Why Vaccinate Your Honey Bees?

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Contagious honey bee diseases, such as American Fouldbrood Disease, can cause significant economic harm to the honey bee industry and devastate honey bee populations. For bacterial diseases, the use of antibiotics can result in bacterial resistance and negatively impact overall hive health. Vaccination can be a promising alternative to protect honey bee colonies and the food supply chain.

The Cost of Disease

Honey bees are subject to a variety of bacterial, viral, fungal, and parasitic pathogens (i.e., disease causing agents) that negatively affect colony health and productivity. According to estimates in the U.S. alone, lost annual revenue due to disease is estimated at $400 million and growing (1).

Listed by the World Organization of Animal Health as a notifiable disease worldwide (2), American Foulbrood (AFB) is the most devastating bacterial disease affecting honey bees. There is no cure for AFB. Destroying infected honey bee colonies and beekeeping equipment is the only way to contain the spread of the disease, resulting in significant economic losses for beekeepers.

AFB is caused by the spore forming bacterium *Paenibacillus larvae*, a specialized pathogen with only one established host, the honey bee larva. Larvae first become infected when fed AFB spore-laden food by nurse bees. Once in the midgut of a larva, the AFB spores begin to rapidly multiply. In the process of replication, the bacteria release enzymes which digest larval tissue, leading to sepsis and death of the larva.

Paenibacillus larvae spores (i.e., the dormant form of the bacteria) are resistant to most forms of destruction (pressure, chemicals, desiccation, and antibiotics) and persist in the environment for decades, serving as a continuous source of infection (3). Honey bee colonies often harbor background spore concentrations, averaging 158 spores per bee. When bacterial spore loads within a colony increase to 228 spores per bee, the colony will begin to develop clinical symptoms of AFB infection (4).

The migratory nature of the beekeeping industry for the pollination of agricultural crops contributes to the spread of disease among honey bee colonies. For example, over 2 million of the 2.7 million migratory colonies in the US are transported to California every February to satisfy the annual almond pollination (5). The mass mixing of honey bee colonies from across the country for agricultural crop pollination promotes the transmission of deadly pathogens, including AFB spores, among migratory colonies (6) as well as to nonmigratory colonies and apiaries in surrounding areas. Indeed, *P. larvae* spores have been detected in 50% of honey bee colonies sampled in Canada (7).

Once in an apiary, an AFB infection is quickly spread through natural bee behaviors such as drifting and robbing. Beekeepers can also inadvertently spread the infection by exchanging infected beekeeping equipment between hives and using unsanitized hive tools. In most cases, an AFB infection kills entire honey bee colonies. Treatment with antibiotics may reduce the replicating bacteria, but does not kill the AFB spores, so the disease will recur.

The Problem with Using Antibiotics to Prevent AFB Infection in Honey Bee Colonies

To reduce the potential for economic losses incurred from bacterial infections in honey bee colonies, many beekeepers prophylactically treat their colonies with antibiotics. However, the use of antibiotics in honey bee colonies increases honey bee mortality – up to 50% - by killing the "good bacteria" in the honey bee gastrointestinal tract (i.e., the honey bee microbiome) that contributes to immunity, nutrition, and detoxification among other actions (8). This imbalance of good bacteria in the gut microbiome is known as dysbiosis. Interestingly, laboratory studies have found that an antibiotic acquired dysbiosis is readily transferred to newly emerged bees through social interactions. These results indicate that an antibiotic-mediated dysbiotic microbiome could continue to harm subsequent generations of honey bees, even after treatment cessation (9).

Due to the widespread use of antibiotics in beekeeping, some strains of *Paenibacillus larvae* have developed resistance, and clinical infections occur despite the use of antibiotics (10). Antibiotic resistance is a global public health problem. The overuse and misuse of antibiotics in livestock animals, including honey bees, is a major contributor to the development of antibiotic-resistant bacteria in humans (11). In fact, antibiotic residues have been found above regulatory standards in honey and hive products. Antibiotic residues consumed in our food can produce resistance in bacterial populations in humans (12). For the health and safety of honey bees and humans alike, alternatives to antibiotics that are effective, safe, and sustainable must be implemented.

Vaccines Are an Effective, Safe, and Sustainable Alternative to Antibiotics

Preventing disease is significantly less expensive than treating disease. Vaccination is an effective and safe way to prevent and control the spread of infectious diseases that cause high morbidity and mortality in a population. Vaccines are also used to greatly reduce, and in some cases, eradicate, disease. For example, due to large-scale vaccination campaigns, smallpox was declared to be eradicated in the human population in 1980 (13) and rinderpest, a fatal disease of cloven-hoofed animals, was declared eradicated in 2011 (14). Vaccines prevent 4 million human deaths annually and save countless more animal lives (15).

Vaccines contain weakened or killed parts of a pathogen that triggers an immune response. In vertebrates, the production of antibodies in response to a vaccine allows the immune system to recognize and quickly respond to the pathogen upon subsequent exposure. Although insects do not produce antibodies, their immune system is capable of recognizing specific pathogens. Through trans-generational immune priming (TGIP), insect parents transfer immune elicitors to pathogens in which they were exposed to their progeny, effectively "priming" the immunity of their offspring to these pathogens (16).

Dalan's Honey Bee Vaccine Technology

Dalan's platform vaccine technology works through a biological mechanism called Transgenerational Immune Priming (TGIP), whereby the the queen passes immunity to her daughters before they hatch. The vaccine, containing a killed pathogen, is administered orally to the maternal insect—the queen bee. Attendants caged with the queen are fed queen candy containing the medication. Work carried out in Dalan's laboratories has indicated that the attendants digest the killed pathogen and produce royal jelly containing pathogen particles. The royal jelly is fed to the queen, and as she ingests it, pieces of the pathogen are transported via her fat body to her ovaries where it is deposited in the eggs. The developing larvae are exposed to the pathogen and start to build up immunity before they hatch.

Dalan's Commitment to Beekeepers

Dalan is committed to providing beekeepers with innovative solutions to protect the health of their honey bees. Our experimental vaccines have been rigorously tested with established research designs used in animal vaccine efficacy trials to demonstrate laboratory safety and efficacy.

Vaccination of honey bees against deadly pathogens, like American Foulbrood, is an important step in protecting the health and welfare of honey bee colonies. Healthy honey bees are essential to ensuring a safe and nutritious food supply. We need bees, and bees need us. Let's take care of one another.

About Dalan Animal Health, Inc.

Dalan Animal Health is dedicated to bringing the world transformative animal health solutions to support a more sustainable future. This platform vaccine technology uses transgenerational immune priming, allowing the maternal animal to pass immune modulators (e.g., antigens, anti-microbial molecules) to the next generation larvae before they hatch. Dalan plans to develop vaccines for other honeybee diseases and underserved industries, such as shrimp, mealworms, and insects used in agriculture. The company is headquartered in Athens, Georgia, at the University of Georgia's Innovation Hub.

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