Parasite Induced Behavioral Change in Blood Feeding Insects
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Introduction – Manipulation as a Concept

Changes to host behavior as a consequence of infection are common in many host-parasite associations (Moore, 2002). These changes are important because they can modify an animal’s functional role in the ecosystem and alter their ability to carry and transmit disease. The majority of research in this area focuses on modifications that facilitate transmission, but some alterations have no identifiable adaptive value and others have detrimental effects for both the parasite and host. This paper focuses on parasitic manipulation of insect vectors carrying human diseases such as malaria, leishmaniasis, and trypanosomiasis although there are a plethora of examples demonstrating parasitic manipulation in insect vectors. The majority of vector-borne diseases do not rely on direct mechanical passage but require a period of growth, development, or reproduction within an intermediate host (typically an arthropod). This mutual dependence leads to an interesting situation. Many infected vectors die before a parasite becomes transmissible or they are able to take a blood meal which facilitates transmission from one host to another (Hurd, 2003). Parasites that increase longevity of their host or increase transmission will therefore have higher fitness than parasites that do not. Strategies for increased parasite transmission include increased contact between vector and host (ie increased probing activity or host seeking), reduced vector reproductive output so that energy can be spent elsewhere, and increased vector longevity (Hurd, 2003). Most of the medically important insect vectors are hematophagous meaning they feed on blood. These insects include mosquitoes, tsetse flies, sandflies, and ticks. Each group has a unique biological mechanism for feeding, reproduction,
and predator avoidance which presents us with a wide range of behavioral changes and associated mechanisms for change (Moore and Gotelli, 1996).

Parasites, by definition cause harm to their host, and by their mere presence often cause behavioral change. Whether behavioral changes seen in insects are simply a result of infection or true manipulation is highly controversial. In order to differentiate the two categories we must know the mechanism of change. We must also note which individual is causing the change and who benefits from the altered behavior; the parasite, the host, or both. In some cases behavioral modification is the result of resource exploitation and has no benefit to either the parasite or the host. In others the host will behave in ways that compensate for the detrimental consequence of infection (Lefevre, 2008), and lastly some behavioral changes initiated by parasites are detrimental to the host and facilitate transmission of the parasite. The evolutionary capacity and quick reproductive cycle of parasites is often greater than that of insects. This creates a typical “evolutionary arms race” where both the pathogen and vector are changing in order to fend off the other. Unfortunately for the insect, natural selection tends to favor parasite transmission traits and its fate is left up to the parasite (Lefevre, 2008).

Most parasites change the behavior of their host in order to increase transmission and the likelihood of moving from one host to another in order to complete their lifecycle. However, it is important to note that behavioral modification takes place in more than one direction. Lefevre et al., (2008) suggests that the manipulated behaviors should not be viewed as good for one species or the other; it could be a simple compromise between host and parasite strategies. Grasshoppers (Boorstein and Ewald, 1987), cockroaches (Bronstein and Conner, 1984), and flies (Watson et al., 1992) exhibit behavioral fever as a way to harm the infecting pathogen. In addition to
fighting infection, insects alter behaviors to raise their fitness through increased egg laying, courtship, and parental behavior. In other cases, hosts compensate for parasitism by decreasing reproductive efforts, presumably to enhance survival and ultimately increase the probability of outliving the parasite (Forbes, 1993; Hurd, 2001). Animals within the insect world are amazingly diverse and have formed a plethora of ways to deal with parasitism. Hocking (1971) made an interesting point when he said “rarely has so much work yielded so little consensus of opinion.” Adaptive changes are not always considered under the category of manipulation but are dependent on the presence of pathogens within vectors and are therefore included in this paper.

**Modification of Leishmania infected Sandflies**

*Leishmania* is a blood born parasitic infection caused by a protozoan parasite within the genus *trypanosoma*. It is transmitted by sandflies and ultimately resides in the blood of vertebrate hosts such as humans, canines, ungulates, and rodents. Sandfly is a general term referring to any species or genus of flying, biting, bloodsucking insect. Infection of the sandfly begins after an infective blood meal is consumed. The ingested amastigotes (ovoid body form) transform within the blood meal to become one of several promastigote morphological forms (Killick-Kendrick, 1979). At the end of the digestion process parasites within the blood meal avoid expulsion during defecation by attaching to the flies midgut microvillar border (Pimenta, *et al.* 1992). While attached to the midgut the parasites undergo another transformation becoming attached haptomonad promastigotes, free-swimming promastigotes, or highly motile and non-dividing metacyclic promastigotes. The metacyclic promastigotes are believed to cause behavioral change in their intermediate host (sandfly) by colonizing the anterior region of the
midgut and preventing optimal blood feeding. In addition to physical blockage, *Leishmania* promastigotes secrete a proteophosphoglycan rich promastigote secretory gel which ultimately causes the behavioral change. Sandflies experiencing this blocked state are not efficient blood feeders and will have to probe their host more frequently in addition to feeding longer. Increased host interaction and probing of vertebrates increases the likelihood of transmission and regurgitation of the infective metacyclic promastigotes.

Only female sandflies will engage in blood feeding behavior and will do so exclusively as they prepare for brooding of eggs and require specific proteins. While various sandflies (horseflys, noseeums, and gnats) have different lifecycles they all require blood feeding and will experience behavioral change (increased probing and longer feeding) via a similar mechanism. Rogers *et al.* (2001) explored the role of promastigote secretory gel in the origin and transmission of *Leishmania* and found that it did not alter a sandflies desire to attempt to feed or insert its proboscis into a feeder, but it did have a strong negative effect on the ability of flies to take a full blood meal. It is easy to assume that a fly who does not receive a full blood meal would subsequently continue to probe its host and also probe for a longer period of time but support for this theory was not found (Rogers *et al.*, 2001).

It is important not to overlook the fact that parasites can affect the behavior of their invertebrate hosts in an indirect manner as well. Sandflies are known to probe *Leishmania* infected hosts more often than non-infected hosts. Sandflies are attracted to these infected hosts via modified odor plumes which act as a nasal stimulant (O’Shea, 2002). In some cases the disease agent will decrease vertebrate host defenses making feeding on an infected host less risky than feeding on a non-infected host.
Modification in Malaria Infected Mosquitoes (Genus *Anopheles*)

Malaria is another blood-borne protozoan parasite causing behavioral change in its host. Human malaria (*Plasmodium falciparum*) is transmitted solely by female *Anopheles* mosquitoes and is of great importance to human health because it kills between one and three million people each year. In order for a mosquito to become infective it must take a blood meal from an infected mammalian host. Seven to ten days after ingestion the sporozoites invade the salivary glands of the mosquitoes. Transmission between hosts occurs as the mosquito tries to blood feed and injects saliva into the wound of its host. Uninfected mosquitoes produce apyrase which prevents blood clotting at the wound site and ultimately aids in feeding. Malaria sporozoites infect and affect the apyrase producing region of mosquito salivary glands which increases the median time for locating blood and therefore probing activity as well (Ribeiro, 1985; Rossignol, 1984). In addition to altering mosquito probing and feeding Rossignol *et al.* (1985) shows that malaria has the ability to alter hemostasis within its mammal hosts making infected rodents easier to feed on than their uninfected counterparts. In a similar fashion to leishmania infected sandflies, we find mosquito feeding success was greater on infected animals than non-infected animals indicating that more probing activity occurs on non-infected animals, naturally increasing the liklihood of transmission. The intensity of sporozoite infections do not alter the probing rate of their host indicating that the presence of infection has an all-or-nothing effect and does not depend on number of infective sporozites (Wekesa, 1992).

The mechanism for reduced apyrase activity and behavioral modification in mosquitoes is not completely understood. These changes could occur via tissue invasion, or via inhibitor proteins produced directly by the mosquito. Either way, it is interesting to see that increased
probing behavior occurs only after the sporozites in the salivary glands have become infectious. A study using Anopheles stephensi and Plasmodium yoelii nigeriensis shows that mosquito feeding behavior is altered differently depending on the life stage of the parasites. Plasmodium oocysts act in a different direction than mature protozoans and will actually decrease feeding persistence of mosquitoes, increasing the likelihood of living long enough for malaria sporozites to become infectious and be transmitted (Anderson et al., 1999).

Modification of Trypanosome infected Tsetse Flies (Genus Glossina)

Tsetse flies are important disease vectors for both African Sleeping Sickness (Trypanosoma brucei and gambiensis) and Chagas Disease (Trypanosoma cruzii). While Chagas disease is most frequently transmitted by blood feeding vectors it does not rely solely on these individuals and it is possible that the selective pressures for parasite resistance or behavioral modification may be different in this group. Contaminated foods and trans-ovarial transmission also aid the transmission process for this parasite. Tsetse are similar to other large flies, but can be distinguished by three visual characteristics; when resting their wings are folded completely so that one wing rests directly on top of the other, they have a long proboscis extending directly forward, and the proboscis is attached to the bottom of their head by a large bulb.

The lifecycle of African Sleeping Sickness and Chagas disease causing trypanosomes is very similar to that of leishmania causing trypanosomes in sandflies. Both develop in the blood of their host and ultimately affect the salivary glands, which is where they develop to maturity and become infectious. Transmission rates of these parasites are altered by reducing blood meal location efficiency of hosts and increasing the probing rate (Hurd, 2003). Transmission of blood borne trypanosomes can occur in both a mechanical and biological way. Mechanical
transmission typically occurs when a blood feeding fly is interrupted and immediately goes to another host to feed. During this transition from one host to another blood from one host can be regurgitated to another with no significant development of the parasite occurring. Biological transmission requires that the parasite develop and reach sexual maturity within the tsetse fly. This is more common than mechanical transmission and flies that become infected with trypanosome larvae will often remain infected for the rest of their life. While blood seeking behavior is the most studied behavior of tsetse flies and modified significantly by parasites the most conspicuous change in foraging behavior occurs when they perceive a host in the area and immediately shift to intermittent, fast upwind flight (Moore, 1993).

**Modification of Lyme Disease (Borrelia burgdorferi) infected Ticks**

Ticks are classified into one of two categories based on the thickness and flexibility of their chitinous exoskeleton; Argasid and Ixodid. Although Argisidae (soft) and Ixodidae (hard) ticks have similar mouthparts they vary greatly in their feeding strategies and ability to transmit disease. Both families of ticks contain a mouth with two lateral palps, paired chelicerae, and a barbed hyposome which is inserted into its host during feeding. The mouth parts of Argasid ticks are not visible from the top the way they are on Ixodid ticks.

Ixodid ticks are excellent vectors for disease transmission because they feed for extended periods of time (days to weeks). This class of ticks transmits a huge variety of pathogens including but not limited to bacteria, rickettsiae, protozoa, and viruses. These ticks have three distinct life stages and take only one blood meal during each stage which reduces the likelihood of parasites being transmitted from one animal to another during any one life stage. However, the
prolonged feeding bouts increase development time for pathogens which inherently increases chance of transmission during feeding. Ixodid ticks serve as the primary vector for Lyme disease.

Ticks can become infected with Lyme disease during any one of their blood-feeding life stages but nymphal ticks are responsible for the majority of infections in the United States. Their smaller size makes them less conspicuous than adults and allows for longer feeding bouts. Due to developmental time constraints transmission of *B. burgdorferi* is uncommon if a tick feeds for less than forty-eight hours. Behavioural changes associated with infection in this system include altered reaction to light, maneuverability, and host seeking. Nymphal ticks that are infected with *B. burgdorferi* show increased phototaxis meaning they will move toward a light source, increased attraction to vertical surfaces, and will quest at greater heights than their uninfected counterparts (Lefcort and Durden, 1996). These altered behaviors increase the likelihood of a tick finding a mammalian host and once again affect the likelihood of transmission in a positive way. Behavioral changes are more frequently seen in adult ticks but the changes occur in an opposite direction than those seen in the nymphal stages. Adults become less maneuverable and have difficulty overcoming physical obstacles; they were also less active, and quested at lower heights (Lefcort and Durden, 1996). Questing is a behavior in which ticks crawl to the uppermost portion of grass or leaves and stand with their front legs extended. Ticks use Haller’s organ on their appendages to measure levels or carbon dioxide in the air, but also rely on pressure, heat, and cerci to identify a passing host.

**Implication of Behavioral Change on Vector Control and Disease Management**

Understanding the behavior of blood-feeding insects is important from both a biological and medical standpoint. Even when parasite transmission is not necessarily affected, it is clear
that parasitized hosts behave differently than uninfected conspecifics indicating that they may segregate themselves in space or time (Moore and Gotelli, 1990). Sampling methods used to determine the presence of insects and pathogens often fail to take altered behavior of hosts into account. A historical comparison of seven trap methods showed that the number of flies caught, sex, and parasitism did vary based on method of capture (Harley, 1967). Insect collectors spend a lot of time determining which trap type to use but often make their decision based on number of individual collected or general behavior of the species without taking into account parasitism.

The majority of research on behavior of blood feeding insects focuses solely on blood-seeking but there are many behaviors we can use to control or identify subgroups. For example, it is not uncommon for us to see changes in activity level of infected insect hosts. *Aedes aegypti* mosquitoes experience reduced activity when infected (Berry et al., 1987), *Culex pipiens* mosquitoes experience inhibited flight (Hawking and Worms, 1961), and *Glossina spp.* tsetse flies experience increased feeding and probing behavior (Jenni et al., 1980). Parasites such as these affect habitat preference and temporal activity patterns which can change a fly’s host choice (Edman et al., 1985). Parasite induced behavioral changes in activity, habitat, nutrition, and feeding patterns of hematophagous insects are likely to alter an insect’s host-seeking behavior and often can even create a new ecological niche for this distinct population.

Unfortunately, the majority of integrated pest management plans within the United States target general populations of insect vectors. While many blood feeding insects are simply annoying and we do not want them in our back yards, the ones carrying parasites and disease agents relative to human health should be of greatest concern. Several classes of insecticide are used in the United States but most of them target and kill entire populations of insects instead of
identifying the individuals of concern. Examples of these insecticides include methoprene which mimics juvenile hormone and prevents insect larvae from pupating to adulthood. Others, like dichlorodiphenyltrichloroethan (DDT) act on the central nervous system of the insect rendering it basically functionless. Contact irritants seem to be a more humane way of dealing with insects because they act by making certain surfaces (such as walls human dwelling) unappealing to insects and therefore decrease the number of insect host interactions that occur. While these insecticides to not decrease the population of vector carrying insects they can aid in decreasing the number of vector borne disease cases in humans.

Blood feeding insects serve an important role in maintaining the functionality of our ecosystem. While most hematophagous insects are considered pests it is important to recognize their function before ultimately trying to eradicate a species or large group of insects. Many of the blood feeding insects serve as food for fish, birds, bats, and other insectivorous insects. Larvae of black flies are suspension feeders helping to clean our rivers and streams by filtering out bacteria and microorganisms. Detritivorous mosquito larvae help remove overgrowing algae and leaf litter in our ponds and other non-flowing bodies of water. Decreased water health and detritous build up has terrible effects on an ecosystem, and eradication of insect species undoubtly decreases the biodiversity of an area. As we being to understand more about the behavior of insects in general, and the behavior of parasitized insects specifically, I hope we can find a way to coexist with insects. A good understanding of insect behavior can help us avoid interactions with diseased insects through altering our own behavior. We can also use this knowledge to target our pesticide development toward unwanted or dangerous insects in a specialized manner.
References


