What's the Buzz About Bees and Antibiotics?

by Elina L. Niño, Ph.D. | Pacific Veterinary Conference Speaker

Honey bees (*Apis mellifera*) are fascinating insects belonging to the order Hymenoptera. They live in colonies within nests and live in complete darkness relying on pheromones and direct contact for communication. They are highly social and are referred to as having a eusocial structure which means that they exhibit a reproductive division of labor (the queen produces all of the female workers); they have overlapping generations (the "mother" queen lays up to 1200 "daughter" eggs per day during the reproductive season); and they conduct cooperative care of young (It takes a village!). Drones (male bees) and queens mate in flight, after which the drones die and the queen comes back to the colony to start egg-laying. Workers do all of the other tasks in the colony (brood rearing, cleaning, building the nest, etc.). Each individual worker will go through a transition from being an "in house" bee earlier in life to becoming a forager later on. Foragers collect nectar and pollen from plants and this behavior allows us to capitalize on their contributions to pollination.

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As of January 1, 2017, beekeepers are required to have a prescription or a veterinary feed directive from a veterinarian who has established a veterinarian-client-patient relationship in order to purchase antimicrobials and administer them to their honey bees. The ruling by the FDA is in response to growing concerns about antibiotic resistance. For more information, visit: https://www.fda.gov/downloads/AnimalVeterinary GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf.

Honey bees are an integral part of United States agriculture and their contribution is valued at approximately $20 billion in the United States alone (Frankie et al. 2014). They are the primary managed pollinator for over 30 crops in California including almonds, alfalfa, onions, many other vegetables, fruits, and nuts. However, unprecedented colony losses of up to approximately 45 percent per year are being reported in the United States, and somewhat lower losses in Europe. It is now widely accepted by scientists and beekeepers alike that these losses are most likely due to a myriad of factors including the presence of pathogens and pests, pesticide exposure, and poor nutrition availability due to habitat loss.

Very often, beekeepers have to rely on various chemistries for the management of pests and pathogens. For example, parasitic varroa mites that feed on bee hemolymph and fat bodies, and transmit viral pathogens and suppress the bee's immune response, are commonly controlled with synthetic (e.g., amitraz) or bio-derived (e.g., thymol-based) miticides. In addition to viruses, honey bees are threatened by various bacterial and fungal pathogens.

Of the bacterial pathogens, American Foulbrood (AFB) and European Foulbrood (EFB) are the two that are of most concern to beekeepers. They should also be of most interest to veterinarians because AFB and EFB treatments are affected by the new FDA rule (see FDA Guidance for Industry 213) on antibiotic use in livestock. This new rule requires beekeepers to get either a veterinary feed directive (VFD) or a prescription from a veterinarian in order to obtain antibiotics for treatment of these diseases.

AFB is caused by a Gram-positive, spore-forming bacterium called *Paenibacillus larvae*. It is arguably worse than EFB since its spores can remain infectious for decades and can resist extreme conditions (reviewed in Genersch 2010). Spores infect only larval honey bees which are the most susceptible

Photo by Rob Snyder, Bee Informed Partnership; Northern California Tech-Transfer Team.

Figure 1: Typical signs of American Foulbrood including "melted larvae," perforations on capped cells, and oozing from within capped cells.

within the first 36 hours after hatching. Within a few days after infection, spores utilize proteases to break down larval tissues into a brown, foul smelling mass, hence the name foulbrood (Figure 1). This larval tissue mass can be scrambled with a toothpick (or a similar tool) and once pulled, it can rope out a few inches without breaking. This is very typical of AFB. Eventually, the mass dries into a hard, blackish scale that can contain millions of spores.

The causative agent of EFB is *Melissoccocus plutonius*, also a Gram-positive bacterium that does not form spores (reviewed in Forsgren 2010). Like with AFB, bacteria infects young larvae that usually die when 4–5 days old.

Photo by Bernardo Niño, University of California Davis.

Figure 2: The appearance of a healthy honey bee brood. Larvae are pearly white and C-shaped like a grub, while the wax cappings protecting the pupae are convex and do not show any damage.

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The larvae will change color from pearly white (Figure 2) to yellow and eventually brown then grayish black, and they usually die with their bodies twisted upward (Figure 3). If the infection overwhelms the colony, it can give off a sour smell, which might not be as offensive as the AFB smell which is described as being sulfurous. Finally, unlike with AFB, the larval remains do not rope out.

While an experienced beekeeper is usually able to identify these two diseases in a colony, to confirm the infection one can use the available diagnostic tools. For diagnosis in the field, commercially available

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AFB and EFB diagnostic test kits can be utilized. The infection can be confirmed by sending samples to a diagnostic laboratory. Currently, one such laboratory is the USDA-ARS Bee Lab in Beltsville, Maryland which provides diagnostic services for beekeepers and regulatory officials free of charge (https://tinyurl.com/jrbbjpb). Since veterinarians now must diagnose diseases before providing a VFD or prescription, I would recommend that interested veterinarians establish a relationship with their County Agricultural Commissioner's office as the existing apiary inspectors might be able to provide additional field assistance.

The three antibiotics that are currently registered for use in honey bees are oxytetracycline, tylosin, and lincomycin. As of January 1, 2017, these medications require either a VFD for those applied in feed, or a prescription for those applied in water. As of December 1, 2016, oxytetracycline was the only one approved for use in medicated feed. A word of caution—AFB has been shown to have developed a resistance to this antibiotic but samples can be sent to the USDA Beltsville laboratory to determine if specific colonies harbor bacteria susceptible to oxytetracycline. To provide either a VFD or a prescription, the beekeeper and veterinarian need to establish an appropriate veterinary-client-patient-relationship as regulated by the state of California. Note that a veterinarian can approve an extra label use as long as it is in compliance with extra label drug use regulations.

Photo by Rob Snyder, Bee Informed Partnership: Northern California Tech-Transfer Team.

Figure 3: Larvae infected with the causative agent of European Foulbrood are characteristically yellow and die in a twisted position with the anterior portion of the body pointing upwards in the cell.

Antibiotics do not kill AFB spores so some states mandate the abatement of AFB-infected colonies. California is one of those states and beekeepers are required to burn AFB-infected bees and certain equipment such as frames, while the hive boxes, tops, and bottoms must be sanitized by scorching. Detailed information can be found here https://tinyurl.com/z8ga9bf. It is worth noting that, in order to reduce the possibility of cross infection between apiaries and/or colonies, those involved in colony inspections should practice proper sanitation practices after visiting each apiary.

While this directive has caused a bit of a stir among beekeepers, it is certainly a welcome step in minimizing the overuse or improper use of antibiotics in food-producing animals. There will likely be an adjustment period for all involved, but in the meantime please feel free to contact the extension apiculture program at the University of California in Davis (elnino@ucdavis.edu) and we will do our best to be of service. ■

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Dr. Niño received her Ph.D. in entomology from Penn State University in 2012. She is an assistant specialist in apiculture with the cooperative extension located in the Department of Entomology and Nematology at UC Davis. Through various extension activities, Dr. Niño works to support beekeepers and the beekeeping industry. Dr. Niño's research interests encompass basic and applied approaches to understanding and improving honey bee health and particularly queen health.

References: Forsgren, E. (2010). European foulbrood in honey bees. Journal of invertebrate pathology, 103, S5-S9 | Frankie, G. et. al. (2014). California Bees and Blooms: A Guide for Gardeners and Naturalists. Berkeley: The regents of the University of California. Heyday Press | Genersch, E. (2010). American Foulbrood in honeybees and its causative agent, Paenibacillus larvae. Journal of invertebrate pathology, 103, S10-S19.

Additional Useful Resources: American and European Foulbrood (2014). Bee Health. eXtension.org http://articles.extension.org/pages/71150/american-and-european-foulbrood#.U_-WlXbp8_c Accessed on February 13, 2017