Honey bee hearts

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At a recent family dinner, we discussed the plight of honey bees. Everywhere bees are disappearing, and a new syndrome has been coined: “Colony collapse disorder.” The etiology is unknown, though proposed causes include loss of habitat, parasites, and pesticides.

The conversation ended with agreement that the cause must be found and rectified. Knowing that I am a cardiologist, one young family member chirped in, “Maybe the honeybees are having heart attacks!” There was giggling and laughter. Kids love to be silly and say nonsensical things. “Honey bee poo!” What a ridiculous statement. Obviously, bees aren’t sedentary, don’t overeat, and are not known to smoke or develop diabetes. Do they even have hearts? Surely, they can’t have heart attacks!

But how in the world would I know? Nothing in my training or clinical practice concerned honeybees. I know about Kounis syndrome: acute myocardial infarction brought on by bee stings,¹ but this is something altogether different. If bees have hearts, and if they can have heart attacks, is it possible that humans are a cause? Could colony collapse syndrome be Kounis syndrome in reverse? Despite two decades spent caring for humans, I am no expert in the diseases of nonhuman animals, either large or small. So, what is true? And what is poo?

I decided to search for an answer using taxonomy. Over the last 300 years, scientists have systematically categorized all living creatures, placing them into categories using a method developed by a Swedish scientist named Carl Linnaeus in the 1700s. His method created a tree of life with branches that connect all living things. At first, his tree had only two branches: plant kingdom and animal kingdom. With the advent of microscopy, more forms of life have been discovered and new branches added, including eukaryotes, prokaryotes, protists, fungi, and archaeobacteria. The branch

of animals divides into phylum, class, order, family, genus, and species. It is a remarkable system that predates genetics or the discovery of DNA. All organisms within a classification have certain shared characteristics. All plants, for example, are autotrophs capable of making their own food. The animal kingdom contains heterotrophs, organisms that rely on intake of nutrition from external sources. In general, animals eat other organisms, often plants or plant products. Like us, honeybees are animals.

When we think of bees, if we think of them at all, we inevitably visualize honeybees. How many people know that honeybees are domesticated animals, similar to cows or horses? They exist only through the efforts of human intervention. Honey bees resemble wild bees in the same way that my miniature poodle resembles a wolf, which is to say just a little. The domestication of bees occurred during the agricultural revolution of the past 10,000 years, and pollination by bees remains crucial to food production today. But most bees remain wild and live solitary lives without hives or queens. They come in a much greater variety of shapes, colors, and sizes and make up an estimated 20,000 different species. Unfortunately, they, like honeybees, are suffering colony collapse syndrome.

Almost all animals have a cardiovascular system. There are a few exceptions such as jellyfish. These aren’t fish (and aren’t made of jelly) and have no circulatory system. They are composed of thin sheets of cells that rely on diffusion of oxygen and nutrients from the surrounding water to supply metabolic needs and carry away waste. Few animals can be structured in this fashion.

Honey bees are phylum Euarthropoda and class Insecta. Within the insects, they are classified as order Hymenoptera, family Apidae, genus *Apis* Linnaeus, and species *Apis mellifera* Linnaeus. Yes, Carl Linnaeus categorized the honey bee himself in 1758. All members of the class Arthropodia,

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including insects, have what is termed an “open” cardiovascular system. Their bodies are filled with an extracellular fluid termed *hemolymph* that lacks hemoglobin or red blood cells. Hemolymph is not confined within vessels but circulates freely in the extracellular space. There is a heart or, rather, hearts that form a tube running from the abdomen to the head. The hearts work in tandem and are made up of muscle cells that pump rhythmically, creating circulation of hemolymph from the abdomen to the head and back again. This may seem strange, but a similar design lives in our own lymphatic system. Modern imaging techniques have allowed visualization of circulation within living insects, revealing a dynamic process with regular “heart rates” and measurable hemolymph flow comparable to that seen in higher animals. Hemolymph circulation must be important; otherwise, why would insects expend the energy and effort? Which led me to a thought. Could cessation of hemolymph flow be the honey bee version of a heart attack?

The simplest, closed cardiovascular systems are found in worms, including earthworms. These simple creatures have most of the organs for which modern physicians have developed subspecialties, making them popular dissection subjects for high school biology classes. There are two major vessels: a ventral vessel that moves blood from front to back and a dorsal vessel that moves blood from back to front. The earthworm heart is not a single pump but a series of five pumps in parallel. Earthworm blood, unlike honey bee hemolymph, contains hemoglobin. However, the hemoglobin is dissolved in solution rather than contained within red blood cells. Step on an earthworm and red “blood” seeps out.

Hearts that are similar to ours, having chambers and valves, are first seen in vertebrate animals (those with “back bones,” phylum Chordata). Lamprey, a primitive vertebrate, have simple hearts consisting of three chambers. They also have blood that packs hemoglobin into red blood cells. These are huge multinucleated affairs that contain sevenfold more hemoglobin than their smaller human cousins.

One closest “relative” in taxonomy is the chimpanzee: Chordata, Mammalia, Primates, Hominidae, *Pan*, *Pan troglodytes*. We share 98.8% of our genetic makeup and are thought to have diverged from a common (yet unknown) ancestor about 6 to 7 million years ago. Few know that the first human cardiac transplant was performed not by Christiaan Bernard in South Africa but by Dr. James Hardy at the University of Mississippi Medical Center on January 23, 1964.² The recipient was a 60-year-old man, but the donor was a chimpanzee selected for its large size (45 kg). Chimpanzee hearts are so similar to our own that they can serve as replacements. Severe immune rejection of the transplanted organ and the rapid demise of the patient extinguished enthusiasm for xenotransplantation for several decades. More recently, “Baby Fae” received a baboon heart at Loma Linda Medical Center in 1984 and survived 21 days after surgery. Interest in xenotransplantation has been revived

with the advent of gene editing and its potential to defeat rejection.

Human beings are Chordata, Mammalia, Primates, Hominidae, *Homo* Linnaeus, *Homo sapiens* Linnaeus. Yes, our old friend Carl Linnaeus classified *Homo sapiens* as being within the family Hominidae along with our cousins, chimpanzees. Unlike *Pan troglodytes*, however, the species *Homo sapiens* has the intelligence and planning needed to develop chemicals and pesticides. A recent pesticide family, the neonicotinoids, has been developed by modifying the chemical structure of nicotine. These compounds are water soluble and can be absorbed into plants, giving them tobacco plant-like resistance to insects. Unfortunately, these compounds can find their way into the nectar gathered by bees. Several observers have noted that the development and use of neonicotinoids has paralleled colony collapse disorder.

We are familiar with nicotine as a product of tobacco plants and the cigarettes and cigars made from their leaves but rarely ponder why these plants make nicotine in the first place. It turns out that nicotine, like manmade neonicotinoids, binds to acetylcholine receptors. In mammals, nicotinic acetylcholine receptors are located in cells of both the central nervous system and peripheral nervous system. These receptors are activated by acetylcholine but also bind and are activated by nicotine. In humans, the binding is relatively weak. In insects, nicotine binds strongly. Nicotine-mediated activation of receptors in humans increases neural transmission, but in insects it blocks receptors, resulting in loss of function. Acetylcholinesterase, the enzyme that degrades the natural neurotransmitter acetylcholine, cannot break down nicotine or neonicotinoids, preventing their clearance.³

Insect “hearts” are dependent on neural networks. Both insect neuron activation and myocyte contraction are dependent on acetylcholine receptors. If poisoned by neonicotinoids, honey bee hearts could slow or even stop. Loss of hemolymph circulation may play a role in the death of bees exposed to these agents.

Who knew? Other than that curious child at my dinner table.

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