Mem. Inst. Oswaldo Cruz, Rio de Janeiro, Vol. 82, Suppl. III: 1-3, 1987
Intern. Symp. on Insects

VECTOR SALIVATION AND PARASITE TRANSMISSION

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Saliva of blood-sucking arthropods contains substances that counteract the host's hemostatic and inflammatory reactions, allowing the arthropod to locate blood and keep if flowing during the blood meal. Parasites may manipulate this system in order to achieve increased transmission, both to vertebrate and to invertebrate hosts. Additionally, salivary pharmacological substances may locally immunosupress the delivery site, allowing initial colonization of the vertebrate host by the parasite.

Until recently, the function of the saliva of hematophagous arthropods was problematic. Coagulation seemed to be the sole potential impediment to ingestion of blood, and thus evidence of some anticoagulant in saliva became the logical research focus. Of course, vessel feeding insects generally feed so rapidly that no clot can form within the mouthparts, a fact that prevented serious consideration of any anticoagulant role of saliva. Students of the subject even disputed the role of saliva in blood-feeding (Hudson et al., 1960; Mellink & Van Zeben, 1976; Rossignol & Spielman, 1980). Indeed, modern authors tend to view solely the antigenic properties of vector saliva as an impediment to feeding (Johnston & Brown, 1985).

Recent findings demonstrated antihemostatic and antiinflammatory components in the saliva of blood feeding arthropods, substances that function by preventing the host from reacting to the trauma associated with the insect's mouthpart (Ribeiro, 1987). Aggregation of platelets establishes hemostasis much more rapidly than does coagulation (Mustard & Packham, 1977). Arthropod saliva, indeed, inhibits such platelet activity. Platelet inhibitory activity characterizes saliva of blood-sucking bugs (Ribeiro & Garcia, 1981; Ribeiro & Sarkis, 1982), mosquitoes (Ribeiro et al., 1984, 1985), sand flies (Ribeiro et al., 1986), tsetse (Mant & Parker, 1981), and ticks (Ribeiro et al., 1985). The function of saliva is illustrated by the prolonged period of nonfeeding probing experienced by non-salivating bugs (Ribeiro & Garcia, 1981a) and mosquitoes (Ribeiro et al., 1984). Feeding in these insects frequently is aborted. Indeed, blood finding behavior of mosquitoes has been presented in a model in which successful blood-findings is a function of the probability of locating blood either inside blood vessels or in hematomas (Ribeiro et al., 1985a). Saliva appears to facilitate blood-finding by promoting hematoma formation, thereby enlarging the food source volume presented to the feeding stylets of the insect.

In addition to anti-platelet activity, blood sucking bugs contain anti-histamine, antiserotonin and anti-thromboxane activity (Ribeiro, 1982; Ribeiro & Sarkis, 1982). The tick *Ixodes dammini*, in addition to anti-platelet activity contains a kininase, prostaglandin E_2, considerable immunosuppressive activity (Ribeiro et al., 1985), an anaphylatoxin inactivating enzyme (Ribeiro & Spielman, 1986) and an anti-complement activity (Ribeiro, 1987). The sand fly *Lutzomyia longipalpis* contains a peptide inducing a long lasting erythema that may help the fly to obtain blood from the capillaries from which they feed (Ribeiro et al., 1986). These activities prevent host inflammatory reactions that may disrupt vector feeding.

The vector-host interface may be represented as a co-evolutionary arms race in which vectors seek to neutralize their host's antihemostatic and antiinflammatory components, while the hosts seek to recognize salivary antigens and counter their effects by mounting local inflammatory reactions. An understanding of the features of this interface may help us to understand how vectors and their hosts may have co-evolved. Studies on this subject address the molecular basis for host specificity of blood sucking arthropods as well as the complexity and diversity of the reaction of vertebrate skin to arthropod saliva. Features of this interface may profoundly affect transmission of vector-borne disease, and knowledge of the biochemical and pharmacological properties of injected saliva may provide an important variable in the crucial initial stages of adaptation of an

arthropod-borne pathogen to its vertebrate host (Stebbings, 1974; Wikel, 1980).

Parasites use various mechanisms to manipulate their host's behavior to maximize their transmission to a new host. Parasite-induced salivary pathology may be one such mechanism, enhancing transmission from invertebrate to vertebrate host. *Plasmodium gallinaceum* sporozoites reduced salivary apyrase in *A. aegypti* without affecting volume of salivary output (Rossignol et al., 1984). Duration of probing by infected mosquitoes was increased, and their biting rate on a host was doubled (Rossignol et al., 1986). *Trypanosoma rangeli*-infected *Rhodnius prolixus* demonstrated a similar behavior; their probing time was greatly enhanced, and the bugs were eventually unable to feed (Anez & East, 1984). Similarly, *Aedes triseriatus* infected with La Crosse virus tended to probe more and engorge less than uninfected siblings, and transmission rates increased as the level of probing increased (Grimstead et al., 1980). Vector-borne parasites may facilitate vector feeding through the hemostatic disorders they commonly induce in vertebrate hosts, thus enhancing transmission from vertebrate to invertebrate host. Indeed, mosquitoes located blood faster in Rift Valley fever virus-infected hamsters or *Plasmodium berghei*-infected mice than in uninfected animals (Rossignol et al., 1985). Thus, parasites manipulate both the vertebrate host's hemostatic components and the vector's salivary antihemostatic properties to achieve maximum transmisision.

Additionally, pharmacological activities in vector saliva may induce local immunosuppression of the host with consequent enhancement of parasite transmission. In a laboratory model of leishmaniasis, salivary gland homogenates of the fly *Lu. longipalpis* enhanced the growth of *Leishmania major* when co-injected in mice foot pads (Titus & Ribeiro, 1988). Indeed, as little as five percent of one pair of salivary glands coinjected with 10 parasites were the difference between having or not having an established infection three weeks later. With larger innocula, the presence of saliva induced an increase in the number of parasites of several orders of magnitude in the same time span. Acquisition of tick-borne diseases may be profoundly affected by the vector's saliva, which contains immunosuppressive activities (Ribeiro, 1987; Makoul et al.,, 1985). Indeed, host immune reaction to vector's saliva may modify the course or suppress disease transmission, a fact empirically observed before in at least three different systems including a virus, a bacteria and a protozoan parasite (Feinsod et al., 1975; Alger et al, 1972; Alger & Harant, 1976; Wikel, 1980). Knowledge of the molecular basis for such host-vector interfaces may lead to rational development of novel disease control methods.

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