Self-Medication in Animals

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Science **340**, 150 (2013);
DOI: 10.1126/science.1235824

ECOLOGY

Self-Medication in Animals

Animal self-medication against parasites is more widespread than previously thought, with profound implications for host-parasite biology.

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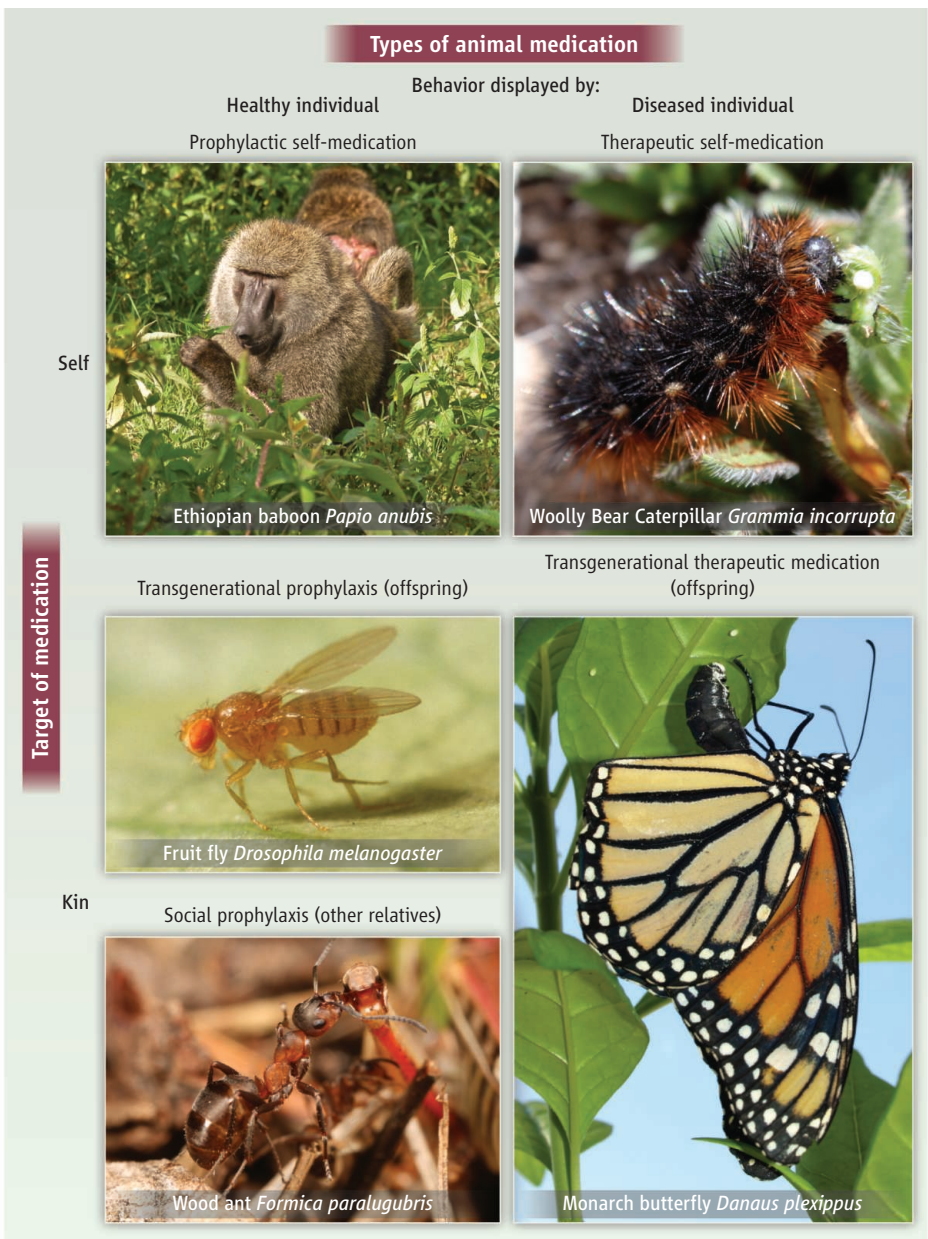
The concept of antiparasite self-medication in animals typically evokes images of chimpanzees seeking out medicinal herbs to treat their diseases (*1*, *2*). These images stem partly from the belief that animals can medicate themselves only when they have high cognitive abilities that allow them to observe, learn, and make conscious decisions (*3*). However, any concept of self-medication based solely on learning is inadequate. Many animals can use medication through innate rather than learned responses. The growing list of animal pharmacists includes moths (*4*), ants (*5*), and fruit flies (*6*). The fact that these animals self-medicate has profound implications for the ecology and evolution of animal hosts and their parasites.

Janzen (*2*) was the first to describe cases in which diseased vertebrates appeared to select secondary plant compounds with antiparasitic activity. Consequently, self-medication has often been defined as the antiparasitic use of secondary plant chemicals or other non-nutritive substances by herbivores (*1*). However, boundaries between nutrients, medicines, and toxins are permeable and are often defined only by the ingested dose of a chemical (*7*). Thus, whereas traditional examples of animal medication involve animals eating specific plants only when diseased (*1*), recent examples include animals increasing the ingestion of particular chemicals that are already in their diets (*4*).

Animals may use chemicals to relieve symptoms that are not caused by parasitic diseases, but we restrict our discussion to self-medication as a defense against parasites. Such defenses can come in two general forms (see the figure). In therapeutic medication, diseased individuals alter their behavior to medicate in response to parasite infection (*4*). In contrast, prophylaxis is used by infected and uninfected individuals alike to prevent parasite infection, often in response to high parasite risk (*5*).

Therapeutic and prophylactic medication can be further divided depending on the target of medication (see the figure). Much work has focused on cases in which animals medicate themselves, including baboons and woolly bear caterpillars (*1*, *4*, *6*), but animals may medicate their offspring or other genetic kin instead. Fruit flies have been shown to preferentially lay their eggs in high-ethanol food when they detect the presence of parasitoid wasps (*8*); this reduces infection risk in their offspring (transgenerational prophylaxis). Wood ants incorporate antimicrobial resin from conifer trees into their nests, preventing microbial growth in the colony (*5*) (social prophylaxis). Parasite-infected monarch butterflies can protect their offspring against high lev-



Types of animal medication.

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Published by AAAS

els of parasite growth and virulence by laying their eggs on antiparasitic milkweed (*9*) (transgenerational therapeutic medication). These studies show that we should deemphasize the "self" in self-medication and base medication studies on an inclusive fitness framework.

There are many examples in which a behavior is strongly implicated as medication, but in which a fitness advantage for the actor remains to be demonstrated. Primates commonly ingest plant materials with antiparasitic properties but with little or no nutritional value. For example, they chew the bitter pith of *Vernonia amygdalina* and swallow rough plant leaves whole (*1*). Chewing bitter pith may release antiparasitic compounds, whereas swallowing rough leaves whole is apparently a means of physically expelling intestinal parasites (*1*). However, it remains to be shown whether parasite infection triggers the behavior and whether the behavior increases host fitness. Similarly, a recent study has suggested that house sparrows and finches add high-nicotine cigarette butts to their nests to reduce mite infestations (*10*), but it is unclear whether the birds gain higher fitness from the behavior.

To conclude definitively that a behavior is an adaptive form of therapeutic medication, several conditions must be met. First, the behavior involves the ingestion or external application of a third species or chemical compound. Second, the behavior must be initiated by parasite infection. This sounds easier to establish than it is. For example, it is hard to determine whether a behavior seen in a particular animal in a field study is a result of parasite infection or whether something else caused that individual both to be infected and to display the behavior. Manipulative experiments, in which some individuals are infected and others are left as uninfected controls, are the best way to evaluate this condition. Third, the behavior increases the fitness of the infected individual or its genetic kin. Fourth, the behavior is costly to uninfected individuals; if it were not, all individuals would display it (*4*). Fifth, the behavior is relevant in the natural environment of the host; showing the existence of medication with artificial diets alone does not demonstrate its relevance in nature.

The conditions are similar for prophylaxis, except that prophylaxis is displayed in response to parasite risk rather than infection. It may also be difficult to demonstrate costs if prophylaxis has evolved into a fixed phenotype over time.

We have omitted an oft-cited condition for self-medication: that the behavior must reduce parasite infection or fitness (*10*). The reason for our omission is that medication behavior may enhance host fitness by increasing tolerance of infection (allowing the host to maintain fitness despite being infected) without reducing parasite fitness (*11*).

Many published cases do not yet satisfy all these conditions, but animal medication is clearly much more widespread than originally thought. It is therefore important to understand how animal medication affects the ecology and evolution of host-parasite interactions. We argue that there are at least four major consequences of animal medication.

First, when animal medication reduces parasite fitness, we expect to observe effects on parasite transmission or virulence. Neither consequence has received much attention yet, but two studies indicate that medication can indeed influence the interactions between hosts and their parasites. For example, when gypsy moth caterpillars consume foliage high in phenolics, it reduces transmission of a polyhedrosis virus and facilitates moth outbreaks (*12*). There is also preliminary evidence that medication affects virulence evolution: increasing parasite virulence is predicted from models of medication behavior by monarch butterflies using toxic milkweed (*13*).

Second, animal medication should affect the evolution of animal immune systems. Immune responses are costly, suggesting that animals should not use or evolve immunity when they do not need it. Animal medication provides an alternative to cellular and humoral immune responses and may thus result in a reduction or loss of such immune responses. This hypothesis has not yet been tested formally, but there is suggestive evidence. Perhaps most strikingly, honeybees use a series of behavioral immune mechanisms, including the incorporation of antimicrobial resin into their nests (*14*). Analysis of their genome suggests that honeybees lack many of the cellular and humoral immune genes of other insects, raising the possibility that their use of medicine has been partly responsible—or has compensated—for a loss of other immune mechanisms (*14*).

Third, host-parasite interactions are often used to explore patterns of local adaptation, yet surprisingly few studies provide evidence for adaptation of parasites to their local hosts or vice versa (*15*). Most of these studies are based on experiments in which hosts and parasites from multiple populations are exposed to each other in sympatric and allopatric combinations. By not allowing hosts to behave naturally, such studies preclude animals from medicating themselves or their kin. Thus, if animals have locally adapted to their parasites through medication behaviors, studies must be designed such that animals can display their naturally evolved behaviors. It is our expectation that when this is done, more studies will find that hosts have locally adapted their behavior to their parasites.

Finally, the study of animal medication will have direct relevance for human food production and health. Disease problems in agricultural organisms can worsen when humans interfere with the ability of animals to medicate. For example, increases in parasitism and disease in honeybees can be linked to selection by beekeepers for reduced resin deposition by their bees (*14*). A re-introduction of such behavior in managed bees would likely have great benefits for disease management. In addition, as self-medicating animals, humans still derive many of their medicines from natural products, and plants remain the most promising source of future drugs. Studies of animal medication may lead the way in discovering new drugs to relieve human suffering.

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Acknowledgments: We thank M. Bushman, C. Gowler, Z. Lynch, K. Leon, M. Maudsley, and A. Pierce for discussion. J.C.d.R. and M.D.H. are funded by NSF grants DEB-1019746, DEB-1257160, and DEB-1256115, and T.L. is funded by Agence Nationale de la Recherche grant 11-PDOC-006-01.

10.1126/science.1235824