
Parasitic Stress and Self-Medication in Wild Animals

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I. INTRODUCTION

In the physical sciences, "stress" is defined as the force per unit area, or pressure, acting upon a solid body, resulting in the deformation (strain) of the solid. At low stresses the strain is said to be elastic, directly proportional to the stress and reversible; the solid returns to its original shape after the stress is removed. As the stress increases the elastic limit is reached, after which the strain is said to be plastic, increasing exponentially with increasing stress and non-reversible. Plastic deformation continues until the rupture strength is reached, at which point the material breaks.

The term stress was adopted by biologists to refer to factors that interfere with the maintenance of homeostasis, the effects of which range from the minor, temporary and easily reversible, to the complete breakdown of homeostatic mechanisms (Cannon, 1935). As applied to vertebrates, the term "stress" is generally used to denote stimuli that elicit a specific set of physiological responses, particularly the release of corticosteroids (Vander, 1981; Kopin, 1995; Mims *et al.*, 1995). However, these responses are not characteristic of all taxa, so this definition is not inclusive. Stresses can also be defined more broadly as aversive stimuli (McGrath, 1970; Selye, 1976), regarded as selective forces, and studied along with the adaptations that have evolved to reduce their negative effects (see Thornhill and Furlow, this volume). Under this view, stresses can take a myriad of forms, as indicated by the wide range of topics included in this volume.

Along with competition and predation, parasitism is one of the main sources of biotic stress facing all organisms. For the purposes of this discussion, parasites will be functionally defined as organisms that live in or on a heterospecific

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animal (the host), draw their nutrients primarily from the host, and have the potential to reduce its fitness. Therefore, this definition includes both endoparasites and ectoparasites, but excludes micropredators or animals that use their hosts solely for shelter. Second, both macroparasites (helminths, arthropods) and microparasites (viruses, bacteria, protozoa, fungi) are included. Finally, parasites need not be harmful all the time, or even most of the time. Parasites can often coexist with their hosts without causing any measurable deleterious effects, but parasites are also opportunistic, and can quickly increase in numbers and overwhelm a host weakened by other forms of stress, such as malnutrition or reproduction (Walzer and Genta, 1989).

To counteract actual or potential fitness losses due to parasitism, animals have evolved a variety of anatomical, physiological and behavioral adaptations, and parasites have developed an equally impressive array of countermeasures to bypass these defenses (Behnke and Barnard, 1990). In some cases parasites have even evolved ways to manipulate their hosts' behavior for their own interests (e.g., Bethel and Holmes, 1973, Brassard *et al.*, 1982; Maitland, 1994). The effects of parasites on host behavior include the manipulation of host behavior by parasites (reviewed by Moore and Gotelli, 1990), and host behavioral adaptations for protection against parasitism (reviewed by Hart, 1990; Møller *et al.*, 1993).

Recently, it has become recognized that animal diets may also be shaped by the need for protection from parasites. Foraging behavior evolves primarily to meet the need of a nutritionally adequate diet. However, just as foraging behavior can be affected by predators (e.g., Milinski and Heller, 1978; Krebs, 1980; Sih, 1980, Edwards; 1983, Abrahams and Dill, 1989; Lima and Dill, 1990), and competitors (e.g., Baker *et al.*, 1981; Milinski, 1982; Millikan *et al.*, 1985), some features of diet selection seem to have evolved to stave off, or reduce parasitism. These adaptations can include the avoidance of foods that are also potential sources of parasitic infection, the use of prophylactic substances, and the consumption of therapeutic substances (Phillips-Conroy, 1986; Lozano, 1991). Self-medication includes the latter two types of responses.

Although in this chapter I deal largely with self-medication in the context of feeding, it may also occur under other circumstances, including the use of plants with potentially antibacterial chemicals for nest material (Wimberger, 1984; Clark and Mason, 1985), and the topical application of antifungal and antibacterial compounds (Ehrlich *et al.*, 1986; Baker, 1996; Gompper and Hoylman, 1993). In this chapter I first incorporate self-medication into the broader phenomenon, namely, the effects of plant chemicals across several trophic levels, and categorize self-medicating behavior into two basic forms: prophylactic and therapeutic. In the body of the chapter I review in detail current evidence in the published literature

for the occurrence of self-medication in non-human vertebrates. Finally, I discuss behavioral mechanisms that may play a role in self-medication, and highlight potential implications for other areas of research.

II. SELF-MEDICATION

The effects of secondary plant metabolites are not always limited to the herbivores that consume them, but may also affect the herbivores' predators, parasites and parasitoids. For example, in several herbivorous insects susceptibility to pathogens differs depending on the plant upon which the hosts feed (e.g., Hare and Andreadis, 1983; Krischik *et al.*, 1988). Such interactions have long been studied in the general framework of chemical ecology, mostly in insects (reviewed by Duffey, 1980, Price *et al.*, 1980). Nonetheless, animals in other taxa are also able to ingest secondary plant metabolites and accumulate them in their tissues. These compounds can make prey unpalatable to predators (e.g., Brower, 1958; Rothschild, 1972; Hay *et al.*, 1990; Pennings, 1994; Daly *et al.*, 1994), or less susceptible to parasitoids (e.g., Campbell and Duffey, 1979). Sequestered compounds, specifically carotenoids, can also play a role in sexual selection by altering the showiness of secondary sexual ornaments in males (e.g.; Kodric-Brown, 1989; Zuk, 1992; Milinski and Bakker, 1990; Hill, 1994), although it is unknown whether these traits are important in sexual selection because they indicate foraging ability or immunocompetence (Endler, 1980; Lozano, 1994). It is therefore clear that plant chemicals can have effects across several trophic levels. The use of secondary plant metabolites by vertebrates for the purpose of self-medication can be viewed as a special case of this broader phenomenon.

Janzen (1978) was probably responsible for bringing to the forefront of western scientific inquiry the idea of self-medication in non-humans. He compiled anecdotal accounts of unusual feeding habits by several species of mammals. For example, just before starting long trips, Indian elephants (*Elephas maximus*) reportedly feed on *Entada schefferi* (Leguminosae). Indian wild boars (*Sus scrofa*) consume the roots of *Boerhavia diffusa* (Nyctaginaceae), a plant used in traditional medicine as an anthelmintic. Sumatran rhinoceroses (*Didermocerus sumatrensis*) have been observed eating copious quantities of the tannin-laden bark of mangroves (*Ceriops candoleana*, Rhizophoraceae). Janzen pointed out that energy requirements and chemical avoidance were probably not adequate to explain these observations, and raised the possibility that animals use plant secondary metabolites as stimulants, anthelmintics, laxatives, antibiotics, or as antidotes for previously consumed toxins.

Despite this apparent taxonomic and behavioral diversity, self-medication can take only two functionally distinct forms, preventative (prophylactic) and therapeutic (Phillips-Conroy, 1986; Lozano, 1991). The two processes yield different predictions and require distinct behavioral mechanisms. By viewing self-medication under a more general framework, these behaviors need not be studied as a series of isolated cases, but rather can be considered in terms of common elements.

For example, the consumption of food items for preventative purposes would be related to the risk of parasitism, but not necessarily to the presence of parasites. The biological effects of these medicines may be aimed solely at the infectious stage of the parasite, and could have no effect at all on established parasites. Furthermore, the consumption of medicinal substances may not vary substantially among individuals within a population, but could differ considerably between populations. Lastly, if the risk of parasitism is predictable, seasonally for example, dietary shifts may be largely genetically determined, and not depend on individual or social learning. This also means that the consumption of prophylactic food items will probably be difficult to demonstrate conclusively, even for a single parasite-host-medicine system, because the consumption of these food items would likely be integrated with the regular diet.

On the other hand, in cases of therapeutic self-medication, only sick individuals would be expected to consume medicinal substances. These food items would not be expected to be in the animal's regular diet, and would only be consumed upon infection. Therapeutic medications would probably be more potent than preventative ones, and consequently would carry a greater risk of negative side effects. Medicinal substances could be aimed at the infection, in which case their biological effect would be directed at parasites already established within the host. Alternatively, the purpose of medicinal substances could be to alleviate discomfort, similar to the use of medicines for the common cold by humans, and have no effect at all on the parasites. In either situation, the ability to self-diagnose, prescribe, seek, and consume the appropriate medicine requires a fairly complex mechanism of individual and/or social learning.

III. PROPHYLACTIC SELF-MEDICATION

Studies have not always made clear the distinction between preventative and curative self-medication. As previously indicated, the difference is that therapeutic self-medication is a specific response to a particular situation; that is, the deliberate consumption of medicinal substances by ill individuals. In this section I discuss instances in which secondary plant metabolites seem

to affect parasites or disease, but, so far, there is no evidence suggesting intentionality. The classification of the following behaviors as preventative self-medication is therefore not definitive, as further work may show that these behaviors are also examples of therapeutic self-medication.

A. GEOPHAGY IN PRIMATES

Geophagy, the deliberate consumption of soil, dirt, or rock, has been observed in several herbivorous and omnivorous mammals (reviewed by Kreulen, 1985). Geophagy may be used to control gut pH (Oates, 1978; Davies and Baillie, 1988), to meet nutritional requirements of trace minerals (Davies and Baillie, 1988; Johns and Duquette, 1991), to satisfy a specific hunger for sodium (Mahaney *et al.*, 1990), and/or to detoxify secondary plant metabolites (Johns and Duquette, 1991). Recently, it has also been suggested that some primates may use geophagy to combat intestinal problems, particularly diarrhea (Mahaney *et al.*, 1995a,b).

Geophagy has been studied in the context of self-medication in Japanese macaques (*Macaca fuscata*) (Mahaney *et al.*, 1993), rhesus macaques (*Macaca mulatta*) (Mahaney *et al.*, 1995a), mountain gorillas (*Gorilla gorilla*) (Mahaney, 1993; Mahaney *et al.*, 1995b), and chimpanzees (*Pan troglodytes*) (Mahaney *et al.*, 1996, 1997). Analyses of the soils consumed by these four species have detected at least one of three mineralogically similar clays: halloysite, metahalloysite, and kaolinite, the last of which is the principal ingredient of the commercial antidiarrheal KaopectateTM (Vermeer and Ferrell, 1985). So far, support for the idea of geophagy as self-medication is limited to these mineralogical analyses. There have been no studies relating geophagy to the incidence or risk of diarrhea, nor have there been studies on the physiological effects of these clays in nonhumans.

B. STIMULANT USE IN BABOONS

Hamilton *et al.* (1978) classified food items consumed by chacma baboons (*Papio ursinus*), into four categories: (1) animals, (2) fruits and seeds, (3) leaves, and (4) "euphorics". The fourth group consisted of plants that were widely available and consumed consistently, but only in minute quantities. Furthermore, these plants were known to be hallucinogenic and highly toxic to humans, and presumably also to other mammals (Hamilton *et al.*, 1978). These "euphorics" included *Croton megalobotrys* (Euphorbiaceae), *Euphorbia avasmontana* (Euphorbiaceae), *Datura innoxia* (Solanaceae), and *D. stramonium*. Subsequent authors (Huffman and Seifu, 1989; Wrangham and Goodall, 1989) have cited this study as an example of self-medication; however, aside from labeling these plants as "euphorics",

Hamilton *et al.* (1978) did not speculate on their possible role(s). There has been no further work with this system.

C. ANTISCHISTOSOMAL DRUG USE BY BABOONS

Phillips-Conroy (1986) examined the diet of baboons along the Awash River Valley, Ethiopia, which is divided by waterfalls into two distinct habitats, with water flow being faster upstream, but slower after the falls. The valley was populated by anubis baboons (*Papio anubis*) above the falls, and hamadryas baboons (*Papio hamadryas*) and anubis-hamadryas hybrids below the falls. The risk of schistosomiasis infection varied for these populations because snails (*Biomphalaria* sp.), the intermediate hosts of *Schistosoma* spp., were absent upstream from the waterfalls, but were abundant downstream. Finally, although the shrub *Balanites aegyptica* (Balanitaceae) was common throughout the valley, only downstream from the falls did baboons consume its leaves and fruits. *Balanites* fruits contain diosgenin, a hormone precursor. Phillips-Conroy (1986) suggested that *Balanites* is consumed because it hinders the development of schistosomes, but experimental in schistosome-infected mice showed that ingestion of diosgenin increases the number of schistosome eggs in the liver; it enhances the disease (Phillips-Conroy and Knopf, 1986).

D. ANTIBACTERIAL FOLIAGE AS NEST MATERIAL

Several bird species place in their nests fresh vegetation that does not constitute part of the nests' structure. Wimberger (1984) noted that fresh plants probably contain more volatile secondary compounds than does dried vegetation, and he hypothesized that birds use these plants to repel or even kill ectoparasites. Using data from egg collections of North American and European Falconiformes, and based on the premise that nest reuse leads to increased parasite transmission, Wimberger (1984) showed that Falconiformes that reused their nests in successive years were more likely to use green foliage in their nests, and those that did not were less likely to do so. Clark and Mason (1985) conducted a similar comparison using selected North American passerines and found that cavity nesters were more likely to use green foliage than were open cup nesters (Table I).

Clark and Mason (1985) also demonstrated that plant use by starlings (*Sturnus vulgaris*) was not random, as the plants selected did not simply reflect the availability in the surrounding areas. Furthermore, preferred plants were more effective at reducing the hatching success of lice (*Mencanthus* sp.) eggs and inhibiting bacterial growth than a random subset of the available vegetation. Subsequently, they showed experimentally that leaves of wild carrot (*Daucus carota*, Umbelliferae), one of the preferred

TABLE I
 USE OF GREEN PLANTS AS NEST MATERIAL IN RELATION TO NEST REUSE AND TYPE OF NEST
 AMONG FALCONIFORMES AND NORTH AMERICAN PASSERINES, RESPECTIVELY (EXPECTED
 FREQUENCIES IN PARENTHESES; FROM WIMBERGER, 1984; CLARK AND MASON, 1985).

	Use of green Vegetation		X ²	p
	Present	Absent		
a) Falconiformes (n = 48)				
Reuse nests	22(17.5)	8(12.5)	8.28	<0.005
Build new nests	6(10.5)	12(4.5)		
b) North American Passerines (n = 137)				
Enclosed nests	18(9.1)	9(17.9)	16.4	<0.001
Open nests	28(36.9)	82(73.1)		

species, significantly reduced the number of fowl mites (*Ornithonyssus sylviarum*) in starling nests (Clark and Mason, 1988). The decrease in mite abundance had no effect of nestling growth, but nestlings from nests with carrot leaves had higher hemoglobin levels than chicks from control nests.

Therefore, it seems fairly clear that starlings select nest material with insecticidal and antibacterial properties. However, contrary to what would be expected according to the chemically-mediated parasite-protection hypothesis, starlings add green vegetation to their nests only during nest building, and, unlike Clark and Mason (1988), not while eggs or young are in the nest. Also, males that reuse a nest box during one breeding season, whether because the first brood fledged or was lost, collect less foliage than males nesting concurrently but for the first time (Gwinner, 1997). Finally, the hypothesis does not explain why only males add green vegetation to their nests, and first-year males use less fresh vegetation than older males (Clark and Mason, 1985). Several other hypothesis, not necessarily alternative, have been proposed to explain the use of green vegetation in nests. Green foliage may serve to attract females (Fauth *et al.*, 1991; Gwinner 1997) and actually be a rudimentary bower; it may be used to cover debris and keep the nest clean; it may advertise nest occupancy, or it may prevent egg desiccation. It would be interesting to know whether other species behave similarly, and whether starlings use more green foliage in response to higher levels of parasitism.

E. ANTING AND FUR RUBBING

Anting refers to a behavior in which birds rub crushed ants throughout their plumage. Birds also ant by lying on ant nests and letting ants crawl

over their plumage. This behavior occurs in a variety of birds (Potter, 1970) and it has been suggested that anting is used to soothe irritated skin, help with feather maintenance, and prevent or reduce the abundance of skin parasites (Potter, 1970; Clunie, 1976; Ehrlich *et al.*, 1986). Birds also "ant" with other invertebrates, plants, and inanimate objects, such as millipedes (Clunie, 1976), lime fruit (Clayton and Vernon, 1993) and mothballs (Clark *et al.*, 1990), all of which have some antiparasitic properties. Anting has also been observed in mammals (Bagg, 1952; Hauser, 1964; Longino, 1984).

An analogous behavior, fur rubbing, occurs in some mammals. Baker (1996) observed capuchin monkeys (*Cebus capucinus*) in Costa Rica rubbing their fur with the fruits of several species of *Citrus* (Rutadeae), and with the leaves or stems of the vines *Piper marginatum* (Piperaceae) and *Clematis dioica* (Ranunculaceae). These plants have a wide range of bioactive compounds and are used in traditional medicine to treat a variety of ailments. White-nosed coatis (*Nasua narica*) have been observed coating their bodies with *Trattinnickia aspera* (Burseraceae) resin. Although information on the medicinal uses of *T. aspera* is limited, Gompper and Hoylman (1993) suggested this behavior serves a medicinal function. In conclusion, support for the idea that anting and fur rubbing are primarily antiparasitic behaviors is still largely anecdotal; more detailed and experimental studies are presumably forthcoming.

IV. THERAPEUTIC SELF-MEDICATION

In contrast to prophylactic self-medication, evidence for therapeutic self-medication is more compelling, and has attracted considerably more attention. This evidence comes from a single source: chimpanzees at Gombe National Park and the Mahale Mountains, Tanzania, but it is very diverse in nature. Conclusions are based on direct observations of chimpanzees in the wild, fecal analyses, traditional medicine, and biochemistry. Several other plants may be involved, but most work has concentrated on the possible therapeutic use by chimpanzees of three specific plants.

A. *ASPILIA*

The first report of a possible case of therapeutic self-medication was based on several peculiarities of the consumption of leaves of *Aspilia pluriseta* (Compositae), *A. rudis* and *A. mossambicencis* (Wrangham and Nishida, 1983). Field observations of chimpanzees and subsequent fecal analyses revealed that entire leaves were swallowed without being chewed. Instead, these leaves were taken singly and rolled around the mouth before being

swallowed. It was later suggested that this feeding technique may facilitate the intake of any existing medicinal substances via the buccal mucosa (Newton and Nishida, 1990). At Gombe consumption occurred only during the morning, but at Mahale it occurred all day. Finally, there was no between-individual variation in the tendency to consume *Aspilia* leaves. Based on these observations and the widespread use of *Aspilia* in traditional medicine, Wrangham and Nishida (1983) suggested that these leaves are consumed because of their pharmacological effects. However, because of the lack of individual variation and because, at Gombe, consumption occurred only during the morning, Wrangham and Nishida (1983) concluded *Aspilia* was probably used as a stimulant, rather than as a medicine.

It is difficult to draw conclusions about the seasonal variation of *Aspilia* consumption. At Mahale, the percentage of chimpanzee feces containing *Aspilia* leaves was highest in January and February (Wrangham and Nishida, 1983). In contrast, at Gombe, the presence of *Aspilia* leaves in fecal samples was highest during June and July, but behavioral observations indicated that consumption peaked in January, November and May (Wrangham and Goodall, 1989) (Fig. 1). Further work has shown that

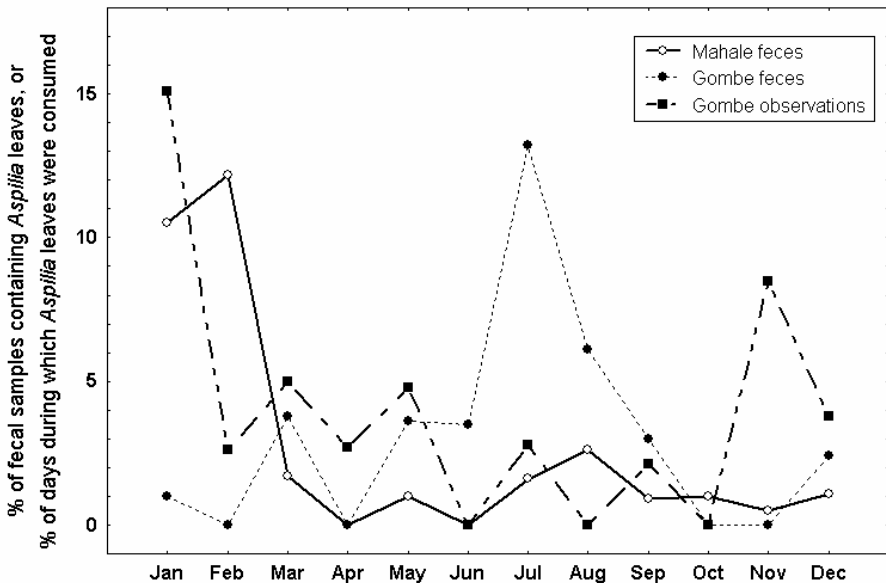


FIG. 1.-Seasonal variation of *Aspilia* consumption by chimpanzees at Mahale and Gombe, based on fecal samples and behavioral observations (From Wrangham and Nishida, 1983 and Wrangham and Goodall, 1989).

the prevalence of infection by the intestinal nematode *Oesophagostomum stephanostomum* is highest during the rainy season (November to March), but there are no seasonal patterns in the prevalence of two other intestinal nematodes: *Trichuris trichiura* and *Stongyloides fuelleborni* (Huffman *et al.*, 1997).

Several secondary metabolites have been obtained from other *Aspilia* species (Mabry *et al.*, 1977; Bohlmann *et al.*, 1984; Ganzer *et al.*, 1992). Methanol extracts of *A. mossambicensis* leaves have limited biological activity against a variety of insects, herbs and fungi (Ohigashi *et al.*, 1991a). In contrast, chloroform extracts of dried leaves yielded thiarubrine-A, a naturally occurring phototoxic compound also found in other species of Compositae (Rodriguez *et al.*, 1985). In the presence of UV-A light, thiarubrine-A is toxic to several bacteria and viruses, and at least one free-living nematode, but its toxicity decreases in the absence of light. Under acidic or alkaline conditions thiarubrine-A readily changes into thiophene-A, which is toxic only in the presence of UV-A light (Towers *et al.*, 1985; Hudson *et al.*, 1986, Table II).

Page *et al.* (1992) found thiarubrine-A in the roots of *A. mossambicensis*, but were not able to isolate it from samples of either fresh or dried leaves. They did, however, isolate two diterpenes, kaurenoic acid and grandiflorenic acid from dried leaves, and showed that these compounds stimulate contrac-

TABLE II
IN VITRO TOXICITY OF THIARUBRINE-A AND THIOPHENE-A^a

Organism	Thiarubrine-A		Thiophene-A		Ref.
	Light	Dark	Light	Dark	
<i>Caenorhabditis elegans</i>	++	+	nt	nt	1
<i>Saccharomyces cerevisiae</i>	++	++	nt	nt	1
<i>Candida albicans</i>	++	++	++	-	1
<i>Staphylococcus albus</i>	++	-	++	-	1
<i>Bacillus subtilis</i>	++	++	nt	nt	1
<i>Streptococcus fecalis</i>	++	-	nt	nt	1
<i>Escherichia coli</i>	++	+	+	-	1
<i>Pseudomonas flourescens</i>	-	-	nt	nt	1
<i>Mycobacterium phlei</i>	++	+	nt	nt	1
Murine cytomegalovirus	++	-	nt	nt	2
Sindbis virus	++	-	nt	nt	2
T4 bacteriophage	+	-	nt	nt	2
M13 bacteriophage	-	-	nt	nt	2

1=Towers *et al.* (1985)

2=Hudson *et al.* (1986)

^a ++ = highly toxic, + = weakly toxic, - = no effect, nt = not tested.

tions of a guinea pig uterus *in vitro*. Observations of chimpanzees revealed that at Gombe more females than males selected *Aspilia* leaves, and the number of days in which *Aspilia* leaves were consumed was also significantly higher for females (Wrangham and Goodall, 1989), which led Page *et al.* (1992) to suggest that pregnant chimpanzees consume the leaves of *A. mossambicensis* to induce labor. This hypothesis would predict increases in *Aspilia* consumption by pregnant females as they approach their due dates, and perhaps even by females ill-suited to carry their fetuses to term. However, there is no information on *Aspilia* use by pregnant females, nor any evidence to indicate that *Aspilia* induces labor *in vivo*. This idea has not received further consideration.

Conclusions based on the chemical analyses must be considered tentative for at least two reasons. First, it is difficult to build a case for self medication based on the ingestion of thiarubrine-A, the biological activity of which is markedly decreased, or completely absent, without light. Given its properties, thiarubrine-A seems an unlikely medicinal substance, except if used as an external antibiotic (see Ehrlich *et al.*, 1986; Gompper and Hoylman, 1993; Baker, 1996). Second, two subsequent studies (Page *et al.*, 1992, Huffman *et al.*, 1996) have failed to detect thiarubrine-A in leaf samples of *A. mossambicensis*, as first reported by Rodriguez *et al.* (1985). If indeed only the roots of *A. mossambicensis* contain thiarubrine-A, then its biological activity is irrelevant to leaf-eating chimpanzees. However, it has recently been suggested that the leaves of *Aspilia sp.* and other suspected medicinal plants may not be consumed because of their chemical properties, but rather because of their characteristically rough surfaces, which may aid in the mechanical removal of intestinal parasites (Messner and Wrangham, 1996; Huffman *et al.*, 1996).

B. *VERNONIA*

The recognition of *Vernonia amygdalina* (Compositae) as a possible chimpanzee medicinal plant was also the result of detailed field observations (Huffman and Seifu, 1989). An adult female, dubbed CH, was observed during two consecutive days, for a total of about 11 hr. For 35 min during the afternoon of the first day CH foraged almost exclusively on the branches of *V. amygdalina*, a plant that was not consumed by other members of her group. When feeding on *Vernonia* she chewed the young branches, sucked and swallowed the pith juice, and discarded the remaining fibers. During the afternoon of the first day and the morning of the second day, CH spent an unusually long time lying down and very little time foraging; she seemed to have trouble defecating, and her urine seemed unusually dark. Her behavior and urine color returned to normal in the afternoon of the second

day. Interestingly, CH had previously been observed swallowing leaves of another plant, *Lippia plicata* (Verbenaceae), presumably also for medicinal purposes (Takasaki and Hunt, 1987).

Huffman *et al.* (1993) observed another adult female, dubbed FT, for a total of about five hr, over a period of 2 days. During this time she fed on clay from a termite mound and on at least four species of plants, among them *V. amygdalina*. Like CH, FT did not consume the leaves of *V. amygdalina*, but instead chewed, sucked and discarded young branches. A fecal sample obtained during the afternoon of the first day was yellowish and liquid, and contained 130 eggs of the intestinal nematode *Ternidens sp.* per gram of feces. A second stool sample, obtained in the morning of the next day, was solid, and contained only 15 eggs per gram of feces. Huffman *et al.* (1993) also presented data on normal infestation levels, based on repeated fecal sampling of seven other individuals. However, these data were not detailed enough to determine whether the decrease in *Ternidens* eggs in FT was within the normal range of daily variation, in the absence of *Vernonia* or clay consumption.

Several factors, including herbivory, can affect the production and distribution of secondary metabolites within individual plants (Rhoades, 1979; Karban and Myers, 1989), so care must be taken to ensure that the leaves used for analysis are a suitable representation of those consumed (e.g., Huffman *et al.*, 1996). Representative samples collected from the actual *Vernonia* plants consumed by FT showed that, contrary to expectations, the concentrations of two biologically active compounds, vernonioside B₁ and vernodalin, was higher in young leaves than young stems (Huffman *et al.*, 1993, Ohigashi *et al.*, 1994). Several other secondary metabolites have been extracted from *V. amygdalina* (Kupchan *et al.*, 1969; Ganjian *et al.*, 1983; Ohigashi *et al.*, 1991a,b; Jisaka *et al.*, 1992a, 1993a), and, as expected, the biological activity of these compounds is diverse. Extracts from *V. amygdalina* deter insect herbivory (Ganjian *et al.*, 1983), are toxic to schistosomes (Jisaka *et al.*, 1992b; Ohigashi *et al.*, 1994), and have antitumoral (Kupchan *et al.*, 1969), antibacterial (Jisaka *et al.*, 1993b), and antioxidant (Igile *et al.*, 1994) properties. Like *Aspilia*, *V. amygdalina* is used widely in Africa by humans as a medicinal plant for a variety of ailments.

C. *RUBIA*

Wrangham (1995) examined the relationship between a parasitic tapeworm infection and the peculiar habit of leaf swallowing by chimpanzees. Fecal droppings containing whole leaves of *Aneilema aequinoctiale* (Commelinaceae) and *Rubia cordifolia* (Rubiaceae) were found sporadically throughout six years. Tapeworm fragments were detected in these droppings

on 14 occasions, spanning 7 months. During this time, the frequency of droppings containing tapeworm fragments and whole leaves was significantly greater than expected. Wrangham (1995) concluded that heavily infected chimpanzees purposely swallow whole leaves, which cause the shedding of tapeworm proglottides. However, Wrangham conceded that, because proglottid shedding is part of a tapeworm's normal life-cycle, leaf swallowing is not necessarily an effective method of tapeworm control.

Another study (Messner and Wrangham, 1996), also involving *R. cordifolia*, is the only one so far in which the biological activity of a presumed medicinal plant has been compared with that of other plants comprising the regular diet of chimpanzees. Messner and Wrangham compared *R. cordifolia* to six other plants, but found no differences in their toxicity to free-living adults or larvae of *Strongyloides* spp.

V. SKEPTICISM

Although the idea of therapeutic self-medication in animals has been discussed for over a decade, only in the semipopular literature have we seen a healthy dose of skepticism (Sapolsky, 1994, his pun). Sapolsky raised three main concerns: the absence of controls with which to compare the biological effects of these presumed medicinal plants, the lack of and need for studies *in vivo*, and the absence of clearly demonstrated behavioral mechanisms by which therapeutic self-medication can arise and be maintained in a population. I will deal with the first two points here, and with behavioral mechanisms in the subsequent section.

Currently, there is adequate evidence that some plants are consumed under unusual circumstances, and that the leaves or roots of these plants have secondary compounds with uterotonic, antiviral, antibacterial and/or anthelmintic properties. Little else is required if the goal is merely to identify bioactive compounds present in chimpanzees' diets. However, if we consider that all plants have secondary metabolites, and that the main role of these chemicals is protection from herbivores, fungi and bacteria, it is not particularly surprising to find that, for any given plant, even if selected at random, some of these secondary metabolites will be biologically active. The presence of bioactive secondary metabolites in suspected medicinal plants is therefore not conclusive evidence. At best, it can be concluded that, when ill, some chimpanzees deviate from their normal diet.

To demonstrate that plants are consumed to deal with specific diseases, we need to know the ailment affecting an individual, and show not only that the plant parts consumed alleviate this condition, but that their effect is greater than that of plants that make up a healthy individual's regular diet.

Alternatively, it is probably difficult to determine the exact relationships between specific diseases and their corresponding medicines, so, when ill, individuals may simply choose plants containing a wide spectrum of biological effects, akin to taking a general antibiotic. In these cases, these plants would not be necessarily effective against the disease, but they would be expected to contain more and/or stronger biologically active compounds than plants normally consumed. Third, therapeutic medicines may be consumed to alleviate the symptoms of the disease, and have no effects at all on the pathogen itself. In such cases medicinal plants would be expected to contain analgesics and other compounds that affect only the host, and not the parasite. Whether an animal consumes medicinal plants as general antibiotics, or to deal with specific diseases, or merely the symptoms of disease, comparisons with other plants comprising the animal's regular diet are needed before firm conclusions can be drawn.

There has been only one study in which such controls have been used. Messner and Wrangham (1996) found no differences in the biological activity against *Strongyloides* spp. between methanol extracts of *R. cordifolia* and six other plants regularly eaten by chimpanzees. Messner and Wrangham pointed out that these results do not necessarily mean that *R. cordifolia* does not affect intestinal nematodes because (1) the extraction method may have failed to obtain all bioactive compounds, (2) the nematodes used in this test were not the parasitic stage, but rather free-living adults and larvae, and (3) *in vitro* tests are a poor replacement for the complex interactions that may occur *in vivo*. Unfortunately, these same caveats would have also been valid had Messner and Wrangham (1996) found significant differences between the biological activity of *R. cordifolia* and the other six plants.

However, Messner and Wrangham (1996) did raise an important point: experimental tests *in vivo* are needed. Understandably, *in vivo* trials may not be practical or ethical in wild chimpanzees, so they must take a back seat to observational and to phytochemical studies. Furthermore, chimpanzees at Gombe and Mahale have been the focus of ongoing research for several decades, so it would be undesirable to carry out invasive experiments with these populations. Nevertheless, such studies are necessary if we wish to understand the effects of these plants, and could perhaps be conducted with chimpanzee populations elsewhere, captive chimpanzees, or other primates.

VI. BEHAVIORAL MECHANISMS

Therapeutic self-medication requires fairly complex and interesting behavioral mechanisms of food selection. However, as Sapolsky (1994)

pointed out, this aspect has received little attention in the self-medication literature. In this section I discuss food selection mechanisms that may be involved in therapeutic self-medication, dealing first with individual learning and then with social learning. The following discussion is not meant to be a critical review of the literature on the mechanisms of food selection, and is based largely on several comprehensive reviews (Rozin and Kalat, 1971; Galef, 1976, 1996; Rozin, 1976; Bandura, 1977).

A. INDIVIDUAL LEARNING

If therapeutic self-medication is learned individually, a series of steps must take place. First, upon infection by a parasite, or when the infection reaches a particularly uncomfortable level, the host must begin sampling unfamiliar food items, and in some cases overcome their natural aversion to new foods and bitter-tasting plants (Garcia and Hankins, 1975). The infected animal must then chance upon a medicinal plant and fortuitously consume it in sufficient quantities for the plant to be effective against the offending parasite. Upon recovery, which may occur many hours after the medicinal plant was consumed, the animal must return to its regular diet.

Several relevant mechanisms have been demonstrated experimentally in rats (*Rattus norvegicus*), apparently the preferred species for experimental work on the mechanisms of food selection. Richter (1943) showed that rats faced with a limited number of single-nutrient food items were able to select a nutritionally adequate diet. Furthermore, rats with deficiencies of specific nutrients were able to obtain these nutrients by altering their diets.

In theory, the ability to obtain a balanced diet may be the result of specific hungers, under strict genetic control, without the flexibility of learned behavior. For every single nutrient it requires, an animal could have the ability to sense physiological deficiencies, and recognize its presence in food. The animal would need the physiological mechanisms to identify each nutrient individually, presumably by taste or smell, and to monitor constantly for deficiencies. This would mean a separate monitoring and identification system for each essential amino acid, vitamin, and mineral.

Clearly, such a system would seldom be necessary or particularly useful. Specific hungers do exist, but they are limited to extremely important nutrients. For example, carnivores need not be concerned with individual nutrients, as each prey item provides them with a full range of essential nutrients in an adequate balance. Domestic chickens (*Gallus gallus*) have a specific hunger for water that includes the ability to taste it, but not identify it visually (Hunt and Smith, 1967). It is therefore possible to have dehydrated newly hatched chicks walking through water and being completely unaware of the obvious solution to their problem. They soon learn

to identify it visually, but only after having pecked at it and tasted it. The adult blowfly (*Phormia regina*) has specific hungers for sugar, water and salt, and its feeding response is under direct control of separate internal and external chemoreceptors for each of these nutrients (Dethier, 1969). Most mammals have a specific hunger for water (Rozin, 1976). Among primates, sodium hunger has been shown in humans (Beauchamp *et al.*, 1990) and baboons (Denton *et al.*, 1993). Given the large number and unusual nature of chemicals involved, it is doubtful that specific hungers play a role in therapeutic self-medication. Whereas the rule of thumb "when suffering from dehydration, drink plenty of water" could be solely under genetic control, the directive "when suffering from malaria drink water from under a cinchona tree, or better yet, chew on the tree's bark" is far more complex and more likely to be a learned response.

In the absence of specific hungers, diet selection must be the result of learned preferences for suitable diets, or learned aversions for inadequate diets. Rozin (1967) observed that the behavior of rats toward their regular, palatable, but nutritionally deficient diet was similar to their behavior toward highly unpalatable diets. In both cases rats approached the food tray tentatively, spilled some food, and then moved away and chewed on some inedible object. These rats were quick to consume any new diet, regardless of whether it was nutritionally adequate. These observations showed that diet changes in rats are not the result of learned preferences for new, or nutritionally adequate diets, but rather the result of a learned aversion for the initial, nutritionally deficient diet.

Whether diet changes are the result of aversions or preferences, several problems arise when attempting to apply diet selection mechanisms to therapeutic self-medication. Self-medication requires that animals consume unusual food items temporarily and maybe exclusively, and then revert to their regular diets. This process does not entail a permanent preference for the alternative diet, or a permanent aversion to the regular diet. It may be possible to explain self-medication in terms of a dual aversion, first to the regular diet, and then to the medicine. However, this would be possible only if the initial aversion to the regular diet is strong enough to cause the initial shift, yet mild enough to be subsequently forgotten.

Another problem for a self-medicating animal is learning to associate its recovery with its diet over the past several hours, and not with other events that may have occurred concurrently. Experiments in rats have shown that aversions do not develop to the location or the type of food container, but are limited to the nutrient-deficient food itself. Garcia and Koelling (1966) exposed rats to taste, sound and light stimuli, paired with either electrical shocks or poisoning, via injection or radiation. Poisoned rats learned to

avoid the taste, but not the sound or light, whereas shocked rats developed an aversion to the light and sound, but not the taste. This experiment showed that certain associations between stimuli are learned more easily than others. Specifically, visceral responses are more likely to be associated with food consumption, which suggests that intestinal ailments would be more likely associated with medicines consumed orally, and external ailments with topical medicines.

A self-medicating animal must not only learn to associate its recovery with food, but also determine which food, out of the several items that may have been consumed, is responsible for its recovery. While trying to find an adequate diet, rats do not sample alternative foods randomly. Instead, their sampling pattern facilitates the possibility of associating recovery with a specific item. Feeding bouts are temporally separated and include only one new food source, and only a few new foods are sampled each day (Rozin, 1969). So far, no studies have dealt specifically with the food sampling behavior of sick chimpanzees.

B. SOCIAL LEARNING

Social interactions play an important role in every aspect of chimpanzee behavior; hence much of their knowledge concerning ways to interact with their environment does not necessarily come from individual experience. Food preferences may be influenced by the food choices of conspecifics, so self-medication may not be learned *de novo* by every individual.

Although the effects of social learning on self-medicating chimpanzees have not been studied yet, several potentially relevant mechanisms have been demonstrated experimentally in other species. For example, in rats, protein deficiency increases the effect of social learning on diet preferences (Galef *et al.*, 1991). These results suggest that sick animals in poor condition may be more likely to alter their diets. It has also been demonstrated that rats are more likely to learn the unfamiliar, rather than the familiar or usual diet of their demonstrators (Galef, 1993). In spotted hyenas (*Crocuta crocuta*), individually learned food aversions can be attenuated and even eliminated by the observation of conspecifics feeding on the avoided food (Yoerg, 1991). In red-winged blackbirds (*Agelaius phoeniceus*) aversions can develop from observing conspecifics becoming ill after consuming a food item (Mason and Reidinger, 1982), which shows that blackbirds learn to associate visual cues of illness in conspecifics with particular foods. However, there have not been any studies demonstrating the reverse: the ability to associate the recovery of a sick conspecific with its consumption of a specific food item.

VII. IMPLICATIONS

A. CONSERVATION ECOLOGY

The many ways in which animals interact with their environment are seldom readily apparent. Self-medication in wild animals may be one such relationship that we are only now beginning to recognize, much less understand. This lack of knowledge further demonstrates that we do not have the ability to reconstruct natural ecosystems; therefore, conservation ecology requires the protection of entire communities, with all their species and interrelationships intact (Clayton and Wolfe, 1993). Captive breeding programs can be successful at preserving individual species, but do not preserve the relationships of an animal with its natural environment. Hence, the preservation of species should be considered as an important fail-safe option, but only part of more holistic conservation ecology strategies.

The existence of self-medication may also affect the ease with which animals can be reintroduced to the wild, especially in cases for which knowledge about self-medication is culturally transmitted. Depending on the extent to which self-medication and other parasite avoidance behaviors are culturally transmitted, naive animals being returned to their natural environment may be subjected to unusually high parasite loads. The negative effects of parasites may be further exacerbated in host populations with heavily fragmented habitats, a factor that should be considered in designing biological reserves (Loye and Carroll, 1995).

B. FORAGING THEORY

Optimal foraging models were initially based on the assumption that the primary goal of foragers was to maximize net energy or protein intake (Stephens and Krebs, 1986). Other factors, such as the risk of predation (e.g., Milinski and Heller, 1978; Sih, 1980; Edwards, 1983; Abrahams and Dill, 1989; Lima and Dill, 1990), and the effects of intraspecific (e.g., Baker *et al.*, 1981; Milinski, 1982) and interspecific (e.g., Millikan *et al.*, 1985) competition, have been subsequently incorporated into diet choice models, and increased their predictive powers. The effects of parasitic infections on foraging behavior have also been examined (e.g., Crowden and Broom, 1980; Milinski, 1984; Giles, 1987). So far, however, diet choice has been largely ignored as a way in which potential hosts could actively reduce parasitism.

Diet choice has also evolved under the selection pressures brought about by parasites. It is therefore reasonable to expect that optimal diets are not only nutritionally and energetically adequate, but also take into account

the potentially detrimental effects of parasites. Hosts could alter their diets to counteract the risks of parasitism by (1) avoiding food items that are common sources of parasites, (2) selectively consuming certain food items to decrease their susceptibility to parasites, and (3) actively consuming foods with antiparasitic properties upon infection (Lozano, 1991). As evidence of self-medication continues to accumulate, future diet choice models must consider the effects of parasitism.

C. BEHAVIORAL MECHANISMS OF FOOD SELECTION

Diet preferences evolve under many constraints, including parasitism, so it is easy to envision that plants with antiparasitic properties may become part of an animal's regular diet. In contrast, therapeutic self-medication requires a sick animal to deviate away from its regular diet, and seek and consume medicinal substances. It requires intentionality, and is, by necessity, a learned behavior. It is sometimes difficult for even well-documented phenomena to be generally accepted without clear mechanisms by which they can occur. So far, self-medication cannot be explained in terms of experimentally demonstrated food selection mechanisms, so it may prove to be an interesting challenge, if it is to be demonstrated conclusively.

D. HUMAN MEDICINE

Although estimates vary, it is generally agreed that a large proportion of our current medicinal drugs derives from plants (Fansworth *et al.*, 1985; Balandrin *et al.*, 1985; Caldecott, 1987; Mckenna, 1996). The resources are not available to sample every species, so the identification of plants with potential medicinal uses is a major impediment in the discovery and development of new medicines. It has been repeatedly stated that the study of self-medication in non-human animals may lead to the discovery of new medicinal compounds (Cowen, 1990, Newton, 1991, Clayton and Wolfe, 1993; Rodriguez and Wrangham, 1993; Sapolsky, 1994). However, this is not supported by the cases studied so far.

As noted above, one important reason to suspect that chimpanzees consume certain plants for medicinal purposes is that these plants are also used in human traditional medicine. So, in essence, it was already known that these plants may have medicinal properties. It is possible that further research will indeed yield new medicines. However, the search for new pharmaceuticals cannot be considered the primary goal of this line of research, for we would probably fare much better by exploring plants used in traditional medicine (e.g., Johns, 1990; Johns and Chapman, 1995; Wagner, 1995) instead of plants used by self-medicating chimpanzees.

VIII. SUMMARY AND CONCLUSIONS

Parasites present a ubiquitous selective force that has led to the evolution of a vast array of behavioral adaptations. The need to avoid and reduce parasites can affect foraging patterns and diet choice, and conceivably lead to self-medicating behavior. Self-medication can be viewed as a specific case of the more widespread phenomenon of chemical interactions across trophic levels. Despite the many apparently disparate examples suggestive of self-medication, it can take only two functionally distinct forms: preventative, and therapeutic. These two processes require separate mechanisms, and yield different and explicit predictions. By viewing it in a more general framework, self-medication can be studied in terms of common elements, instead of isolated examples.

Rodriguez and Wrangham (1993) proposed the term "zoopharmacognosy" to describe the scientific study of the use of plants by wild animals for the prevention and treatment of disease. Current research on therapeutic self-medication is still solely limited to chimpanzees at Mahale and Gombe, but work could be carried out with other populations or other taxa. The multidisciplinary nature of this relatively new field means that problems can be tackled from many different angles, and many avenues of research are still open. Contributions are possible from ethologists, biochemists, parasitologists, pharmacologists, behavioral ecologists, immunologists, psychologists, and statisticians, whether working directly on the field, or simply being aware of the possibility of self-medication in wild animals when conducting other lines of research.

Finding out that baboons indulge in the recreational use of pharmaceuticals, or that chimpanzees practice a primitive form of medicine may challenge some individuals' convictions regarding the uniqueness of humans. Understandably, public interest is high, and discussions on self-medication have not been limited to academic media (Bower, 1986; Cowen, 1990; Sears, 1990; Gibbons, 1992; Strier, 1994; Sapolski, 1994). On the other hand, most scientists would probably consider such findings extraordinary, but not necessarily disturbing. Scientific interest, therefore, results from more than a mere fascination with newly discovered behaviors; as noted above, the study of self-medication in wild animals may have implications on a variety of related fields. Although several recent synopses (Wrangham and Goodall, 1989; Newton, 1991; Huffman, 1993; Rodriguez and Wrangham, 1993; Huffman and Wrangham, 1994) have presented the evidence for self-medication as being fairly conclusive, I must conclude that the evidence for therapeutic self-medication in non-humans is still only suggestive. Nevertheless, the possibility of prophylactic or therapeutic self-medication in nonhumans remains a fascinating prospect, and is certainly a fertile ground for further innovative research.

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