Why Vaccinate Your Honey Bees for AFB?

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American Foulbrood (AFB) disease can cause significant economic harm to the honey bee industry and devastate honey bee populations. 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, *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 AFB vaccine, containing pieces of killed *P. larvae*, is fed to the honey bee queen. It is free of chemicals, preservatives and is non-GMO (1). In laboratory studies, one-day old larvae fed 200 times the number of spores needed to incite an AFB outbreak in nature, were up to 50% more resistant to developing an AFB infection when their queen was vaccinated with Dalan's AFB vaccine compared to larvae whose queen received a placebo (17). These results indicate the vaccine has a much higher efficacy under natural conditions where spore numbers are lower and behavioral defenses of honey bees, such as hygienic behavior, grooming behavior and propolis deposition also contribute to reduce pathogen loads. In addition, vaccination had no negative effects on queen or hive survival (17) (Figures 1-2). Increased immunity to AFB in honey bees may help them deal with the other multiple stressors to which they are exposed.

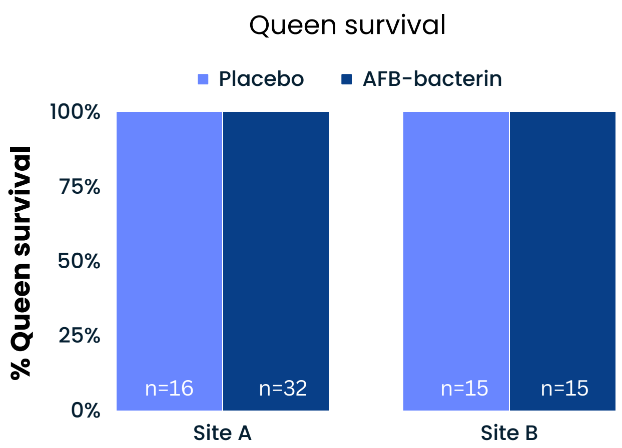

Figure 1. Queen survival after 8 day vaccination at each study site. Vaccination had no significant impact on queen survival. See citation 17 for full information.

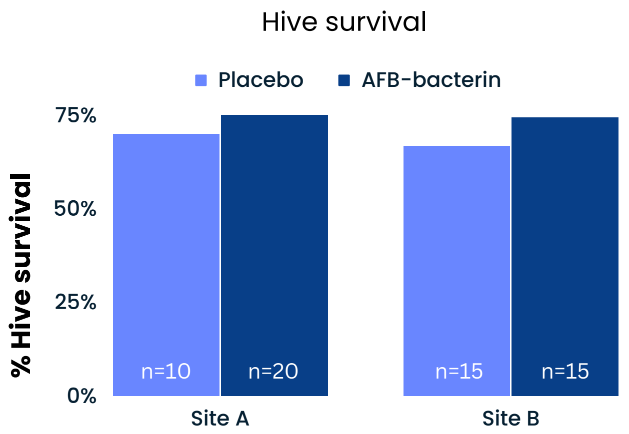

Figure 2. Hive survival after queen placement after a 3 month monitoring period. Vaccination had no significant impact on hive survival. See citation 17 for full information.

Dalan's commitment to beekeepers

Dalan is committed to providing beekeepers with innovative solutions to protect the health of their honey bees. Our AFB vaccine has 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.

LITERATURE CITED

1. Dalan Animal Health. (2023). https://www.dalan.com/

2. World Organization for Animal Health. (2023). Infection of honey bees with Paenibacillus larvae (American Foulbrood). Terrestrial Animal Health Code. Chapter 9.2.Article 9.2.1. https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/?id=169&L=1&htmfile=chapitre_paenibacillus_larvae.htm

3. Milbrath, M. (2021). Honey bee bacterial diseases. In Kane, T., & Faux C. Honey bee medicine for the veterinary practitioner. John Wiley & Sons.

4. Stephan, J., de Miranda, J., Forsgren, E. (2020). American foulbrood in a honeybee colony: spore-symptom relationship and feedbacks between disease and colony development. BMC Ecol. (20)15. Doi: 10.1186/s12898-020-00283-w

5. American Beekeeping Federation. (2018). Pollination facts. https://abfnet.org/pollination-facts/

6. Martinez-Lopez, V., Ruiz, C., De La Rua, P. (2022). Migratory beekeeping and its influence on the prevalence and dispersal of pathogens to managed and wild bees. International Journal for Parasitology: Parasites and Wildlife 18.

7. Zabrodski, M. et. al. (2022). Establishment of apiary-level risk of American foulbrood through the detection of Paenibacillus larvae spores in pooled, extracted honey in Saskatchewan. Scientific reports, 12(1), 8848. https://doi.org/10.1038/s41598-022-12856-4

8. Raymann, K., Shaffer, Z., Moran, N. (2017). Antibiotic exposure perturbs the gut microbiota and elevates mortality in honeybees. PloS Biol 15(3): e2001861. https://doi.org/10.1371/journal.pbio.2001861

9. Kowallik, V,, Das, A., Mikheyev, A. (2022). Experimental inheritance of antibiotic acquired dysbiosis affects host phenotypes across generations. Front. Microbiol. 13:1030771. doi: 10.3389/fmicb.2022.1030771

10. Miyagi, T., Peng, C., Chuang, R., Mussen, E., Spivak, M., Doi, R. (2000). Verification of oxytetracycline-resistant American foulbrood pathogen Paenibacillus larvae in the United States. Journal of Invertebrate Pathology 75(1). Doi: 10.1006/jipa.1999.4888.

11. Martin, M., Thottathil, S., Newman, T. (2015). Antibiotics overuse in animal agriculture: A call to action for health care providers. American Journal of Public Health 105 (12).

12. Noori, A., Khelod, S., Al-Ghamdi, A., Javed Ansari, M. (2012). Antibiotic, pesticide, and microbial contaminants of honey: Human health hazards. The Scientific World Journal (12). https://doi.org/10.1100/2012/930849

13. World Health Assembly, 33. (1980). Declaration of global eradication of smallpox. World Health Organization. https://apps.who.int/iris/handle/10665/155528

14. World Organization for Animal Health. (2011). Joint FAO/OIE Committee on global rinderpest eradication. OIE Final report. https://www.woah.org/app/uploads/2011/05/final-report-may2011.pdf

15. Centers for Disease Control and Prevention. (2023). Global immunization fast facts. https://www.cdc.gov/globalhealth/immunization/data/fast-facts.html

16. Cooper, D., Eleftherianos, I. (2017). Memory and specificity in the insect immune system: Current perspectives and future challenges. Frontiers in Immunology (8). Doi: 10.3389/fimmu.2017.00539

17. Dickel, F., Bos, N., Hughes, H., Martín-Hernández, R., Higes, M., Kleiser, A., Freitak, D. (2022). The oral vaccination with Paenibacillus larvae bacterin can decrease susceptibility to American Foulbrood infection in honey bees—A safety and efficacy study. Frontiers in Veterinary Science (9). Doi: 10.3389/fvets.2022.946237