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Birds, Bees, and Butterflies

"Did you know that monarch butterflies use drugs?" I ask.

It is October 2022, and I am sitting at an outdoor table at the St. Marks National Wildlife Refuge located on the southern side of Florida's Big Bend, right on the water of the Gulf of Mexico. Behind me is a white lighthouse. To my left I can look out over Goose Creek Bay, where I saw dolphins earlier. In front of me is a lagoon with alligators. Standing around the table are twenty people, varying in age from about three years old to seventy years old. We are at the St. Marks Monarch Butterfly Festival, held every year on the fourth Saturday of October. It is one of my favorite weekends of the year. For more than a decade, my students and I have made the six-hour drive from Emory University in Atlanta, where I am a professor, to attend the celebration of monarch butterflies. We come here to tell people about monarchs, and the research we do on them.

"Just like us, monarchs get germs," I say to a little girl wearing a tutu and dress-up butterfly wings. Holding the butterfly for her to see, I explain that these germs make the monarchs very sick. "They cannot go to the doctor like you or me, but luckily they can find medicines in the plants they eat."

Most people who know about monarchs are aware of their amazing migration.[1] As temperatures drop and the days get shorter, monarch butterflies from the United States and Canada embark on an amazing autumn journey. Flying as many as forty-five hundred kilometers, they travel to oyamel fir forests in the Transvere Neovolcanic Belt in Central Mexico. From late October to late November, and coinciding with the Mexican celebration of Day of the Dead, hundreds of millions of monarchs make their way into the high-altitude forests. They form clusters on the trees. Although each monarch weighs about as little as a medium-sized paperclip, some branches break under the weight of the thousands of monarchs that huddle together. Monarchs overwinter at these sites until February and March, when they mate and fly back north. On their way south, many monarchs follow the coast of the Gulf of Mexico to reach their overwintering sites. And lots of these monarchs stop in the refuge at St. Marks. On a good day, we see thousands flying through the refuge, feasting on the nectar of the abundant salt bushes and other flowering plants.

Amazing as monarch migration is, though, it is not the reason I started studying monarchs. I like to tell people that I study monarchs because they get sick. This takes many people by surprise. Accustomed as we are to becoming sick ourselves, and taking our pets to the vet, few of us think of wild animals becoming ill. But they do. Just as humans encounter a whole collection of disease-causing viruses, bacteria, worms, and protozoans throughout our lifetime, so do birds, bees, and butterflies. The most common disease in monarchs is caused by a one-celled parasite called *Ophryocystis elektroscirrha*.[2] Because its name is difficult to pronounce, many people refer to the parasite simply as "OE." This parasite is somewhat related to the parasites that cause malaria in humans, and it is no joke for monarchs. The parasite forms millions of spores on the skin of the monarch and pokes little holes in the monarch body. If the parasite does not kill the monarch, it causes dehydration and weight loss. Infected monarchs cannot fly well. So, instead of completing their journey to the overwintering sites in Mexico, they die along the way.[3]

Sitting at the table in St. Marks, I show people how we figure out whether monarchs are infected. My students and I like to call it the monarch health check. Like nurses and doctors, we wear examination gloves as we stick a clear plastic sticker to the abdomen of the butterfly (it does not hurt them), then place the sticker on a paper index card. We use a microscope and check for little black parasite spores. I show the festival visitors the parasites when we find them.

Then I tell them something truly remarkable. *Monarch butterflies are expert doctors*. Just as humans use drugs to treat parasitic infections, so do monarchs. As it turns out, I tell my audience, when faced by this horrendous OE parasite, monarchs are not helpless. They can seek out medicinal plants that reduce infection and relieve disease symptoms.

POISONOUS PLANTS

I started studying the parasites of monarchs in 2005 when I moved to the United States for a research position. While I was initially interested in studying the basic biology of these parasites, I quickly became interested in the interactions between the parasites, the monarchs, and the caterpillars' sole food source, milkweeds. Like many other butterflies, monarchs are specialist herbivores, meaning they eat only specific plants as caterpillars. For monarchs, their specialized diet consists only of milkweeds. There are actually many kinds of milkweed, in many forms and sizes, but most are in the same genus, *Asclepias*. When we rip off their leaves, they ooze white latex that looks like milk—hence the name.

In addition to producing latex, milkweeds produce a class of chemicals known as cardenolides. These steroid chemicals are toxic to most animals, and the plants use them to deter herbivores.[4] Monarchs can tolerate them, though. What's more, the caterpillars, while feeding on the plants, store the toxic chemicals in their own tissues.[5] This is what makes monarchs poisonous to their predators. Monarchs have bright orange wings, lined with black lines and white spots, which they use to tell birds and other predators they taste bad.[6]

When I started studying monarchs, it was a well-known fact that monarchs use cardenolides to protect themselves against predators. But with my interest in parasites, a question soon started forming in my brain. I knew of studies that had shown that other types of toxic chemicals, found in other plants, can kill disease-causing viruses of insects.[7] And that made my colleagues and me wonder: Could the cardenolides found in milkweeds be toxic to OE parasites? Were the monarchs using plants not just as food, but as medicine?

To answer that question, I set up an experiment with two groups of monarch caterpillars—one group fed on only tropical milkweed and the other fed on only swamp milkweed. All caterpillars (a total of 240) were exposed to OE by feeding them milkweed with parasite spores. I knew from published studies that tropical milkweed (*Asclepias curassavica*) has more cardenolides than swamp milkweed (*Asclepias incarnata*). After the caterpillars became butterflies, we tested how many of the monarchs had become infected and how sick they were. If cardenolides could protect against parasites, we would expect the monarchs who had fed on tropical milkweed as caterpillars to experience less illness. The result was exciting: in the group of monarchs that had fed on tropical milkweed as caterpillars, 20 percent fewer monarchs became infected than those that had fed on swamp milkweed. And the tropical milkweed–fed caterpillars that did become infected had less than half the number of parasites and were a lot less sick, living up to twice as long.[8] All in all, our experiment suggested that highly toxic milkweed not only wards off predators but also acts as a potent antiparasitic drug.

The next question was as logical as it was unlikely. Was it possible that monarchs could intentionally take advantage of these medicinal milkweeds? Would sick monarchs be able to specifically use highly toxic milkweeds as a form of medicine? In 2008, I had taken a position as assistant professor at Emory University. There, my team and I carried out a series of experiments in which we offered infected and uninfected female butterflies medicinal tropical milkweed and nonmedicinal swamp milkweed in big flight cages. We counted the numbers of eggs that these females laid on each species. What we found is that infected butterflies laid way more eggs on medicinal plants than on nonmedicinal plants.[9] Uninfected butterflies did not. In other words: when monarch mothers are infected, they prefer to lay their eggs on medicinal milkweed.

That infected monarchs prefer to lay their eggs on medicinal plants is remarkable. It is even more remarkable when we think about who they are actually protecting. Diseased monarchs do not benefit from the medicinal plants themselves. They are already infected and have suffered the consequences. They cannot cure themselves. What they also cannot do is avoid the spread of parasites to their offspring. The parasites form

FIGURE 1.1. A female monarch butterfly lays eggs on a medicinal milkweed, which will reduce infection and disease symptoms in her offspring caterpillars. Photo by Jaap de Roode.

millions of spores on the butterflies' abdomens, and every time the butterfly lays an egg on a milkweed plant, some of these will inevitably get stuck to her eggs and the milkweed leaves.[10] But what the mother butterfly *can* do is choose to lay her eggs on medicinal plants. When her babies hatch from their eggs, they will ingest the parasites. But they will also ingest the medicinal milkweed. And this reduces the chance that the parasites take hold. Should the caterpillar still become infected, the plant reduces the growth of the parasites, and thereby relieves disease symptoms. Thus, rather than medicating herself, a monarch mother medicates her offspring—and she does so even before those offspring are born. A wonderful case of "mother knows best."

TEENY-TINY BRAINS

As I was studying monarch medication, I realized that many other animals use drugs as protection against disease. (I fully realize that humans are animals. But for the sake of simplicity, I will use the term "animals" specifically for nonhuman animals throughout this book). In the 1980s, primatologists had discovered that chimpanzees can use the toxins and hairy leaves of plants to treat intestinal worm infections. I found other studies that showed that goats and sheep are their own medical doctors too. And while many scientists traditionally believed that animals needed big brains to be able to medicate themselves—a bias mostly driven by the fact that chimpanzees are our closest living relatives—this idea did not jibe with the data.

I learned that woolly bear caterpillars and wood ants can use medicine too. Thus, animals with brains smaller than a pinhead can be just as good at medicating as those with brains like our own. What this suggested to me is that animal medication is common across the animal kingdom. I became fascinated with this idea, and that fascination eventually grew into this book. In the coming chapters, we'll explore all of these examples, and more.

Over the last four decades, scientists have discovered that animals do in fact seem to seek out medication (though, as we'll see, defining exactly what this means is a tricky task): animals of all shapes and sizes use a vast array of plants, fungi, toxic animals, chemicals, and other natural products to fight infections and alleviate disease. And they can do so in four different ways. First, animals can use "prophylaxis," which is when healthy animals choose to eat foods and antiparasitic compounds *before* they get sick to stay healthy and prevent disease. Japanese monkeys that live in areas with more parasites eat more antiparasitic plants than monkeys that live in areas with fewer parasites.[11] In Ethiopia, baboons that are at greater risk of schistosome infection increase their worm resistance by eating more toxic berries.[12] Second, animals may use "therapeutic medication." This is the use of medicinal compounds when the animal is already infected: chimpanzees suck the toxic juice out of bitter plants when sick with parasitic worms, and woolly bear caterpillars use toxic alkaloids to kill parasitic fly maggots. A third form of medication is "body anointing," where animals as diverse as lemurs, cats, and coatis rub antiparasitic substances into their fur to deter parasites such as mites, lice, and mosquitoes. Finally, animals may use "fumigation," by which they add antiparasitic substances to their living or sleeping quarters. Fumigation is used widely by birds, who line their nests with aromatic plants that kill mites, ticks, and lice. It is also used by ants and bees, which fill their nests with antimicrobial tree secretions to prevent disease.

Some scientists have described all these different behaviors with the word "zoopharmacognosy."[13] The term derives from the root words “zoo” (animal), “pharma” (drug), and “gnosy” (knowing). Other scientists prefer to describe the different behaviors as “animal self-medication.” I do not particularly like either term. To me, the word “zoopharmacognosy” suggests that animals know that they are medicating themselves (they may not: the behaviors they display could be fully innate, as we will see in chapter 8). And the term “animal self-medication” suggests that animals exclusively medicate themselves (they do not—as we already saw, monarch butterflies medicate their offspring). I believe a more inclusive term to describe all these different behaviors is “animal medication,” and that is what I will use throughout this book.

Demonstrating that animals use medication is difficult. I will discuss this in the next few chapters, highlighting the use of observational studies and experiments. For now, I want to make two important points. First, I will spend most of this book discussing behaviors that allow animals to fight against infection—that is, dealing with parasites and pathogens that make them sick. The reason for this focus is not only because parasites and pathogens are extremely important for animal evolution but also because most of the well-described examples of animal medication involve defenses against infections. That said, infectious diseases are not the only reason animals use medication. As this research continues, we are learning that animals may use medicine to treat wounds or relieve sore joints.[14] Orangutans, for example, mix specific plants with saliva and rub the mixture either into wounds,[15] or onto different body parts, which reduces inflammation.[16] Scientists have also suggested that pregnant animals may use particular plants to induce labor. Pregnant and lactating sifaka females increase consumption of tannin-rich plants, which is associated with increased body weight and stimulation of milk secretion.[17]

There are also reports of animals using drugs for recreational use. The concept of drunken monkeys is quite popular indeed. And reports of drunken elephants ransacking buildings can count on a wide readership. After a herd of 50 elephants raided a shop that sold a fermented drink in 2012, local police spokesman Asish Samanat commented in an online news outlet: "They were like any other drunk—aggressive and unreasonable but much, much bigger."[18] (Although it is entertaining to assume that animals consume alcohol to get drunk, a recent analysis suggests that primates actually eat fermented fruits because the fermentation process breaks down toxic chemicals that would otherwise make the fruits inedible, and because it provides a food source during times when fresh fruit is unavailable.[19]) Wound treatments, pregnancy care, and alcohol use fall outside the scope of this book, but if you are interested in learning more about these fascinating behaviors, I recommend the excellent book *Wild Health* by Cindy Engel.[20]

The second point I want to make is that it is not always obvious that a specific animal behavior is a form of medication. As I will discuss in the next few chapters, the most important criterion for animal medication is that the behavior helps the animal: either by reducing or avoiding infection, or by alleviating disease. But infection can also change behaviors in ways that are not beneficial to animals. On the contrary: it turns out that parasites and pathogens are masters at manipulating animal behaviors for their own benefit.[21] This means that when we see an infected animal change its behavior, we cannot simply assume it is medicating. Instead, it may be the parasites and pathogens doing the talking.

That animals can use medicine is now supported by many studies, and I chose to write this book to share the many fascinating stories of how animals use medication to protect themselves against parasites and pathogens. I also wanted to introduce the people who have provided us with these stories, showcasing how scientists from many different backgrounds, and in different continents, have been driven by an innate interest in understanding the natural world. As we will see, those scientists share a common belief: the study of animals is not only interesting in itself but can also teach us about how we can tackle the many parasites and pathogens that continue to inflict death and suffering on humans, domesticated animals, and pets.

The goal of this book is therefore twofold. First, I want to make the case that animals are highly evolved experts at medicine. They may not speak Latin, be trained in bedside manners, or write prescriptions, but they have evolved a plethora of ways to keep infectious diseases at bay through rather sophisticated medicine.

The second goal of this book is to show that we can benefit from studying animal doctors. Yes, most researchers studying animal medication are driven by a basic curiosity to understand the natural world. But as we will see, we can use insights into the medication behaviors of goats and sheep to increase animal health and reduce antibiotic resistance at farms and in the livestock industry. We can apply the antiparasitic behaviors of bees to improve beekeeping. And work is underway to develop bug repellents from compounds discovered by cats. Many scientists studying animal medication believe that their research may ultimately lead to the discovery of drugs that we can use to treat our own diseases.

Some would argue that our modern chemistry and technology equip us well enough to come up with new drugs from scratch.[22] But consider this: over the last forty years, more than half of the new antibacterial drugs and 45 percent of the antiparasitic drugs that hit the market for human use were derived from natural products. These include compounds from plants, bacteria, and fungi.[23] With the ongoing threat of infectious disease, and the ever-growing number of pathogens that evolve resistance to the drugs we rely on, it is more important than ever to study animal medication—and to apply the medical knowledge of animals to the health of humans and domesticated animals.

We'll explore all these ideas in future chapters. But before we get to those exciting applications, let's start by asking how a sick chimpanzee sparked the birth of a new scientific field.

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