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Preface

Honey bee disease overview

Sexual reproduction of many crops and the majority of wild plants is dependent on animal pollination through insects, birds, bats and others, with insects playing the major role. Among the insect pollinators, solitary and social bees provide most pollination in both managed and natural ecosystems. Most of the world's staple foods, including wheat, corn, and rice reproduce without insect pollination. These crops account for 65% of global food production, still leaving as much as 35% depending on pollinating animals (Klein et al., 2007). In part due to the massive scale and homogeneity of modern agriculture, the majority of crops requiring pollination are dependent on managed pollinators, and especially on managed honeybees (Aizen et al., 2008).

The presumption of ample honey bees for crop and ecosystem pollination was severely challenged in the past several years by enigmatic declines of honey bee colonies in the United States and some European countries (Aizen and Harder, 2009; vanEngelsdorp et al., 2007). These losses are defined by a rapid loss of adult worker bees in colonies and the lack of apparent symptoms, leading to the nebulous label of 'Colony Collapse Disorder' (CCD). CCD is distinct from other forms of colony collapse described in this issue in that dead bees cannot be found in the vicinity of the hive, and food stores are not touched by robbing bees or honey bee comb pests for several weeks after the collapse. This disorder is not universal and, in fact, global populations of honey bee populations are increasing (Aizen and Harder, 2009). Further, similar episodes are apparent for specific geographic regions over much of the recorded history of beekeeping (vanEngelsdorp and Meixner, 2010). Nevertheless, this phenomenon has triggered an aggressive search for abiotic and biological causes, including pathogens.

Due to the link between animal pollinators and global food security, any decline of managed honeybees and the loss of wild pollinators are of increasing concern. Although there is an ongoing discussion of whether or not we are facing a 'global pollinator crisis' (Allsopp et al., 2008; Ghazoul, 2005a, 2005b; Steffan-Dewenter et al., 2005) there is no question that many solitary and social bees are declining (Ghazoul, 2005a, 2005b; Steffan-Dewenter et al., 2005). Given the increasing dependence on honeybee pollination in North America and Europe (Aizen et al., 2008), the unquestioned decline in managed honeybee colonies in these regions is alarming. Undoubtedly, the global health of honeybees is at risk. Honeybee well being is negatively affected by the intensive use of pesticides and fungicides in agriculture (Barnett et al., 2007; Desneux et al., 2007; Karise, 2007) and the chronic exposure to acaricides needed to combat the parasitic mite *Varroa destructor*. Furthermore, destruction and fragmentation of natural and semi-natural habitats as well as land-use intensification in agricultural landscapes have significant negative effects on honeybees and other pollinators (Kremen et al., 2007; Rathcke and Jules, 1993;

Steffan-Dewenter and Westphal, 2008; Tschamtkke et al., 2005). In addition and perhaps most importantly, honeybees are attacked by parasitic mites (*Varroa destructor*, *Acarapis woodi*, *Tropilaelaps* spp.), fungi (*Nosema* spp., *Ascosphaera apis*), bacteria (*Paenibacillus larvae*, *Melissococcus plutonius*), numerous viruses, and scavengers (from beetles and mice to bears) during any life stage. For some of these parasites and pathogens the consequences for individual bees and colonies are known, while for others they remain elusive. Still, it is clear that they all in one way or another reduce the fitness of their honeybee hosts.

Detailed knowledge of the pathogenesis of infections is fundamental for understanding and foreseeing the impact that an infectious pathogen will have on its host. In addition, understanding a pathogen's multiple ways to exploit its host is a prerequisite for the development of effective cures or measures to combat infections. Also the interactions (neutral, additive, synergistic, antagonistic) between different pathogens can best be evaluated with a strong understanding of the individual threats. In bee pathology, research was concentrated on the host for decades, neglecting the molecular analysis of the various bee pathogens and the fact that differences in the virulence of these pathogens can have an impact on both disease progression and the resulting impacts on bee hosts. A basic lack of understanding of bee pathogens has hampered the development of sustainable disease prevention and control strategies in the past. Considering the present dire situation of apiculture in many countries there is urgent need to change this situation. We need concerted action from specialists of all areas of honeybee biology, infection biology, and toxicology in order to explain what is going on in bee hives and to develop effective cures and rational disease prevention strategies based on these results.

This special issue of the Journal of Invertebrate Pathology on bee health aims to collect state-of-the-art knowledge on various bee pathogens in order to provide a solid and up-to-date background for those interested in honeybee infection biology. Only if research in the field of honeybee pathology is conducted at the cutting edge of science will we be able to address the pressing questions for sustaining honeybee health and preventing colony losses due to disease. CCD has greatly increased awareness of the fragility of honeybee pollination, and provided additional motivation and resources to understand honeybee pathology. We anticipate that this interest will lead to great fundamental and applied successes for honeybee research.

The issue starts with a historical review of managed honey bee populations in Europe and the United States and the factors that may affect them (vanEngelsdorp and Meixner). This review gives a broad and comprehensive overview of the global development of managed honeybee populations with special emphasis on the situation in North America and Europe. The review dissects the

current situation with colony losses in some areas and an increase of managed colonies in other areas resulting in an overall global increase in colony number of 45%, which still does not meet the increasing need for managed pollinators. When reviewing the underlying factors responsible for historical and recent colony losses, the main focus lies on the various pathogens and parasites implicated in these losses. However, other factors including pesticides, genetically modified crops, the environment, and socio-economic factors, just to name a few, also receive the appropriate space. The authors conclude that many of the factors included in their review influence the profitability of beekeeping, which by itself may have the most dramatic effect on managed populations of honey bees.

A total of three papers review the historical and recent developments in honeybee virology. More than 18 viruses infect bees and here we focus on those with the greatest impact on bee health.

One of the most prevalent honeybee viruses, deformed wing virus (DWV) is analysed by Joachim de Miranda and Elke Genersch. This virus and its genus (Iflavirus) have received abundant attention of late, in part from their clear impacts on honey bee health and in part because they have provided endless variations on what it means to be an insect pathogen. The authors document the diverse ways in which this virus is transmitted, from vertical transmission via both parents to horizontal transmission with or without the help of mite parasites. More broadly, the authors present a novel and parsimonious lexicon for describing disease or the lack thereof when this and other pathogens come into contact with bees. They also discuss quite recent hypotheses to explain how this virus makes the leap from covert to overt infection status and the resulting impacts on individual bees and their nestmates. Finally, they use comparative genomics to discuss how particular amino acids might play a role in Iflavirus translation and, ultimately, virulence for their bee hosts.

Chronic bee paralysis virus (CBPV), arguably one of the first viruses with described symptoms in bees (Aristotle is credited with this), is one of the latest to have been described at the genome level. Magali Ribière, Violaine Olivier and Philippe Blanchard, who were responsible for shepherding this virus into the 'genetic age', describe that journey and present a logical model explaining how this virus and associated proteins interact with each other and are inherited. This is arguably one of the most complex and divergent bee RNA viruses, and one that seems destined to form its own quirky family at some point soon. Bee paralysis is a widespread phenomenon, and the role this virus plays in that disease merit much future study.

Three related viral species, the complex of acute bee paralysis virus (ABPV), Kashmir bee virus (KBV), and Israeli acute paralysis virus (IAPV), are described by Joachim de Miranda, Guido Cordoni and Giles Budge. These three viruses are genetically closely related and share a number of biological characteristics which are thoroughly described. Particular emphasis is put on the molecular variability within this complex, a characteristic that makes both reliable diagnosis and correct classification especially difficult. For those interested in honeybee virus detection and diagnosis this review outlines the problems related to virus variability and gives extremely useful hints on how to solve these problems and avoid misinterpretation of the results. This review also deals in detail with the enigma of IAPV, including the proposed role of this virus in CCD, an apparent tendency for genome integration, and possible bee counter-defence via RNAi. Published results concerning these issues are discussed critically, presenting reasoned comments and placing published data in the context of the wider literature. Through a balanced analysis of IAPV and the remaining dicistroviruses, this review will prove to be a valuable asset for the field of honeybee virology.

Two chapters deal with bacterial pathogens of bees. In a comprehensive review of the aetiological agent of American Foulbrood,

Paenibacillus larvae, Elke Genersch links historic research with more recent advances. The background for the latest reclassification of the pathogen is described in detail, placing the bacterium in its historical context. Understanding the pathogenesis and epidemiology of the disease has increased considerably in the last few years and these advances are highlighted in this review. The fact that *P. larvae* is a most variable pathogen with variable life history strategies is treated in the section covering genotypes and virulence. In particular, recent research indicating that fast versus slow killing strains at the larval level yield opposing levels of virulence at the colony level is presented in some detail. With a better understanding of pathogenesis, epidemiology and virulence of the pathogen, improved methods for disease control may emerge. This is well covered in the section on AFB control. Finally, and perhaps most important, is the section describing how AFB is now entering the molecular era. The sequencing of the host genome, and the new possibilities to study virulence factors in pathogens may reveal as yet unknown interactions between the host and the parasite. So far, pathogenicity islands (PAI) have not been detected in *P. larvae* but recent surveys for the presence of virulence-associated genes are fully discussed.

European foulbrood is somewhat neglected as a honey bee disease. In her review on the subject, Eva Forsgren points out that the severity of the disease is currently increasing in parts of Europe. The causative agent, *Melissococcus plutonius*, along with secondary invaders and opportunists are described in detail and it is concluded that the mechanisms of pathogenesis and the role of secondary invaders in EFB are poorly understood. The detection and diagnosis of EFB is covered in detail with the most recent molecular tools included. After covering EFB control, it is concluded that by employing new techniques, future studies may reveal some of the mechanisms whereby *M. plutonius* infects bees and provide knowledge for the development of improved strategies for the control of EFB.

Reviews are included for two fungal pathogens of bees. An updated overview of chalkbrood disease, an invasive mycosis of honey bees is long overdue. In their comprehensive treatise of the topic, Katherine Aronstein and Keith Murray describe the progressive historic spread of the pathogen *Ascosphaera apis*. The taxonomy, epidemiology, pathogenesis, morphology and reproduction are well covered with much recent information. The section on disease control offers several useful suggestions for apiculture. Of particular interest is the up to date section on methods used in *A. apis* research which includes a detailed overview of culturing and larval bioassays, most useful for the researcher interested in *A. apis*.

Much has been written about microsporidial disease caused by *Nosema* spp. in honey bees, but the field received a substantial jolt in recent years with the discovery of the great geographical spread and abundance of a previously unrecognised pathogen of western honey bees, *Nosema ceranae*. Only described in 1996 (by the author of this review, Ingemar Fries), this species enjoys a nearly worldwide distribution and a proposed major role in honey bee pathology and colony losses. Emblematic of this is the fact that this species, and not the long-known honey bee pathogen *Nosema apis*, was chosen as the first species in the group to tackle complete genome sequencing. Fries describes the historical and current host ranges of *N. ceranae* and offers contrasts with its congener *N. apis* in a diversity of traits important for bee health, from intrinsic growth rates to the invasion of specific tissues and the relative resilience of spores. As a prime candidate for recent worldwide honey bee colony losses, *N. ceranae* is well deserving of the ideas and context provided by this review.

In the most extensive review on the topic to date, Peter Rosenkranz, Pia Aumeier and Bettina Ziegelmann, cover the whole range of issues related to infestations of the parasitic mite *Varroa destructor*. In particular the in-depth coverage of morphology, biology and

behaviour, orientation and host finding, and reproduction of this mite will make this review useful for many years to come. The review also updates and summarises what is known regarding tolerance to mite infestations. Interestingly, it appears as if directed selection for mite resistance has been generally less successful than natural selection. The methods used for mite control are extensively reviewed. The review concludes with some well founded suggestions for urgent future research to aid in providing healthy honey bee stocks.

The issue closes with a review of how honeybees cope with their many pathogens and parasites by mounting individual and communal disease barriers (Jay Evans and Marla Spivak). Pathogens and parasites afflicting honeybees are briefly introduced followed by a profound discussion on physiological, immunological, and behavioural responses of individual bees on one side and group-level behaviours and dynamics within honeybee colonies that can limit disease on the other side. It becomes clear that the versatile strategies of pathogens and the multifaceted immune responses of the host are two sides of the same medal and that it is necessary to know both to understand the complex host-pathogen interactions in the honeybee system.

Compilation of this volume of the Journal of Invertebrate Pathology resulted in part from the special emphasis on bee disease and CCD at the annual meeting of the Society for Invertebrate Pathology held in Warwick, UK in 2008. We thank participants in those symposia in addition to all other authors who have contributed to this volume, all internationally recognised experts in their respective fields. This volume provides detailed discussion of the current status and future prospects for management of bee health which will almost certainly be of ongoing concern.

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Conflicts of interest

There are no conflicts of interest to be declared.

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