Honey Bee Viruses—Pathogenesis, Mechanistic Insights, and Possible Management Projections

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Abstract

Honey bee viruses have gained substantial attention due to their involvement in the collapse of honey bee colonies. This chapter focuses on honey bee viruses linked to honey bee colony losses, specifically those that cause paralysis, those carried by Varroa mites, and those that cause deformed wings. Often virus infections in the colony are dormant and asymptomatic. Asymptomatic infections can convert to active (and visible) symptomatic infections when colonies are exposed to various stresses. These stresses include biological, such as *Varroa destructor*, mechanical, such as the utilization of bee colonies for pollination in net-covered crops, and chemical, such as the use of insecticides harmful to bees. These stresses enable viruses to overcome natural honey bee defenses, by facilitating viral access to the bee blood (hemolymph) and by weakening its immune system. Knowledge and understanding of the cause-and-effect interactions between viruses, stress factors, and honey bees will promote the use of antistress measures to help ameliorate collapse of honey bee colonies. This chapter is the result of intense collaboration between Y.S., instructor in beekeeping for the Extension Service of the Ministry of Agriculture and N.C., researcher of insect viruses and particularly honey bee viruses at ARO. The subjects presented below try to integrate the beekeeping and virus pathology perspectives.

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1 Honey Bee Viruses and Colony Losses

Honey bee viruses have gained substantial attention since the first reports of colony collapse disorder (CCD) where many honey bee (*Apis mellifera)* colonies were lost in the US during 2006–2007 (Cox-Foster et al. 2007; Stokstad 2007). As a result, it became clear to a wider public that bees were in trouble. Several pathogenic viruses were then found to be actively involved in the collapse of honey bee colonies around the world (Cox-Foster et al. 2007; Berthoud et al. 2013; Chen and Siede 2007; Cornman et al. 2012; Genersch et al. 2010; van Engelsdorp et al. 2009).

The most common honey bee viruses currently recognized are acute bee paralysis virus (ABPV), black queen cell virus (BQCV), chronic bee paralysis virus (CBPV), deformed wing virus (DWV), Israeli acute bee paralysis (IAPV), Kashmir bee virus (KBV), sacbrood virus (SBV), and Varroa destructor-1 (VDV-1) (Chen and Siede 2007; de Miranda et al. 2010 2013; de Miranda and Genersch 2010; Ribiere et al. 2010) (see Table 1).

Table 1 Honey bee viruses discussed in this chapter and their symptoms

Virus name	Abbreviation	Clade and family	Symptoms	Transmission by *V. destructor*
Acute bee paralysis virus	ABPV	ABPV-IAPV-KBV *Dicistroviridae*	Paralysis including: trembling, leg paralysis, the inability to fly, and general paralysis that leads to death. No dead bees accumulate in front of the colony	Yes
Kashmir bee virus	KBV			
Israeli acute bee paralysis	IAPV			
Chronic bee paralysis virus	CBPV	Unclassified	Paralysis involving abnormal trembling of body and wings. Inability to fly, crawling at the beehive entrance and on the ground. Bloated abdomens and hairless bees with black coloration on the abdomen. Piles of dead bees accumulate in front of the colony.	No
Deformed wing virus	DWV	DWV-VDV-1-KV *Iflaviridae*	Deformed wings, bloated and shortened abdomens, discoloration, and premature death	Yes
Varroa destructor-1	VDV-1			
Kakugo virus	KV			

Renewed research has identified new viruses infectious to honey bees, such as the various strains of Lake Sinai virus and aphid lethal paralysis virus Brookings strain (Runckel et al. 2011, Cornman et al. 2012). The real impact on honey bee colonies of some of the latter viruses is still unknown [for a comprehensive list of viruses, see (de Miranda et al. 2013, Runckel et al. 2011)].

In this chapter, we will focus on the major honey bee viruses responsible for recent colony losses. We will distinguish between viruses that cause paralysis (acute or chronic) and those that cause the easily recognized symptom of emerging bees with deformed wings (see Table 1).

2 Virus-Mediated Paralysis of the Honey Bee

The paralysis group of viruses Table 1 (de Miranda et al. 2010; Ribiere et al. 2010) may be present in the colonies in covert asymptomatic infections (not visible) with the symptoms described below appearing after the virus progresses to a more virulent form.

ABPV-IAPV-KBV belong to the viral family *Dicistroviridae*, due to the nature and specific organization of the viral genome; a single-strand RNA molecule bearing all the information the virus needs to replicate in the cells of its host (de Miranda et al. 2010).

Symptoms associated with paralysis viruses include trembling, leg paralysis, the inability to fly, and general paralysis that leads to death [most often observed for ABPV and IAPV and less frequently for KBV infections (de Miranda et al. 2010)]. In IAPV-infected hives, a relatively high number of smaller bees are often seen. Some researchers reported dark cuticle pigmentation in adult bees infected with IAPV and in pupae experimentally injected with the virus (Boncristiani et al. 2013; Maori et al. 2007), but in experiments performed with emerging bees fed with highly purified viral stocks, the bees never showed this symptom (Y.S. and N.C., unpublished observations). Paralysis by this group of viruses does not seem to result in accumulation of dead bees in front of the beehive (de Miranda et al. 2010).

IAPV was initially linked to CCD because CCD colonies had high loads of this infectious virus (Cox-Foster et al. 2007; Hou et al. 2014). Interestingly, IAPV was detected in the heads of experimentally infected foragers that showed impaired cognition and homing ability (Li et al. 2013). A recent study showed that IAPV was most abundant in the gut, hypopharyngeal glands, and the nerves of infected adults (Chen et al. 2014). Queens can bear the virus in the gut, spermatheca, and ovary and can lay infected eggs as well (Chen et al. 2014). Newly emerging bees are very sensitive to oral infection (mostly by trophallaxis).

The ectoparasite *Varroa destructor* is able to transmit viruses of this family, though it seems that this happens less frequently than transmission of viruses of the DWV clade (see below). In the USA and Europe, ABPV and IAPV prevalence increases in the summer (Bailey et al. 1981; de Miranda et al. 2010; Chen et al. 2014), while in Israel, its prevalence peaked mostly in the fall (Soroker et al. 2011).

CCD colonies detected in Israel had active IAPV infection with higher viral loads in April and December (Hou et al. 2014). Acute paralysis virus (ABPV) was discovered as a contaminant CBPV viral stocks (Bailey et al. 1963).

CBPV displays a different genomic organization (two single RNA segments of different size packaged in the viral particles) and is not classified in any viral family yet (Ribiere et al. 2010). From sequence analysis (the nature of the genomic information), Lake Sinai viruses display partial similarity to CBPV; however, no specific symptoms were associated with their infections in honey bees (Runckel et al. 2011).

CBPV paralysis involves abnormal trembling of the body and wings. Symptomatic bees are not able to fly and often crawl at the beehive entrance and on the ground, and piles of dead bees can be seen in front of the colony. Bloated abdomens and hairless bees with black coloration on the abdomens were also detected (Ribiere et al. 2010). The virus seems not to be transmitted by Varroa mites (*V. destructor)* (Ribiere et al. 2010). The infection develops slowly, from 6 days to two weeks, depending upon the conditions and probably the viral strain. Following CBPV infections in Israel, we were able to distinguish two types of infections:

1. an individual infected colony shows the typical symptoms of paralysis that are usually detected by the end of the winter and beginning of the spring and,
2. a group of colonies become infected and dead bees pile up in front of the colony during the spring-to-summer transition seasons.

Recently, we found that in most cases, CBPV infections were accompanied by ABPV infections. We are currently investigating whether the type of infections presented above have any correlation with the amount of ABPV present in single- versus group-type infected colonies.

What factors determine the type of infection? It could be the evolution of the virus to more virulent/infective strains, environmental interactions difficult to reveal, and even characteristics of the colony. Research is ongoing to answer this question. CBPV was also reported to be able to prevail in the colony in an asymptomatic state (Ribiere et al. 2010).

CBPV exhibits broad distribution in the infected bee; remarkably high numbers of viral particles were detected in the head. CBPV also prefers the honey bee nervous system. Also, high numbers of viral copies (around 10^9 per μl) were detected in the hemolymph of the infected host. The high preference of CBPV for the bee's nervous system correlates with trembling and other typical paralysis symptoms observed in adult bees from infected hives (Ribiere et al. 2010).

CBPV infects adults, brood, and also eggs, but the virus replicates to higher titers in worker bees (Blanchard et al. 2007). Experimental infections showed that honey bee queens are susceptible to CBPV, probably transmitted by trophallaxis. However, in naturally infected hives, there seem to exist behavioral strategies that prevent the queen from being fed by infected workers (Amiri et al. 2014). Also, CBPV can be transmitted by contact between infected bees and their non-infected

mates, as well as by oral ingestion of infected feces that have high viral loads (Ribiere et al. 2007).

CBPV was sometimes reported in association with *Nosema ceranae* infections (Toplak et al. 2013).

3 Deformed Wing Virus Clade

In this group, we find the viruses of the DWV-VDV-1-Kakugo virus (KV) clade (de Miranda and Genersch 2010). Though KV was mainly associated with aggressive behavior of infected bees and VDV-1 was initially found in Varroa mites, this group forms part of the clade because of the similarity of their genomes with DWV (de Miranda and Genersch 2010; Fujiyuki et al. 2005; Ongus et al. 2004). DWV-VDV-1 and KV belong to the *Iflaviridae* family of viruses [also with a single-stranded RNA molecule similar to the dicistroviruses, but displaying a different organization (de Miranda and Genersch 2010)].

Queens, workers, and brood can be infected with viruses of the DWV clade (de Miranda and Genersch 2010). Vertical transmission by drones and queens was reported as well (Fievet et al. 2006). Horizontal transmission by larval food and trophallaxis was also reported; however, the oral route of infection mostly results in asymptomatic infections. Before the invasion of Varroa, DWV was often present in honey bee colonies as an asymptomatic or mild infection (Gauthier et al. 2007; de Miranda and Genersch 2010). The spread of *V. destructor* throughout the world contributed to the horizontal transmission of DWV, mostly by the ability of the mite to carry and inject the virus directly into the bee hemolymph. This direct injection promotes the conversion of avirulent or low virulent asymptomatic viruses to more virulent viruses that induced symptomatic infections [(Moore et al. 2011; Ryabov et al. 2014) and see Sect. 4.1]. DWV and VDV-1 were shown to replicate in the mite as well but they seem not to harm it (Ongus et al. 2004; Shen et al. 2005; Yue and Genersch 2005; Tentcheva et al. 2006).

Worker honey bees infected with virulent DWV/VDV-1-like viruses displayed wing deformation, bloated and shortened abdomens, and discoloration (de Miranda and Genersch 2010, Zioni et al. 2011, de Miranda et al. 2013) and resulted in premature death of the bees.

DWV has been detected in the midgut of infected workers (Fievet et al. 2006) and in the hemolymph of Varroa-parasitized individuals as well as in the gut, wings, legs, head, thorax, and abdomen (Boncristiani et al. 2009; Shah et al. 2009). High loads of virus were also localized to the heads of infected workers (Yue and Genersch 2005; Zioni et al. 2011). Interestingly, DWV-infected bees showed learning disabilities (Iqbal and Mueller 2007). Moreover, extremely virulent strains may cause premature death of infected larvae parasitized with Varroa, aborting the emergence of worker bees (Martin 2001). The increasing imbalance in the bee population composition in such infected colonies can lead to their subsequent collapse (Dainat et al. 2012a). DWV has a worldwide distribution and in Europe

and Israel, it is the most prevalent virus (Genersch et al. 2010; Soroker et al. 2011; de Miranda and Genersch 2010; Berthoud et al. 2013). In Europe, DWV is highly associated with losses of overwintering colonies (Dainat et al. 2012b; Highfield et al. 2009).

4 An Abrupt Awakening: Stress-Induced Viral Infections

As discussed above, honey bee viruses can be carried by individual bees in an asymptomatic or silent mode. This equilibrium between the host and the pathogen can be broken by the appearance of outside stress factors, such as chemical or biological stresses that can induce replication of dormant viruses. In this section, scenarios of biological, chemical, and other stresses that may cause dormant viruses to replicate and cause symptoms will be covered.

4.1 DWV and the Biological Vector *Varroa destructor*, a Vicious Cycle

The rapid expansion of the ectoparasite *V. destructor* throughout the globe from the Eastern honey bee *A. cerana* to the Western honey bee *A. mellifera* introduced a new stress factor to Western bee colonies since the viruses were mostly asymptomatic (de Miranda and Genersch 2010). Varroa serves as a vector of viruses, thus profoundly changing the manner of transmission (Yue and Genersch 2005). Also, several investigations indicated that Varroa exerts a debilitating immunosuppressive effect in the parasitized bee (Shen et al. 2005; Nazzi et al. 2012). DWV became one of the most prevalent viruses in honey bee colonies and collapsing colonies showing typical symptoms of DWV infections became more frequent (de Miranda and Genersch 2010). Furthermore, the number of Varroa mites that could induce the collapse of a colony at the beginning of the Varroa invasion diminished over time. For example, in Germany at the beginning of Varroa infestation of *A. mellifera,* the colonies were able to sustain high levels of mites, up to 10,000, but nowadays mite levels above 3000 may be enough to cause colony collapse (Boecking and Genersch 2008). Varroa-parasitized bees with deformed wings symptoms showed very high loads of DWV-like viruses (Gisder et al. 2009; Zioni et al. 2011).

During the beekeeping season, when the colonies display high brood activity and rapid population increase (due to the abundant forage), no treatment against Varroa is usually applied to avoid contaminating the honey with chemicals. Thus, the Varroa population increases and concomitantly the DWV-like viruses, which is often unnoticed. But when Varroa treatments begin, the viruses do not necessarily disappear. Harsher climatic conditions, like the European winter or warm Middle Eastern summer, when forage is poor, lead to shortened life span of virus-infected adults and rapid bee depopulation of the colony. Since the colony is unable to replace the lost bees with a strong buildup of younger bees. Thus, despite success in

controlling/combating Varroa, the colonies may collapse with characteristic post-Varroa syndrome.

An insight to the nature of this phenomenon was explained in various studies.

Ongus et al. (2004) discovered VDV-1 that appeared to replicate in the mite. VDV-1 is highly homologous to DWV [about 84% similarity at the genomic level (Ongus et al. 2004)]. In addition, DWV replicates to high loads in the mite and mostly in the head of symptomatic bees (Gisder et al. 2009; Yue and Genersch 2005). Moreover, DWV-symptomatic bees bore recombinant DWV/VDV-1 viruses in their heads (Moore et al. 2011; Zioni et al. 2011). These results suggested that parasitism by Varroa provoked not only a significant increase in viral prevalence and a quantitative change enhancing replication of DWV, but also a qualitative change in the virus, selecting from a mild to a more virulent strain. These hypotheses were confirmed by two studies: one following the invasion of Varroa to the Hawaiian Islands under natural conditions and the second in the UK with experimentally infected hives (Martin et al. 2012; Ryabov et al. 2014). This suggested that either the immunosuppressing activity of Varroa on the honey bee and/or the ability of the virus to replicate to high loads in the mite and in the bee promoted the transformation of DWV and the appearance of DWV-VDV-1 recombinants and virulent DWV strains (Martin et al. 2012; Ryabov et al. 2014).

Nazzi et al. (2012) demonstrated that Varroa and DWV build on weakening of the bee's immune system mediated by NfκB, a protein that regulates its stress-related responses (Nazzi et al. 2012). At high DWV loads (over 10^{15} viral copies per bee), this results in the down-regulation of genes involved in the immune response of the honey bee. Thus, the renewed ability of the virus to change (mediated by Varroa) and replicate to higher loads could benefit the parasite, whose gain could be a reduction in the ability of the bee host to react to it (e.g. to being wounded which is known to trigger immune responses (Nazzi et al. 2012)]. What is the advantage to the virus? Further studies showed that direct injection of DWV into the body of honey bee larvae enabled amplification of the virus and a rapid emergence of DWV virulent strains [DWV-VDV-1-like recombinants (Gisder et al. 2009; Ryabov et al. 2014)].

These data enable us to hypothesize that the mite contribution to the emergence of virulent strains of DWV could be:

1. The rapid accumulation of a variety of DWV variant strains that may even replicate in the body of the mite and,
2. Their subsequent injection directly into the bee hemolymph, overcoming the primary immune defenses of the bee which are normally directed toward pathogens naturally introduced by oral ingestion, a route known to be much less effective (Mockel et al. 2011).

A summary of the Varroa-DWV vicious cycle is presented in Fig. 1.

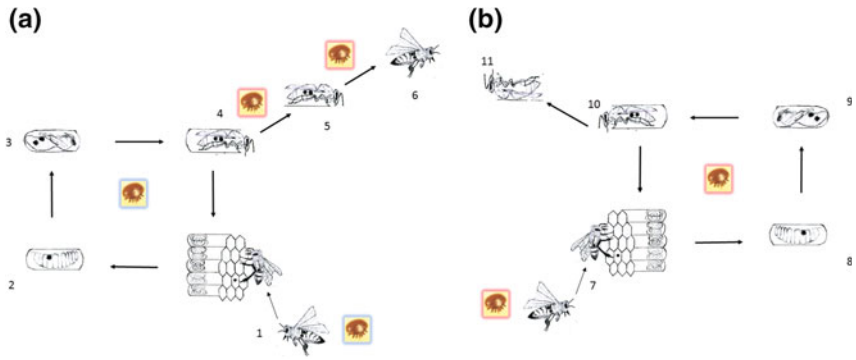

Fig. 1 The Varroa–DWV cycle. **a** Infestation of a new colony by Varroa carrying low DWV loads (blue Varroa) and conversion to highly virulent DWV. 1. Brood infestation. 2. Reproduction. 3. Reproduction and amplification of the viral load. 4. Amplification of DWV-virus injected to the bee hemolymph induces appearance of highly virulent DWV. 5. Emerging bees carrying Varroa with highly virulent DWV (red Varroa) can transmit the DWV-loaded parasite and/or DWV to other bees from the same colony. 6 Foraging bees can transmit the highly DWV-loaded Varroa to other colonies. **b** The Varroa–DWV cycle re-initiates with the red Varroa in the same or in other colonies and brings them to their collapse

5 CBPV Opportunistic Infections and Mechanical Stress

A common observation is that CBPV infections erupt often when the colony seems to be strong (a robust population of adults and brood). Frequently, this eruption was attributed to the mechanical break of the bees' body hairs due to overcrowding of the colony population before swarming; such breakage could facilitate the access of contaminating CBPV to the bee hemolymph (Ribiere et al. 2010).

Another example of stress-induced infections was observed after beehives were put under nets and into greenhouses for pollination. Keeping up with the increasing trend in Israel to utilize honey bee hives for pollination in net-covered crops, we noticed an increase in piles of dead bees in the front of those hives. These bees displayed the characteristics typical of CBPV-induced paralysis and death. Diagnosis performed in the laboratory showed that they were highly infected with CBPV (viral titers of above 10^9 particles per bee). To confirm our initial findings, we introduced a group of colonies at the entrance of net-covered crops at two locations in the country, and kept an equal number of control colonies uncovered, at open crop conditions. We found that the hives located at the covered crops' entrance quickly contracted CBPV (Slabezki, Y, Dag, A. and Chejanovsky N, Manuscript in preparation).

These findings support the hypothesis that mechanical stress caused cuticular damage to the pollen/nectar-loaded honey bee foragers by their collision with the nets in an attempt to return to the hive, providing the virus quick access to the insect hemolymph, and thus overcoming the insect defenses.

6 DWV and Insecticide Exposure—Insecticide Spread and Virus Emergence

Some insecticides were documented as causing stress responses in honey bees (Blacquiere et al. 2012). This resulted in temporarily banning the use of three neonicotinoids by the European Union (Gross 2013). A recent study showed that application of the neonicotinoid clothianidin weakened the immune defenses of recently emerged worker bees (Di Prisco et al. 2013). Furthermore, it involved the repression of expression of another member of the NfκB family (Di Prisco et al. 2013). Under these circumstances, DWV-dormant infections with low levels of viral replication were promoted to replicate DWV at high levels, comparable to those observed in symptomatic infections.

The stress situations presented above referred to induction of particular viruses. However, we and others have observed the simultaneous or progressive appearance of several pathogenic viruses upon weakening of honey bee defenses by biological, chemical, or environmental stresses. These superinfections then contribute to the rapid deterioration of the colony.

7 Prophylaxis Methods and Antiviral Approaches

7.1 What Can We Learn from Stress-Induced Infections?

The three cases discussed in detail above exposed a link between stress induction, weakening of the immune system of the bees, and the activation of lethal viral infections (summarized in Fig. 2) and suggest that if we adopt appropriate measures, we should be able to maintain the damage to colonies at sustainable levels. If we "beekeepers" look at treatment according to the different elements that can co-act to weaken a colony, beekeepers should be able to attain a comprehensive treatment.

7.2 Can We Treat Viral Infections?

From the point of view of virus treatments, we should aim to reduce:

1. The conversion of avirulent strains to virulent strains.
2. Block the replication of viruses.
3. Reduce the possibility of their transmission.

7.2.1 Conversion of Avirulent Strains to Virulent Strains

As we discussed above, Varroa is an active vector of viruses and promotes their direct access to the host hemolymph overcoming bee defenses. This direct infection

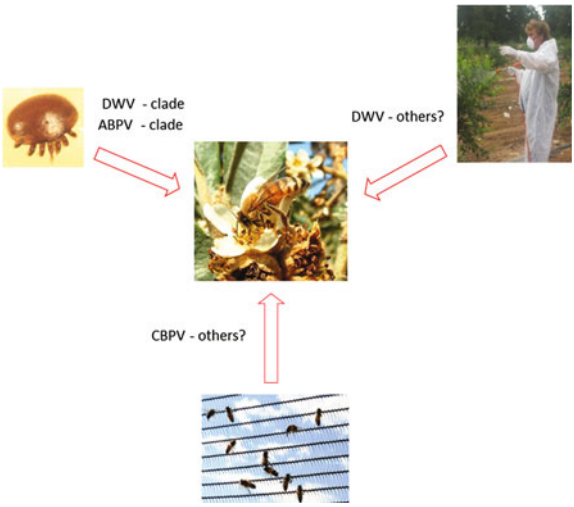

Fig. 2 Biological (e.g. mites), chemical (insecticides, miticides), and mechanical stressors can induce dormant and new honey bee virus infections

route facilitates conversion of viruses from avirulent to virulent strains. To interrupt this process, we (beekeepers) should aim to diminish the effect of Varroa by controlling the mites. The timing and dose of treatment should be applied early in the season, which is crucial to avoid virus conversion (from low virulent to highly virulent strains).

However, some Varroa treatments can induce stress in bees and incidentally increase the virus too. For example, it has been reported that coumaphos and fluvalinate treatments can induce changes in certain honey bee genes related to immunity, detoxification, behavioral maturation, and nutrition (Boncristiani et al. 2012; Schmehl et al. 2014). Thus, applying thoughtful, professionally assisted treatments against Varroa (and even alternating control measures to avoid the emergence of resistant Varroa mites) could diminish its long-term impact on bee health. Successful breeding of bees to resist Varroa infestation might achieve similar results (Locke et al. 2014; Rinderer et al. 2010; Buchler et al. 2010).

Knowledge of the insecticides used on the crops in the vicinity to the bee colonies could prevent the replication of undesirable highly pathogenic viruses. From a long-term perspective, it will be important to coordinate insecticide applications (type and timing) with honey bee colony placement and more strongly advocating the use of honey bee-friendly insecticides (if these even exist).

Proper nutrition, such as pollen (or protein-based feeding), was shown to reduce the impact of the pesticide chlorpyrifos; and it can help to reduce the negative impact of some insecticides (Schmehl et al. 2014). In contrast, excessive reliance on feeding sugar syrup may have detrimental effects, since they may have a negative impact on the performance of the honey bee immune system (Galbraith et al. 2015).

In other cases, such as mechanical stress, using nets that could be less damaging to the bees, or even working in other types of covered crops, would help.

7.2.2 Block Replication of Viruses

Viruses replicate only in the body of their hosts, yielding high numbers of viral particles (virions) that propagate the infection. During this process, multiple copies of the viral genome that encodes the genetic information for its propagation are produced (from a million to a billion copies). In addition, new variations of the original information (variants) are produced, and the chance that these variants convert from an avirulent to a more virulent virus and infectious strains (viral strain) increases with the increase in the number of virions produced.

Thus, blocking the ability of viruses to replicate may reduce the chance of the emergence of more virulent and infectious strains. Sometimes the host (in this case the honey bee) can develop such blocking, but little is known about the ability of different bee races to resist viral infections. Much more research needs to be supported in these areas.

On the other hand, a promising approach is based on the fact that it is possible to target the replication of honey bee viruses by utilizing biological tools that mimic or enhance the host immune response. This approach is based on what is known as the RNA interference response (Niu et al. 2014). This natural response detects the presence of foreign (non-host) RNA, such as the genome of RNA viruses of the honey bee, and promotes their specific degradation when the virus is trying to replicate (Niu et al. 2014). During this process, the viral genome is chopped into useless pieces by the honey bee immune defense mechanism. It became clear that it is possible to induce this response by producing in vitro (in the laboratory) molecules of double-strand RNA. Double-stranded RNAs, or (dsRNAs), are short molecules with one strand and its mirror copy). Such RNA strands carry small bits of the genetic information for specific viruses. Subsequent injections or feeding of these RNA molecules to honey bees triggered the RNAi response. This resulted in the inhibition of the ability of the virus to replicate in the honey bee. This was shown for SBV, DWV, and IAPV (Desai et al. 2012; Liu et al. 2010; Maori et al. 2009). Furthermore, in the case of IAPV, it was revealed that the administration of dsRNA protected the colonies from viral infection (Hunter et al. 2010). However, in the latter case, RNAi was administrated concurrently with IAPV, and it remains to be demonstrated that its application postinfection is efficient to diminish/ameliorate viral damage (Hunter et al. 2010).

From the very beginning of animal and plant virus research in the middle of the last century, viruses were considered as mysterious pathogens. However, research has produced drugs and treatments against a series of serious viral pathogens, such as the flu viruses, herpes viruses, human immunodeficiency viruses, small pox virus. These treatments were aimed at stopping the multiplication of the viruses. Thus, it is conceivable that in the future, there will be progress in understanding the replication of honey bee viruses which may yield experimental drugs that could block virus infections or immunize honey bees.

7.2.3 Reduce Their Transmission

Early monitoring of symptomatic viral infections can be used as a preventative measurement. In the case of DWV, for example, observant beekeepers could recognize that the more virulent viral strains were already present (at least in some colonies), and measures can be taken to prevent their spread.

8 Conclusions

There is much more to be learned about bee viruses, such as the natural resistance of different honey bee strains against virus infections, the genetic basis of this resistance, and the effect of human-borne and environmental factors that can upset or maintain bee virus infections. Current research is trying to understand more about these processes.

In the meantime, we hope that this material presented an overall view of virus infections associated with colony losses, the stress factors involved in their acute manifestation, and possible measures that can contribute to ameliorating their impact on your honey bee operation.

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Glossary

Genome A DNA or RNA molecule, depending on the virus, bearing all the information the virus needs to replicate in the cells of its host

Viral genomic copies Number of viral genomes that bear the genetic information that allows the virus to produce more viral particles

Viral loads Usually refers to the number of viral genomic copies which is the most common method of estimating honey bee viruses, but it could also refer as well to the number of infectious virus particles

Viral genomic replication The process by which the virus produces new copies, replicas, of itself, that are packed in new viral particles

Immunosuppression Weakening of the immune system, body defenses

Down-regulation of genes A molecular process that results in lower expression of the proteins that are products of these genes

Genomic homology Similarity of nucleotide sequences between virus genomes

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Yossi Slabezki finished his studies at The Faculty of Agriculture from The Hebrew University of Jerusalem in 1987, specializing in entomology and beekeeping. His research thesis was on factors affecting honey bee swarming. Since then he works at the Israeli Ministry of Agriculture Extension Service in the beekeeping branch focused on resolving honey beekeeping problems: acarology, virology, toxicology, etc. His endeavor is to link between the field and research front back and forth. From this interchange emerge and are implemented the treatments' policy of the honey bee branch in Israel. During these years, Yossi specialized in honey bee pathogens and participated in research projects on *Varroa destructor*, tracheal mites, honey bee viruses, and Nosema. He is also actively involved in prevention of insecticide damage and intoxication of bees as well as in efforts to enlarge the bee-safe foraging areas. Actually, he is the Director of the Apiculture Department at the Israeli Ministry of Agriculture Extension Service and Lecturer of beekeeping at The Faculty of Agriculture of The Hebrew University of Jerusalem.