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FACTORS DETERMINING HUMAN ATTRACTIVENESS TO MOSQUITOES: A REVIEW

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ABSTRACT

Humans are detected by blood-feeding mosquitoes when producing and releasing certain chemical signals, such as lactic acid and carbon dioxide. These compounds help the above-mentioned insects to differentiate humans from other animals by using olfactory receptors located in their antennal olfactory receptor neurons. However, the frequency of mosquito bites varies from person to person due to differences in the composition and quantity of released attractants, which makes certain individuals more prone to infections, transmitted by these vectors. Such infections include malaria, yellow fever disease, West Nile fever, Zika syndrome, among many others. Therefore, it is of high importance to determine which factors affect the releasing of attractants and therefore play a role in the frequency of mosquito bites.

Key words: mosquitoes, factors, human attractiveness.

Introduction

Mosquitoes are widely spread external parasites that cause a number of vector-borne diseases (Komar et al. 2001). Although climate plays a significant role in their transmission, it is not the only factor of importance (Brown 1966). Several studies show that groups of people that live in the same environment, under the same living conditions, differ in the number of mosquito bites – while for some they are quite frequent, others are rarely bothered by mosquitoes (Schreck et al. 1990; Lindsay et al. 1993). Volatile organic substances and heat, released from the human body, navigate the female mosquitoes when they are looking for a host. Each person releases different chemical compounds which explains why preferability varies (Renate et al. 2011). Identifying those compounds can help people that are more prone to mosquito bites protect themselves more efficiently when visiting a country with a higher risk of mosquito-borne diseases. Moreover, those attractants can help in creating better mosquito traps for home use (Barrera 2022; Okumu et al. 2010).

Although it is well established that the release of certain attractants is the main cause for the mosquitos' preferability towards certain individuals, it is not entirely clear what regulates the intensity and composition of said attractants. Genetic predisposition, for example, has only recently been discussed as a possible factor, while the role of others, for example diet, is still a controversial topic This is why the purpose of this review is to discuss the characteristics and role of certain human factors that contribute to mosquito attraction (Martinez et al. 2021).

Mechanisms of mosquito-human interaction

Mosquitoes find a host by using heat, humidity and olfactory and visual stimuli to find a host. Carbon dioxide, ammonia, lactic acid and acetone are some of the most well-established attractants to mosquitoes. Moreover, some substances called "kairomones" are released by humans only and are differentiated only by some species of mosquitoes, hence they attack people exclusively instead of other animals (Sbarbati and Osculati 2006). Furthermore, a kairomone alone, such as carbon dioxide or lactic acid, has a weaker effect as an attractant on mosquitoes, compared to a combination of human kairomones (Dekker et al. 2002). Kairomones are detected by mosquitos using gustatory, odorant and ionotropic receptors, located in the antennae, labellum and maxillary pipes (Ray 2015). Carbon dioxide induces and sustains flight and is the main molecule mosquitoes use to detect a blood source from further away (Raji and DeGennaro 2017).

Humans can produce repellents, as well as attractants. Some of the most efficient repellents include geranylacetone and sulcatone (an odorant found in humans in higher levels, compared to other animals which can be either an attractant or a repellent, depending on its concentration and combination with other chemical compounds). Other compounds can mask mosquito attractants and therefore break the connection between the insect and the compound (Logan et al. 2010).

All in all, the information presented above shows that the combinations of mosquito attractants, the release of repellents and the intensity of the substances all matter in relation to the humans' susceptibility to mosquitoes. Some of the leading factors for higher mosquito attraction in humans include pregnancy, present plasmodium infection, skin microbiota, diet and genetic predisposition (Ellwanger et al. 2021).

Pregnancy as factor

A number of studies show that pregnant women attract a higher number of mosquitoes from species *An. gambiae, An. arabiensis and Mansonia spp.* (Ansell et al. 2002; Himeidan et al. 2004). These results are worrying due to the fatal effects of gestational malaria on pregnant women and the embryo, including stillbirth, preterm delivery, maternal morbidity and mortality (Desai et al. 2007). Pregnant women release higher number of attractants, for example CO2, due to the higher heart and metabolic rates during pregnancy. Pregnancy is also associated with the release of compounds specific to the gestational period that act as mosquito attractants. However, most of the studies are carried out with species from subfamily Anophelinae. It is not yet clear whether or not other subfamilies, such as Culicinae (Zika syndrome) are more attracted to pregnant women.

Malaria infection as factor

Chances that a person may be bitten by a mosquito can increase if said person already suffers from malaria. It has been proven that when infected with the transmissible gametocyte stage of Plasmodium falciparum, humans are more attractive to *An.gambiae* (malaria transmitting mosquitoes).This indicates that the parasite influences the physiology of the host, therefore leading to increased number of attractants being released, leading to the transmission of the parasite in the mosquitoes afterwards (Lacroix et al. 2005). Humans with malaria produce certain volatile compounds in a very specific way, which differentiates them from healthy individuals and even from those with asymptomatic malaria. The produced kairomones form an "odor signature" of the host, also known as "malaria smell". It can be used in highly sensitive tests to diagnose patients, even those with the asymptomatic variant of the illness.

Data shows that thioethers from a specimen of patient's breath are a main component in malaria smell. Such compounds are also the aldehydes heptanal, octanal and nonanal, which are produced in greater amounts by infected patients (Berna et al. 2015).

Interestingly, mosquitoes also suffer changes when infected with malaria. An. Gambiae female mosquitos are more attracted to human kairomones, compared to non-infected ones (Smallegange et al. 2013). This leads to the conclusion that the malarian parasite manipulates its host in order to stimulate transmission. However it should be noted that this can be caused by the effects the parasite has on the immune system and not directly on the host (Markwalter et al. 2024).

Skin microbiota as factor

Some of the bacteria found on the skin, such as *Bacillus cereus, Bacillus subtilis, Staphylococcus epidermidis* and *Corynebacterium minutissimum* produce a notable number of attractants, including butyl isobutsyrate, dimethyldisulphide, butylacetate and butyl-2-methylbutanoate. Moreover, violate products released by sebaceous, apocrine and eccrine glands are metabolized by said bacteria. Therefore, the differences between skin microbiota in different individuals influences the concentration and composition of attractants that are released. On the other hand, distribution of the glands can also determine microbiota composition. Skin irritations, such as eczema, modify skin microbiota and therefore also play a role in susceptibility to mosquito bites. Even though skin microbiota varies from person to person, it stays relatively consistent over time. This further supports the possibility of microbiota being a leading factor in mosquito attraction in humans (Paul et al. 2018; Téllez and Eduardo 2005).

The abundance and diversity of the bacteria greatly influence the release of kairomones. Low abundance and high diversity of bacteria show reduced attractiveness, while high abundance and low diversity lead to increased attractiveness of mosquitoes. Also, there is difference in the groups of bacteria, existing in different parts of the body. Volatile organic material produced in vitro by bacteria from human feet, specifically propionibacteria, corynebacteria and staphylococcus, highly attract An. Gambiae mosquitoes (De Obaldia et al. 2022).

Human diet as factor

In recent years several studies have shown that diet can alter body odor and therefore the perception of mosquitos towards humans. For example, alcohol consumption increases the possibility of mosquito bites from Ae. albopictus. The alcohol used in these studies is beer, which leads to the conclusion that increased beer consumption makes a person more prone to mosquito bites. Further investigation is needed in order to determine whether other beverages have the same effect. The consumption of bananas is also found to be a reason for higher susceptibility to mosquitos, again due to change in body odor. Garlic and vitamin B, previously considered repellents, have no apparent effect on mosquitos (Fernández-Grandon et al. 2015).

Human genetics as factor

Studies with twins have shown that genetics truly influence the frequency of mosquito bites (Kirk et al. 2000). The results are plausible since the production of individually specific chemical signals, composing the human odor signature, is determined by genetic factors, including human leucocyte antigen (HLA) alleles. Though it seems relevant, more research is needed in order to establish a definite connection between this factor and human-mosquito attractiveness (Ellwanger et al. 2021; Verhulst et al. 2013).

Conclusions

Human susceptibility to mosquitoes is influenced not only by external, but also by internal factors, such as pregnancy, malaria infection, skin microbiota, genetics and possibly diet. Some of them are evident (pregnancy, skin microbiota and Plasmodium infection, while others need further investigation (genetic predisposition and diet). The information reviewed in this article is highly relevant due to the epidemiological importance of certain mosquito-borne diseases affecting humans all over the world as well as the need for further improvement of preventive measures against various species of mosquitoes.

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