after controlling for previous exposure to appropriate antigens." Thus, social mechanisms of disease resistance such as herd immunity—the insulation of susceptible individuals from exposure by surrounding them with immune individuals that are incapable of transmitting infection—would be included in this definition. Immunocompetence, in this holistic sense, can also circumscribe colony-level mechanisms of infection control (Hart, Bot, and Brown 2002) and the social enhancement of resistance to infection (Traniello, Rosengaus, and Savoic 2002). An expanded view of immunocompetence would also involve prophylaxis and prevention from initial infection, as well as survival subsequent to the contraction of a disease. In this way, social groups can be said to resist disease, and resistance can be measured in terms of their persistence despite pathogen presence and the challenges of infection. Social behavior can affect exposure risk and, thus, positively impact survival, playing a crucial role in immunocompetence overall.

The study of the significance of behavior to exposure and immunocompetence can be unified from the perspectives of epidemiology (following paths of disease spread) and evolution (describing the survival and fitness consequences of transmission) to create a deeper understanding of disease dynamics in social groups (cf. Bonds et al. 2005). Manipulations can be difficult in non-human populations and in field studies of non-human social species. Theoretical modeling, however, can supplement empirical research to investigate the impact of behavior and social organization on exposure and the induction and maintenance of immunocompetence. Progress in achieving a more complete view of how individual-, group-, and population-level disease dynamics lead to local pathogen spread, affect survival and fitness, and ultimately select for resistance mechanisms could be accelerated by identifying and developing model systems for an integrative approach. A system lending itself to empirical and theoretical
research would allow hypothesis testing to occur in a manner that would ensure a realistic representation of the effect of each studied mechanism of immunocompetence on disease dynamics at the level of the society. In this chapter, we argue that social insects are an ideal model system for an integrated sociobiological and epidemiological approach.

An Accelerated Arms Race: Social Insects and the Selective Pressures of Infectious Pathogens

Disease can seriously impact survival and reproductive success and, as a result, pathogens are potent agents of selection. Pathbreaking studies of the coevolution and epidemiology of animal and plant parasites demonstrate that parasites have exerted significant effects on the evolution of their hosts (Anderson and May, 1982; Ewald 1991, 1994; Andersson 1994; Briggs and Godfray 1995; Rothman and Myers 1996). This is especially true of infectious diseases in group-living species in which interactions among individuals within a dense social structure can lead to increased exposure and transmission relative to solitary animals (Grenfell and Dobson 1995). Recent research has focused on host defenses and life-history traits and the potential fitness costs associated with infection resistance (Schmid-Hempel 1998; Moret and Schmid-Hempel 2000; Hasselquist, Wasson and Winkler 2001; Norris and Evans 2000; Calleri, 2006) using solitary, gregarious, and eusocial insects as models in ecological immunology (Cotter et al. 2004; Pie et al. 2005; Schmid-Hempel 2005).

The focus on immunological and ecological factors in the cyclic nature of epidemics to examine disease dynamics can be adapted to sociobiological research problems by considering the scale of operation of these factors. From this perspective, immunological factors are attributes of the host/parasite association that manifest in individuals, matri/patriline, demographic subgroups, colonies, and populations of colonies, potentially leading to patterns of recurrent epidemics. All inducible colony defenses play important roles in the prevention of establishment and transmission of disease and the induction of resistance. Ecological factors, such as foraging, or competitive or predatory actions that ultimately could lead to the introduction of infected individuals from neighboring colonies of the same or different social insect species, are paramount to understanding exposure, although very little is known about them.

In the same way that disease resistance and its underlying mechanisms
(such as physiological immunity) can be thought of as having been shaped over evolutionary time by a diverse array of disease challenges, social behavior and colony structure have also formed under a set of selective pressures from pathogens. Considering insect immune defenses as “evolved traits” (Schmid-Hempel 2005), and focusing on the interface of insect immunology and sociobiology, we can identify the selective forces that have favored the variety of resistance mechanisms that characterize different species (Schmid-Hempel and Ebert 2003; Pie et al. 2005; Fefferman et al. 2007). By considering the impact of disease on the evolution of social structure and behavior, colony-level mechanisms of immunocompetence can be considered as adaptive responses to the selective pressure of infectious disease.

We predict that the individual and social disease-resistance mechanisms that comprise colony-level immunocompetence will reflect variation in microbial loads associated with nesting and feeding ecology (Cruse 1998; Rosengaus et al. 2003; Bulmer and Crozier 2004, 2005). In eusocial insects, disease transmission risks that are inherent in their nesting ecologies are likely to be high due to the level of relatedness of workers, leading to increased susceptibility to infectious agents due to the lower genetic heterozygosity of nestmates (e.g., Shykoff and Schmid-Hempel 1991). At the same time, the contributions of the individual through selection for adaptive patterns of division of labor, especially when considered in terms of group size and structure, are critical to the survival and reproductive success of the colony. This leads to a trade-off in selection for genetic variation to enhance colony immunocompetence or colony efficiency. The relationships among these variables, however, are far from clear (e.g., Rosset, Keller, and Chapuisat 2005).

Social Insect Ecology, Behavior, and Disease Resistance

The nesting habits of social insects highly recommend them for epidemiological study: they form multigenerational families in environments that are particularly challenging in terms of acute and chronic exposure to pathogens and parasites. Ants and termites—two diverse and abundant groups—nest and feed in soil and decayed-wood environments in which a diverse and abundant microbial community flourishes (Rosengaus et al. 2003). Social insects often live in densely populated colonies and mortality risks may be compounded through inter-individual transmission of infection (Rosengaus et al. 1998; Schmid-Hempel 1998 and references therein).
Adapting to disease has long been considered to have been a major event in the evolution of sociality and diversification of social insects (e.g., Wilson 1971), but only recently has the evolutionary significance of social insect pathobiology been the focus of empirical and theoretical investigation. If mechanisms of disease resistance compromise the energetics of colony operations, we expect they will be selected against, and that mechanisms that afford protective benefits at low cost will be highly unlikely due to the evolutionary responses of the pathogens in question (Figure 24.1). A benefit/cost analysis involving humans is instructive here: to control infectious disease, simple hygiene such as hand washing, a low-cost behavior, can provide significant protective benefits against infection (Daniels and Rees 1999). Analogously, through self-grooming, ants can physically remove microbes and spread the antibiotic secretions of the metapleural gland, but they have been shown to be metabolically costly to produce (Poulsen et al. 2002). Humans have antibiotic dermal peptides (e.g., Harder et al. 1997); their production costs are unknown. Inducible physiological responses such as fever help combat infection, but can also have moderately high costs (e.g., energy loss or febrile seizures; Nesse and Williams 1994). Evolution has also favored the maintenance of a trait with enormous protective benefits against malaria in heterozygotes, but at the high cost of sickle-cell anemia (a disease with a high associated mortality of

Figure 24.1. Individual and societal costs and benefits of defensive mechanisms.
its own, Platt et al. 1994) in homozygotic individuals. Allogrooming can both decrease the likelihood of illness after exposure for the individual contacted, but can also spread infection to otherwise unexposed individuals (Rosengaas and Traniello 1997). Due to heightened levels of interaction in the course of colony function, hygienic behavior can provide significant protective benefits at what would appear to be a relatively low cost. This example provides rich opportunities to study exceptions to theoretical expectations.

In group-living animals, mating system, group size, population density, and parasite transmission are significant to infection risk and control (Freeland 1976, 1979; Hamilton 1987; Reeson et al. 1998; Nunn, Gittleman, and Antonovics 2000; Read and Allen 2000; Cotter et al. 2004). Social insects face similar challenges (e.g., Hamilton, Axelrod, and Tanese 1990; Keller 1995; O’Donnell 1997; Thorne and Traniello 2003; O’Donnell and Beshers 2004). There is ample support for the hypothesis that the presence of pathogens has selected for a variety of disease-protection mechanisms in phylogenetically different groups of social insects. In the haplodiploid social Hymenoptera, there is evidence that behavior, physiology, and biochemistry (as well as colony size and organization, colony and population genetics, and mating system) have been influenced by pathogens (Hölldobler and Wilson 1990; Baer and Schmid-Hempel 1999; Rosengaas et al. 1998; Schmid-Hempel 1998, 2005; Schmid-Hempel and Crozier 1999; Starks, Blackie, and Seeley 2000; Tarpy and Seeley 2006). The biology of the diploid termites (Order Isoptera) reflects individual physiological, life history, and social adaptations, again indicating a prominent role for pathogens (Rosengaas et al. 1998; Rosengaas, Traniello, et al. 1999; Rosengaas, Jordan, et al. 1999; Rosengaas and Traniello 2001; Thorne and Traniello 2003; Traniello et al. 2002; Calleri et al. 2005; Calleri, Rosengaas, and Traniello 2006).

The risks of disease and its subsequent impact on colony fitness are affected by social behavior. Crowding can lead to increased transmission, but if behavior can improve the recovery of infected nestmates or if individual defenses can be summed over a colony’s population to lower susceptibility, then overall mortality can be decreased even if transmission rates are increased. Moreover, the removal, quarantine, or isolation of diseased individuals may counteract the increased exposure risk incurred by group living. Other forms of social interaction, such as allogrooming, which can prove more efficacious than self-grooming (Rosengaas et al. 1998), can be
highly effective in the prevention of disease. Allogrooming is an inducible defense that can be increased through signaling in the dampwood termites *Zootermopsis angusticollis*. Nymphs communicate information about exposure risk (Rosengaus, Jordan, et al. 1999); when individuals encounter lethal concentrations of fungal conidia, they remain in place and vibrate, transmitting substrate-borne signals that cause nearby nestmates to abscend and then increase allogrooming. The signal activates behaviors that are equivalent to the induction of the molecular cascades that govern individual immune response. These signals serve as public service announcements—sending cues to nestmates to up-regulate hygienic behavior and preemptively defend against disease as well as avoid infection.

**Social Insect Immunocompetence**

Insects, in general, have nonspecific and short-lived cellular immune responses such as encapsulation, nodule formation, and phagocytosis, which characterize innate immunity (Hoffmann et al. 1999; Russell and Dunn 1996). For example, some dictyopteran ancestors of termites defend against disease through acquired immunity (Faulhauber and Karp 1992). Humoral immune responses are characterized by specificity and memory (e.g., Hultmark 1994; Hoffman et al. 1999). Specificity in insect immunity has been reported: cercopins, dipterins, drosocin, mucin, and attacin have antibacterial activity; drosomycin appears to be fungicidal (Lemaître et al. 1996; Lemaître, Reichhart, and Hoffman 1997). Although Hamilton (1987) once noted that in insect societies “nothing like the immune system...is known to exist,” recent research has found social insects to have adaptive immunity and produce antimicrobial peptides (Rosengaus, Traniello, et al. 1999, 2007; Lamberty et al. 2001; Bulmer and Crozier 2004; Evans 2004). Social insect disease defenses are likely to have evolved in part from traits present in ancestral solitary and/or presocial species. Because social insects live in groups in ecological circumstances characterized by variation in disease risk (Rosengaus et al. 2003), we expect that adaptive immune system variation will match the qualitative and quantitative nature of pathogen load. That said, acquired immunity is poorly understood in ants, bees, wasps, termites, and other gregarious, presocial, colonial, and eusocial insects.

Immune defenses can be considered on both a colony-level and individual scale (Rosengaus et al. 1999b; Traniello, Rosengaus, and Savoie 2002).
Individual immunity can confer protection against pathogen infection, either by innate or adaptive defense, and the transfer of immunity to nestmates can also confer protection to a naïve individual (Traniello, Rosengaus, and Savoie 2002). Allogrooming reduces the pathogen load of an individual and thus overall exposure risk. Conversely, high levels of immunity in a colony may buffer susceptible individuals from exposure to infection. Studies of herd immunity suggest that substantial protective benefits accrue only after a large percentage of the total population becomes immune (Castillo-Chavez et al. 2002; but see Fletcher 2003).

In addition to providing protection from disease, immunity has associated costs at the individual and colony level. For the individual, mounting an immune response entails metabolic/energetic costs which have been estimated in a variety of systems (cf. Nesse and Williams 1994). There can be additional costs to the individual; physiological responses can have adverse effects. For example, while fever is beneficial, extreme elevation of body temperature can be dangerous (Kluger 1979). Additionally, the actual protective function of an immune system can itself result in autoimmune disorders, which exact severe costs to the health and fitness of an individual (Nesse and Williams 1994). Defense mechanisms at the colony level have costs too. For example, hygienic behavior can result in the culling of particularly susceptible individuals once disease is present in the colony (Rosengaus and Traniello 2001). While this may prove effective in limiting disease spread in the short term (Fefferman et al. 2007), it can negatively impact long-term colony growth.

Social Organization and Infection Control

Colony organization may enhance disease resistance, and colony demography—a chief feature of the social architecture of an insect colony—can impact disease susceptibility. When pseudomutant colonies of Z. angusticollis were exposed to conidia of the entomopathogenic fungus Metarhizium anisopliae, groups with a mixed-instar demographic distribution had significantly higher survivorship than colonies composed only of individuals of a single instar. Same-age groups (10 individuals of the same instar) had more than double the hazard ratio of death than mixed-age groups. Relatively young individuals were the most susceptible to infection (Rosengaus and Traniello 2001). These studies indicate that age-structure can serve as a mechanism of defense against disease and
age- and caste-distribution structures could in part have evolved under the selective pressures of parasitism (Schmid-Hempel and Schmid-Hempel 1993). Indeed, in social insects with worker task specialization, there can be colony-wide up-regulation of hygienic behaviors, which offer greater protection to the colony as a whole (e.g., Hart, Bot, and Brown 2002). Middens workers are more likely to come into contact with pathogenic fungi, which are thus restricted from freely moving to other areas of the nest.

The life histories of basal termites are characterized by plasticity in the reproductive options of individuals and variation in colony social organization that can impact disease resistance (Thorne and Traniello 2003). In these species, cycles of outbreeding and inbreeding associated with the reproductive plasticity can alter genetic heterozygosity and affect innate immu

nity as well as social mechanisms of infection control. For example, low levels of genetic variation in the offspring of inbred supplementary reproductives could result in greater susceptibility to infection. In *Zootermopsis angusticollis*, a single generation of inbreeding significantly reduced heterozygosity and allelic diversity (Calleri et al. 2006). This lower genetic variation in turn affected the resistance of isolated and grouped individuals depending on the mode of transmission of the pathogen used in experimental exposure. Inbred and outbred, isolated and grouped termites inoculated internally with the bacterium *Pseudomonas aeruginosa*, exposed to a low dose of the fungal pathogen *Metarhizium anisopliae* on the cuticle, or challenged with a pseudopathogen (an implanted nylon monofilament) did not differ in immunocompetence. This is because internal infection by bacteria apparently cannot be controlled by social interactions such as mutual grooming and low concentrations of conidia do not impact survival. Inbred termites housed in groups and exposed to a relatively high concentration of fungal conidia, however, had significantly greater mortality than outbred grouped termites, presumably because of a genetic effect on allogrooming or another group mode of disease control. Inbred termites also had significantly higher cuticular microbial loads, likely due to less effective grooming by nestmates. Decreased genetic heterozygosity associated with inbreeding thus appeared to increase disease susceptibility by influencing the efficacy of social behavior rather than physiological immunity.

Finally, living in groups can augment individual immunity in social insects. The ability of *Z. angusticollis* nymphs to resist a fungal pathogen is enhanced in naïve nymphs (i.e., termites having no prior exposure to a challenge pathogen) allowed to associate with immunized nestmates (Traniello,
Rosengaus and Savoie 2002). Increased immunocompetence at the colony level can thus be improved through the social interactions of nestmates that vary in their immune status and ability to resist infection. Although social immunization in termites would appear to be most closely related to vaccination in humans, social immunization involves the up-regulation of immune response in naïve individuals by an immune nestmate(s). Social immunization may, therefore, most accurately be approximated in the realm of human epidemiology by the vertical transmission of immunity from mother to infant through antibodies passed in thecolostrum (the nutrient and immune-factor rich secretions of human mammary glands within the first few days after childbirth and prior to the onset of milk production). In termites this transmission is not limited to parent-offspring interaction. This difference in the mechanistic basis by which groups can achieve greater collective immunity shows an instance where, by limiting the definition of an epidemiological concept to human physiological capability, the underlying theory itself is narrowed. By incorporating a broader (insect-based) concept of individual-to-individual transmission, both vertical and horizontal, of immunity, it may be that human epidemiologists may arrive at more efficient algorithms for socially based inoculation strategies (e.g., a “new and improved chicken pox party”).

**Modeling Disease Resistance in Social Insects**

Attaining a balance between accuracy and simplicity is required for successful modeling in biology (Levin 1992). In identifying useful model systems, researchers attempt to identify commonalities between the system being studied and a more accessible system which serves as a model. The more attributes the two systems hold in common, the greater the applicability and credibility of the model, and the greater its heuristic value. The nature and complexities of some pairs of systems—social insects and humans and how they cope with disease—can initially appear highly divergent. We anticipate that some researchers will balk at the idea of bridging human epidemiology and insect sociobiology, using mathematical modeling as the foundation of the interdisciplinary linkage, but we believe such an approach is timely, appropriate, and fruitful. Social insects can be viewed as an epidemiological system that is simple relative to humans and many group-living vertebrates, and by creating mathematical models based on insect sociobiology and human epidemi-
ology, it will be possible to contribute new insights into traditional problems in both disciplines.

Models can focus at the level of individual action or emergent system-wide properties, so the analysis of social insect behavior and colony epidemiology through computational modeling is a natural extension of more traditional empirical experimentation. The wealth of research in human epidemiology has identified parameters of disease prevention and transmission that are fundamental to the analysis of mechanisms of disease control in social insects, but many of these factors have been neglected or only infrequently examined or explicitly considered in theoretical or empirical studies (Table 24.1).

Even among factors considered in the context of disease, very few have been examined in combination to determine plausible synergistic effects within the scope of human epidemiology and none have, as yet, been examined in social insects. Indeed, as Table 24.1 illustrates, important aspects of the social phenotype of insect colonies that may have been studied in other contexts have yet to be examined in relation to infection. For example, polyethism in social insects is well studied; it has long been known that workers perform tasks (e.g., foraging, nest maintenance, and brood care) in an organized manner to allow the colony to efficiently function. The probability of performing a particular task can be determined by the individual's developmental or physiological state, or can be dependent on the requirements of the colony and/or social interactions (Robinson 1992; Seid and Traniello 2006). The performance of each task may have an associated risk to the individual and cost to the colony (e.g., being eaten by a predator while foraging outside the nest). Task performance can also carry associated disease-related costs and benefits that are rarely studied. Foraging might increase exposure to pathogens, for example, and subsequent contact with an infected nestmate can reduce individual pathogen loads (through allogenousomating and/or spread infection. Processes of task allocation can be described with a set of minimum threshold values, probability distributions, and net contributions to colony function, accurately comprising a detailed mathematical representation of the organization of colony labor. The importance of these factors for withstanding a pathogen challenge can then be examined.

Recently, a few models have been developed using some parameters generally considered within an epidemiological framework to examine disease spread in social insect colonies, specifically showing how nest
Table 24.1. Parameters considered in models of infectious disease prevention and transmission as developed in human epidemiology and insect sociobiology.

<table>
<thead>
<tr>
<th>Effect</th>
<th>Epidemiology</th>
<th>Insect sociobiology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single factor effects</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics/prophylaxis</td>
<td>Yes*</td>
<td>Yes*</td>
</tr>
<tr>
<td>Distribution of antibiotics</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Heritable variation in resistance</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Vaccination</td>
<td>Yes*</td>
<td>No</td>
</tr>
<tr>
<td>Quarantine</td>
<td>Yes</td>
<td>Yes*</td>
</tr>
<tr>
<td>Hygiene</td>
<td>Yes</td>
<td>Yes*</td>
</tr>
<tr>
<td>Exposure</td>
<td>Yes</td>
<td>Yes*</td>
</tr>
<tr>
<td>Transmission</td>
<td>Yes*</td>
<td>No</td>
</tr>
<tr>
<td>Infectivity</td>
<td>Yes*</td>
<td>Yes*</td>
</tr>
<tr>
<td>Attack rate</td>
<td>Yes*</td>
<td>No</td>
</tr>
<tr>
<td>Pathogenicity</td>
<td>Yes*</td>
<td>No</td>
</tr>
<tr>
<td>Virulence</td>
<td>Yes*</td>
<td>No</td>
</tr>
<tr>
<td>Immunity</td>
<td>Yes*</td>
<td>Yes*</td>
</tr>
<tr>
<td>Immunogenicity</td>
<td>Yes*</td>
<td>No</td>
</tr>
<tr>
<td>Herd effect and social immunity</td>
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<td>Yes*</td>
</tr>
<tr>
<td>Population density</td>
<td>Yes*</td>
<td>Yes*</td>
</tr>
<tr>
<td>Age structured susceptibility</td>
<td>Yes*</td>
<td>Yes*</td>
</tr>
<tr>
<td>Division of labor</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Activity level</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Environment structure</td>
<td>Yes</td>
<td>Yes*</td>
</tr>
<tr>
<td><strong>Additive multifactor effects</strong></td>
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<td></td>
</tr>
<tr>
<td>Antibiotics and quarantine</td>
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<td>No</td>
</tr>
<tr>
<td>Antibiotics and immunity</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Antibiotics and vaccination and virulence</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>


Note: Although vaccination, antibiotic protection and prophylaxis are distinct concepts in the context of social insects, in human epidemiology there may be some scenarios in which they operate as the same factor.

*Indicates that the effect of these metrics on disease spread has been measured empirically.
architecture, behavior, social immunity, and nest hygienic behavior can affect disease transmission (Naug and Camazine 2002; Pie, Rosenga, and Traniello 2004; Fefferman et al. 2007). Many aspects of social organization pertinent to disease dynamics within the population of a colony can be empirically determined, such as demography, task allocation, and nest structure. In addition, some of the standard epidemiological metrics employed in human disease studies (e.g., infectivity) have been measured (Table 24.1). The mechanisms that likely govern exposure are more complex, but in the case of social insects, where mechanisms of exposure can be clearly defined and observed, it is possible to measure epidemiological factors to validate models and thus increase our understanding of exposure and the influences of individual behavior and social structure on infection control.

To illustrate the ways in which these standard epidemiological rates rely on exposure and the types of predictive models that can be developed, consider the following mathematical expressions for etiologic- and exposure-based parameters:

\[ E_{X,T} = \text{The probability of exposure, for each worker, in a group of individuals of caste X at time T.} \]

\[ I = \text{The probability of becoming infected from exposure (subscript denotes time since previous infection, with some measure of immunity conferred that influences a current probability of infection).} \]

\[ S_T = \text{The probability of becoming symptomatic at time T, given infection at time T=0.} \]

\[ C_T = \text{The probability of becoming contagious at time T, given infection at time T=0.} \]

\[ M_T = \text{The probability of death at time T, given the onset of symptoms at time T=0.} \]

While it is still possible to consider each of these variables as population-wide transition averages (as is done in traditional susceptible-infected-recovered epidemiological models, also called "mean field approximation" models), this method brings the successive conditional probabilities into the definitions. Standard epidemiological rates can then be defined mathematically: pathogenicity as \( \sum_{T=0}^{n} S_T \), virulence as \( \sum_{T=0}^{n} M_T \), and infectivity as \( I^* C_T \), where \( n \) = the duration of disease until either death or recovery and infection beginning on day 0. Similarly, attack rate may be
defined as $I^* \sum_{T=0}^{n} S_T$, where $n$ is the end of the window for disease expression. Expressed mathematically, these standard concepts in epidemiology are conditional probabilities, building on each other, and each fundamentally relying on the underlying probability of exposure (see Figure 24.2 for a visualization of how these concepts follow directly from exposure risks).

In social insect research, $E_{x,T}$ can be experimentally manipulated and $S_T$, $C_T$, and $M_T$ can all be measured. None of this is possible in human
studies. Pathogenicity, virulence, infectivity, and attack rate can all then be computed, thereby providing known parameter values for use in previously purely theoretical modeling. This allows the testing of predictive models of outbreak scenarios (including the traditional SIR (S = susceptible; I = infections; R = recovered) models)—something which has not been possible in epidemiological modeling on such a scale. Furthermore, the ability to validate models in this way opens the possibility for the theoretical investigation of the efficacy of specific interventions or defenses to combat disease spread by influencing the underlying exposure rates.

By dissecting the system of disease dynamics in this way, we can then examine the roles of individual aspects of social phenotype. By manipulating hypothesized mechanisms of exposure and calculating their effect on dependent metrics, we are able to tease apart the effects of individual behavior and colony structure on disease spread. The demographic distribution of a population and the associated age-specific etiologies of a given pathogen can be recorded. Modes of infection can be isolated and rates of transmission among nestmates and colonies can be determined. The induction and subsequent efficacy of immunity can be tested. All of the standard epidemiological parameters can be investigated and models based on these parameters can provide insight into how each influences patterns of disease in a population. However, social insect colonies provide an opportunity to investigate the effect on disease dynamics of other factors often assumed pertinent, but rarely amenable to experimental manipulation in humans, such as behavioral responses to pathogen presence (e.g., allogrooming, alarm signaling, contact rates between susceptible and infected individuals). Computational models are being developed to examine the effects of such influences in cases where direct empirical manipulation, even in social insects, is difficult (Fefferman et al. 2007).

Infectious disease epidemiology in social insect colonies has begun to examine the effects of social behavior and colony organization through modeling. Naug and Camazine (2002) created a cellular automata model to examine the effects of division of labor and interaction networks among nestmates and colony demography, focusing on transmission rates among colony subgroups as defined by colony size, and using an underlying spatially explicit nest structure. We altered the density of infected workers at the outset of each model run within castes and varied the inter-caste probabilities of transmission to represent differences in their rates of interaction. We then examined the trajectory of disease in a closed population, using the number
of infected individuals at any given time as their metric of comparison. Our results indicate that although the presence of distinct subgroups within the nest was by itself ineffective as a protective measure, when combined with the altered caste-specific replacement rates the two properties were successful at reducing the number of infected individuals. This implies that division of labor within a colony can act in concert with demographic change to provide some measure of protection against disease risks.

Pie, Rosengaus, and Traniello (2004) dealt more explicitly with exposure by constructing both a mean field approximation and cellular automata models of disease in a single termite colony. Here, the effects of disease on colony-wide survivorship were compared, rather than the number of individuals infected at any given time. In the mean field approximation model, contact was based on the density of infected individuals, which was found to have a significant effect on the likelihood of epidemics within the colony. In the cellular automata model, transmission occurred between infected and susceptible individuals if they co-occupied the same cell according to a uniform probability. Nest architecture was found to have increasing protective benefit against colony-wide spread of disease as the nest became increasingly spatially segregated, and thus subdivided. By focusing the cellular automata models on the restrictions of movement in a spatially explicit environment and holding the probabilities of transmission constant subsequent to exposure, these models allowed the examination of the effects of nest architecture and worker activity level on exposure risk.

Fefferman et al. (2007) developed a series of cellular automata models to analyze the relative efficacy of allogrooming, immunity, and nest hygiene in combating pathogen challenges hypothesized to be associated with the transition from solitary to presocial to eusocial life. Nest hygiene was found to provide an immediate survival benefit, and immunity lowered overall disease susceptibility under constant and periodic disease exposure scenarios. Allogrooming increased survivorship in chronically pathogen-challenged colonies, but also increased transmission rates when exposure was recurrent. Colonies having demographics biased toward either young or old individuals had slightly higher mortality than those with evenly distributed demographics. These models indicated that nest hygiene and immunity function on different temporal scales and can interact with demography to lower disease risks and with the age distribution of individuals to lower, to varying extents, pathogen-related mortality risks in social insects. Indeed, nest hygiene had an immediate and significant impact on
improved survivorship. Allogrooming benefited overall survival in the short term, but the advantage was outweighed over time by the loss of protection conferred via socially transmitted immunity. The equilibrium point of the trade-off between the costs and benefits of allogrooming is therefore likely influenced by natural patterns of exposure. The results suggest that infection control systems in social species were built upon the inducible immune defenses and nest hygienic behaviors of solitary and presocial ancestors and served as important preadaptations to manage disease transmission in colonies of incipiently eusocial species.

While social insects are an appealing model system for the study of disease and sociality in all group-living animals due to generalities of the social phenotype, there are a number of equally appealing differences that make them more accessible to study than many other social species. Human behavior is too complex and diverse to model effectively; examining how individual and group behavior can provide infection-control benefits is difficult (if not unethical) through empirical study. The inability to manipulate contributing factors, the lack of replication, and the lack of control/understanding of possible confounding factors (e.g., genetics or environmental conditions) create the need for a simpler model system. Therefore, we have demonstrated that social insects can provide a simplified study system where social structure, behavioral decisions, and their epidemiological impact can be examined empirically on both an individual and colony-wide level, and modeled accordingly.

The use of a simplified biological system that retains crucial but otherwise impenetrable aspects of group living is a powerful tool, allowing the external validation of theoretical models of disease spread that incorporate the substantial effects of behavior and social structure in ways that have not previously been possible. As a model system, social insects offer significant and diverse opportunities for analysis within colonies, between colonies, and/or across populations of colonies. Contact rates among foragers of different colonies can be easily made to represent different populations that vary in rates of emigration and immigration. Additionally, the focus can be on an individual rather than a population.

Socioecoinmunology can help us to understand the selective pressures and constraints that accompanied adaptations to pathogen exposure as insects evolved socially and diversified ecologically, and to identify the infection-reducing benefits associated with colonial life. As we have argued, the ability of social insects to control infection results from the behavioral
and physiological attributes of individuals as well as the social groups in which they reside. The nature of social interactions among nestmates, as well as the mechanisms of disease transmission and pathogen defense, may directly parallel those of other group-living animals. Social insects exhibit both innate and adaptive immune responses to pathogen challenge and some species have social mechanisms of generating immunity (Traniello, Rosengaas, and Savio 2002) that can be thought of as similar to human vaccination. They face both primary and secondary exposure to disease and are vulnerable to a variety of micro- and macro-parasites via many different modes of transmission. Social insect behavior can be observed with relative ease, and colony subpopulations that perform specific tasks with different associated risks of exposure to pathogens can be monitored. Workers are capable of modifying their behaviors in response to the threat of pathogen exposure, including quarantining possibly infected individuals and sending alarm signals that cause nestmates to avoid contaminated areas of the nest. They can generate effective immune responses (e.g., Mackintosh et al. 1998; Rosengaas Traniello, et al. 1999) and regulate pathogen spread with hygienic behavior (Spivak and Gilliam 1998a, b). These behaviors parallel human behavioral interactions (e.g., parents being more frequently exposed to childhood diseases than adults without children, healthcare workers being exposed to a greater diversity of pathogens, etc.) and public health efforts (e.g., Food & Drug Administration recalls of contaminated food, or flags to indicate pollution along public beaches), albeit as the result of local rather than group decision making (e.g., Rosengaas, Jordan, et al. 1999). Finally, as in many group-living animals, social insects exhibit differential susceptibility to some diseases based on the developmental stage of colony members (Rosengaas and Traniello 2001; Evans and Lopez 2004).

Traditionally, modeling social insect biology has been somewhat limited in scope, but the properties of colonies make them ideal biological systems for the study of a wide array of aspects of infectious disease epidemiology. The fact that accurate representation of this biological system in computational models may be verified by empirical investigation presents a unique research opportunity. In no other system is it possible to manipulate as many of the factors directly governing exposure, infection, and disease defense as is possible with social insects. By using empirical studies to test the predictions of models, we can have greater confidence in the accuracy of results of more complicated, purely theoretical investigations than has
previously been possible for epidemiologists to achieve. Investigations in insect socioecoinmunology can advance our understanding of the role of sociality in disease risk and control in both the study of social insects and the field of infectious disease epidemiology in ways that each discipline might not be able to accomplish separately.

Over the last few years, models have begun to set the groundwork for deeper investigation into the epidemiology and socioecoinmunology of insect colonies and provide methods to examine how individual behaviors can have potentially synergistic contributions to colony health and survival. They allow the examination of how colony structure and organization can directly affect exposure, as well as illuminating how disease resistance traits of the solitary ancestors of eusocial species were adaptively expressed within the context of group life (Fefferman et al. 2007).

An entirely new scope of questions about the nature of disease dynamics governed by the social phenotype and influencing its evolution can now begin to be examined: To what extent is disease regulation built on emergent properties of a colony? At what point will compromising colony efficiency lower disease risk and maximize fitness? How does selection for disease resistance at multiple levels affect the ergonomic organization of a colony? How do immunological systems change as a consequence of social evolution and how do they interact with social behavior to control disease? Each of these questions (among many others) are of direct interest, not only as significant and timely questions in sociobiology, but also as a first step toward addressing analogous questions about the structure of human society and disease.

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