Journal of Invertebrate Pathology 103 (2010) S62–S72

Contents lists available at ScienceDirect

Journal of Invertebrate Pathology

journal homepage: www.elsevier.com/locate/jip

Socialized medicine: Individual and communal disease barriers in honey bees

Jay D. Evans [a,*], Marla Spivak [b]

[a] USDA-ARS Bee Research Lab, BARC-East Bldg. 476, Beltsville, MD 20705, USA
[b] Department of Entomology, Univ. of Minnesota, St. Paul, MN, USA

ARTICLE INFO

Article history:
Received 10 June 2009
Accepted 30 June 2009
Available online 11 November 2009

Keywords:
Innate immunity
Social immunity
Hygienic behavior
Pollinator
Colony collapse disorder
Varroa mites
Dicistroviridae
Chalkbrood
Foulbrood

ABSTRACT

Honey bees are attacked by numerous parasites and pathogens toward which they present a variety of individual and group-level defenses. In this review, we briefly introduce the many pathogens and parasites afflicting honey bees, highlighting the biology of specific taxonomic groups mainly as they relate to virulence and possible defenses. Second, we describe physiological, immunological, and behavioral responses of individual bees toward pathogens and parasites. Third, bees also show behavioral mechanisms for reducing the disease risk of their nestmates. Accordingly, we discuss the dynamics of hygienic behavior and other group-level behaviors that can limit disease. Finally, we conclude with several avenues of research that seem especially promising for understanding host–parasite relationships in bees and for developing breeding or management strategies for enhancing honey bee health. We discuss how human efforts to maintain healthy colonies intersect with similar efforts by the bees, and how bee management and breeding protocols can affect disease traits in the short and long term.

Published by Elsevier Inc.

1. Introduction

Honey bees (*Apis mellifera*) provide important pollination services in agricultural settings worldwide and in many natural ecosystems. Honey bees and other pollinating insects are under threat from a variety of natural and anthropogenic causes (Committee on the Status of Pollinators in North America, 2007), ranging from viruses and bacteria to other insects and even mammals (Morse and Flottum, 1997). Thanks to the cultural importance of honey bees during much of modern human history the study of honey bee disease is an ancient topic, discussed in the literature since the ancient Greeks. The advent of modern microbiology and methods for culturing and observing microbes led to the first formal confirmation of several honey bee pathogens. As one example, the causative agent for American foulbrood was identified as a Gram-positive, rod-shaped, spore-forming bacterium labeled *Bacillus larvae* (White, 1906) and since renamed several times, ending with a recent reclassification as *Paenibacillus larvae* (Genersch et al., 2006).

Bee pathology has grown substantially in the past 50 years, with the identification of additional bacterial, fungal, and viral disease agents (Bailey, 1976), and the more recent application of molecular-genetic techniques to track both pathogens (Govan et al., 2000; McKee et al., 2003; Bakonyi et al., 2003; Genersch, 2005, as examples for viruses and bacteria) and bee responses toward those pathogens (Evans, 2006). Research efforts to understand honey bee resistance mechanisms are motivated by desires to breed and manage bees that are naturally resistant to parasites and, more generally, to better understand how an insect host interacts with a diverse set of pathogens. As an example of the former, beekeepers and researchers have long tried to develop lineages of bees with traits that enable colonies to survive attacks from their pathogens and parasites (e.g., Harbo and Hoopingarner, 1997; Spivak and Gilliam, 1998b; Szabo, 1999; De Guzman et al., 2001; Büchler, 2000; Kefuss et al., 2004).

In this review, we will briefly introduce the many pathogens and parasites afflicting honey bees, highlighting the biologies of specific taxonomic groups mainly as they relate to virulence and possible defenses. Second, we will describe physiological, immunological, and behavioral responses of individual bees toward parasites. Honey bees have evolved diverse methods to control the impacts of their many parasites and pathogens. Like all animals, individual honey bees enlist mechanical, physiological, and immunological defenses against disease agents (Evans et al., 2006; Schmid et al., 2008; Wilson-Rich et al., 2008). Third, bees also show behavioral mechanisms for reducing the disease risk of their nestmates (Starks et al., 2000; Spivak and Reuter, 2001a). Accordingly, we discuss the dynamics of hygienic behavior and other group-level behaviors that can limit disease. These group-level dynamics, labeled 'social immunity' (Cremer and Sixt, 2009), provide an underappreciated benefit of living in crowded social groups with respect to reduction of disease. We will contrast the costs and benefits of individual versus social defenses and will address the

* Corresponding author. Fax: +1 301 504 8736.
E-mail address: Jay.evans@ars.usda.gov (J.D. Evans).

0022-2011/$ - see front matter Published by Elsevier Inc.
doi:10.1016/j.jip.2009.06.019

enigma that honey bees show great genetic variation for the expression of their various defenses. Finally, we conclude with several avenues of research that seem especially promising for understanding host–parasite relationships in bees and for developing breeding or management strategies for enhancing honey bee defenses. We will discuss how human efforts to maintain healthy colonies intersect with similar efforts by the bees, and how bee management and breeding protocols can affect disease traits in the short and long term.

2. Parasites and pathogens

Domesticated and free-living honey bees are challenged by viruses, bacteria, fungi, mites and beetles, among others. Particularly enigmatic are the viral diseases of honey bees, most of which have been placed into two lineages of positive-strand RNA viruses, the Dicistroviridae and the Iflaviridae. The iflaviruses contain the agent responsible for one of the first recognized bee maladies (sacbrood virus) along with Deformed wing virus (DWV), a subject for numerous studies on bee pathology and epidemiology (Chen et al., 2005; Martin, 2001; Sumpter and Martin, 2004; de Miranda and Genersch, 2010). DWV is transmitted both vertically (by queens and their mates; Chen et al., 2006; de Miranda and Fries, 2008; Yue et al., 2007) and horizontally, especially via the ectoparasitic mite, *Varroa destructor* (Bowen-Walker et al., 1999; Chen et al., 2004; Shen et al., 2005; Yang and Cox-Foster, 2007; Yue and Genersch, 2005; Gisder et al., 2009). Recent evidence indicates that distantly related mites in the genus *Tropilaelaps* are also likely to be DWV vectors for *A. mellifera* (Dainat et al., 2009; Forsgren et al., 2009). DWV infections at high doses can lead to their definitive pathology and appear to generate negative effects on behavior and learning at lower doses (Iqbal and Mueller, 2007). There appears to be considerable variation among DWV relatives in their ability to cause behavioral changes among infected individuals (Fujiyuki et al., 2004; Rortais et al., 2006). In the Dicistroviridae, the genus *Cripavirus* contains several widespread bee viral pathogens, from Kashmir bee virus (KBV) to Acute bee paralysis virus (ABPV) and Israeli acute paralysis virus (IAPV), all of which can be found across multiple continents (Chen and Siede, 2007; de Miranda et al., 2010). IAPV was unrecognized outside of its type population in Israel until serendipitously discovered by metagenomic sequencing in bee colonies from parts of the United States (Cox-Foster et al., 2007).

Important bacterial diseases include American foulbrood disease (causative agent *Paenibacillus larvae*; Genersch et al., 2006; Genersch, 2010) and European foulbrood disease (causative agent *Melissococcus plutonius*; Bailey, 1983; Forsgren, 2010). The primarily fungal pathogens are *Ascosphaera apis* (cause of chalkbrood disease, Qin et al., 2006; Aronstein and Murray, 2010), *Aspergillus* sp. (stone brood disease, Morse and Flottum, 1997), and two members of the basal fungal lineage the Microsporidia (*Nosema apis* and *Nosema ceranae*: Zander, 1909; Fries et al., 1996; Fries, 2010). Along with their recognized pathogens, bees carry a diverse set of fungi and bacteria with poorly understood health impacts, with likely impacts on their bee hosts that range from pathogenic to benign or beneficial (Gilliam, 1997). Honey bees also harbor scattered parasites ranging from parasitic flies to trypanosomes and amoebae. One method now in use to document the 'neglected' parasites of honey bees and other organisms involves using modern high-throughput sequencing techniques to describe would-be pathogens on the basis of their chromosomes or expressed genes.

3. Mechanical, physiological, and immune defenses

Like all animals, *individual* honey bees of all ages and castes have evolved mechanisms to limit the impacts of their pathogens (Fig. 1a). These mechanisms involve *resisting* pathogens, by building barriers to infection or mounting defense responses once infection has occurred, or *tolerating* pathogens, by compensating for the energetic costs or tissue damage caused by either these pathogens or the bee's own immune responses. Mechanical, physiological, and immune defenses provide the classic route for resisting pathogens. Mechanical barriers include the insect cuticle and epithelial layers, which in many cases prevent microbes from adhering to or entering the body. Physiological inhibitors to microbial invasion can include changes in the pH and other chemical conditions of the insect gut (Crailsheim and Riessberger-Galle, 2001).

Honey bees are known to mount an induced immune response to wounding or pathogen exposure (Evans et al., 2006). Honey bees and other insects possess four major and interconnected routes for responding to parasite exposure; the Toll, Imd, Jak/STAT, and Jnk pathways (Theopold and Dushay, 2007). These pathways consist of proteins to recognize signals from invading parasites, proteins to modulate and amplify this recognition signal, and effector proteins or metabolites directly involved with parasite inhibition (Lemaitre and Hoffmann, 2007). Among the recognition proteins,

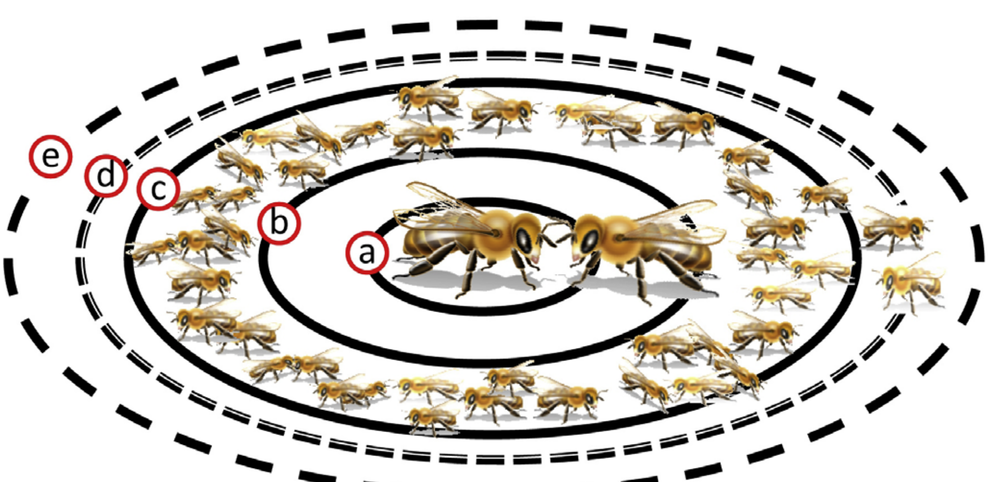

Fig. 1. Levels of defense in honey bee colonies from: (a) individual defenses, (b) pairwise defenses including grooming, (c) colony defenses such as task differentiation, (d) minimizing the entry of infectious agents, and (e) use of resins and other environmentals in colony shielding.