Parasitology Research Monographs 10

Giovanni Benelli · Heinz Mehlhorn
Editors

Mosquito-borne Diseases

Implications for Public Health

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Parasitology Research Monographs 10

Series editor

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Chapter 1
Introduction I: Personal Insights in the Problem: What Remains to Be Done

Giovanni Benelli

Despite decades of extensive research efforts, mosquitoes (Diptera: Culicidae) still play a crucial role among vectors of medical and veterinary importance (Benelli 2015). Indeed, besides the widely known malaria burden, which led to 6.8 million deaths averted globally since 2001 (Benelli and Beier 2017), dengue virus poses at risk 3900 million people in 128 countries (Bhatt et al. 2013). In addition, lymphatic filariasis is still ranked among the most important neglected tropical diseases, and—at the same time—Zika virus outbreaks in the Americas and the Pacific are attracting high public health attention (Petersen et al. 2015; Benelli and Romano 2017), due to the arboviral connection with fetal microcephaly and neurological complications, with special reference to the Guillain–Barré syndrome (Oehler et al. 2014; Benelli and Mehlhorn 2016).

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To effectively manage mosquito populations, a rather wide number of control routes have been attempted, including classic applications of chemically synthesized pesticides, wide employ of long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS), as well as the development of eco-friendly formulations of novel insecticides (covering also nanostructured materials) (Benelli 2016, 2018) and mosquito repellents and field testing of biological control agents and biotechnological tools (Benelli et al. 2016; Bourtzis et al. 2016). However, only few of these tools have been approved by the World Health Organization Vector Control Advisory Group (WHO - VCAG), and there is an urgent need to validate several of them through epidemiological evidences (Benelli and Beier 2017).

The present books present authoritative book chapters written by experts in the field of mosquito vectors and mosquito-borne diseases, to provide an updated overview of the current mosquito research scenario. Key questions formulated—and sometimes addressed—in the present book focus on mosquito morphology, biology, genetics, ecology, and control.

Some of the most relevant ones about mosquito biology and ecology are: which is the updated vector status of mosquitoes widespread in Europe? Which mosquito species are endangering public health in India and other Asian countries? Are mosquitoes able to transmit HIV? What do we really know about the potential carcinogenic action of some pathogens and parasites vectored by several mosquito species?

Concerning mosquito control, crucial issues to deal with are: which are the main drawbacks arising from the use of chemical pesticides? How outbreaks of mosquito-borne diseases can be prevented by proper vector control operations? Do herbal and microbial products represent a challenging solution to develop novel mosquito repellents and insecticides of commercial interest? Which strategies are currently adopted during army field activities to protect humans from mosquito bites? Do long-lasting insecticide-treated textiles have a promising potential in the fight against mosquitoes?

Overall, all these questions urgently need a competent reply from public health experts, epidemiologists, parasitologists, biologists, and entomologists. As co-Editor of the present book, I am aware that this *Parasitology Research Monograph* cannot fully reflect the high diversity of the ideas and new insights rapidly growing in the field of mosquito vector research. Furthermore, I hope that this book will significantly contribute to boost research and applications on successful mosquito control strategies, along with an improved knowledge about the impact of vector biology and ecology, on the success of real-world mosquito control programs.

Conflict of Interest The author declares no competing interests.

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Chapter 2
Introduction II: Why Are Mosquitoes and Other Bloodsuckers Dangerous? Adaptations of Life Cycles and Behavior

Heinz Mehlhorn

The present book deals with recent aspects of bloodsucking arthropods such as mosquitoes, biting flies, fleas, midges, ticks, etc., which exist much longer on earth than the present generations of humans, who are targeted by these nasty contemporaries. Bloodsuckers are not only troublesome but also dangerous due to their ability to transmit agents of diseases such as prions, viruses, bacteria, fungi, and/or parasites, which might even lead to death (Mehlhorn 2016a, b). The transmission may occur during sucking lymph fluid or by oral uptake of blood, when injecting their mouthparts into the blood vessels (e.g., mosquitoes) or sucking at little blood "lakes" being produced by peculiar cutting mouthparts (e.g., tabanids, ticks) (Figs. 2.1 and 2.2).

All known bloodsuckers run their life cycles successfully not only in their typical endemic regions, where they are supported by the slightly but constantly increasing phenomena of global warming, but constantly enlarge their territory due to an enormously increasing globalization process including the daily transportation of goods, persons, and animals from one end of the world to the other. The present book will deal with some selected examples, which give an impression, how vulnerable the world population is. However, it is comforting that epidemics may be successfully blocked as was shown by eliminating, e.g., the bluetongue epidemics of ruminants in the years 2006–2009 (Mehlhorn et al. 2007, 2009; Kampen and Werner 2010; Hoffmann et al. 2009). Another example for a blocking of the spreading of an epidemic was successful, when the Chikungunya virus was imported to Central Italy in

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Fig. 2.1 Scanning electron micrograph of the anterior end of an *Ixodes* tick, which is entered into the skin being cut by two saw-like cheliceres

Fig. 2.2 Light micrograph of a female *Anopheles* mosquito sucking sugar solution by help of its two-channeled, injectable piercing mouthparts

Fig. 2.3 Prof. Dr. Heinz Mehlhorn, Düsseldorf University

the year 2007 (Rezza et al. 2007). However, it is clear that strong efforts are always needed to avoid the spreading of bloodsuckers and thus block transmission of agents of diseases. The present book considers the recent situation and shows the endangering situation. However, it does not consider the transmission activities of other bloodsuckers such as leeches (Nehili et al. 1994), bats (Klimpel and Mehlhorn 2013), or fishes (Mehlhorn 2016a, b) (Fig. 2.3).

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Chapter 3
Mosquito Transmission of HIV: Rare or Not Possible?

Diehl Nora

Abstract From its outbreak till today, HIV (human immunodeficiency virus) caused over 35 million dead. If the transmission of the virus would not be restricted to unprotected sexual contact, needle sharing, blood transfusion, and mother to child transmission, this number would probably be tremendously higher. Luckily, HIV has yet not been documented to be transmitted by mosquitoes. Arboviruses (acronym for arthropod-borne viruses)—the viruses that are transmitted by arthropod vectors—are the cause of severe epidemics worldwide. But why is mosquito transmission restricted to certain viruses? This article elucidates the characteristics a virus needs to be spread by mosquitoes and how HIV fits into this picture.

Keywords HIV · Retrovirus · Arbovirus · Mosquito · Vector-based transmission Biological transmission · Mechanical transmission

3.1 Introduction

At the beginning of the 80s, reports of patients suffering from undefined immunological dysfunctions accumulated. The unprecedented and extremely rapid spread indicated a devastating epidemic. Three years later, a retrovirus—subsequently known as HIV—was identified as the cause of the acquired immune deficiency syndrome (AIDS) (Barre-Sinoussi et al. 1983; Gallo et al. 1984). Followed by the rapid sequencing of the viral genome (Ratner et al. 1985; Wain-Hobson et al. 1985), ongoing research led to the development of a highly active anti-retroviral therapy (HAART)—a drug cocktail which blocks the virus at different stages of its life cycles. With this lifelong therapy, patients nowadays can survive this former deadly illness. However, rarely one-half of worldwide infected person have access to this therapy. More than 75 million people have been infected with the virus since its outbreak and 35 million people died of AIDS-related illness. 36.7 million people were

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Table 3.1 Characteristics of the HI and dengue virus

	HI virus	Dengue virus
Family	*Retroviridae*	*Flaviviridae*
Genome	+ssRNA, size: 9 kb	+ssRNA, size: 11 kb
Baltimore classification	Group 6	Group 4
Envelope	+	+
Mosquito transmission	−	+
Human to human transmission	+	−
Receptors	CD4, co-receptors: CXCR4 or CCR5	Many candidate molecules, e.g., glycosaminoglycans, lectins
Symptoms	Flu-like illness, followed by an asymptomatic phase	Flu-like illness, rarely: hemorrhagic fever
Prognosis	Lifelong therapy, without therapy: deadly	Recovery within 14 days, very rarely deadly
New infections in 2016	1.8 million	390 million

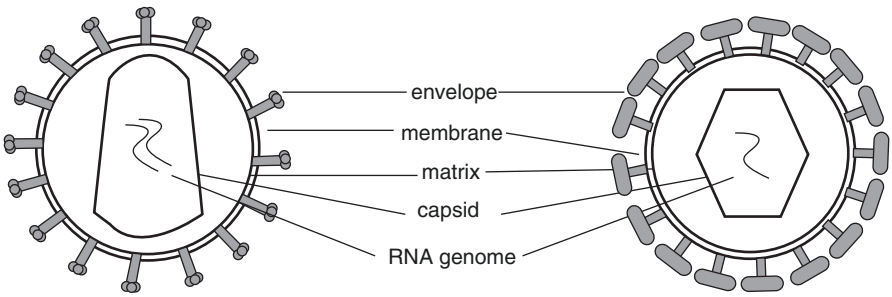

Fig. 3.1 Structure of the HI (left) and dengue virus (right)

living with the virus at the end of 2015 (UNAIDS 2016). Nevertheless, in comparison with the most common mosquito-borne viral disease, the dengue fever, the number of HIV infections seems comparatively small: A recent study estimates that 390 million dengue infections occur annually (Table 3.1) (Bhatt et al. 2013). The dengue fever is caused by the dengue virus, a flavivirus with a positive single-stranded RNA genome (Fig. 3.1), which is mainly vectored by mosquitoes of the genus *Aedes* (principally *Aedes aegypti*). Though not necessarily deadly, this disease can cause hemorrhagic fever, which leads to 22,000 deaths per year. During the last years, the numbers of infections with arthropod-borne diseases increased globally, which is due to increasing mobility, international trade, climatic changes, and approaches to formerly uninhabited areas (Liang et al. 2015). The recent outbreak of the Zika virus, which is likewise a member of the flaviviruses and also transmitted by *Aedes* mosquitoes, in South America, Central America, and the Caribbean, only represents one of several severe threats for human health (Benelli and Mehlhorn 2016).

The lower numbers of people infected with HIV compared to those of, e.g., dengue (Table 3.1) might in part be explained by its different mode of transmission. The main transmission route of the HI virus is via unprotected sexual contact, but also blood, breast milk, and drug needles are origins of infections. However, HIV-containing fluids must directly contact a mucous membrane, damaged tissue, or the bloodstream. Infection via an arthropod vector has not been documented yet. But why are some viruses transmitted by arthropod vectors and other, like HIV, obviously not? This article recapitulates the requirements of a virus to be transmitted by mosquitoes and which of these criteria are accomplished by HIV or not.

3.2 Virus Transmission

Viruses are transmitted by many different routes, while direct transmission between two hosts is the most common way. Thereby, viruses can be embedded within aerosols, body fluids, fecal, or salvia. Depending on the type, they can enter a host orally, intranasally, venereally, or through injured tissue, skin, and mucosa. Another form of virus transmission is mediated by arthropods. This vector-based transmission can either occur mechanically or biologically. In case of mechanical transmission, a vector carries the pathogen on its contaminated mouthparts from one host to another without being infected itself. In case of biological transmission, however, the virus enters the vector to replicate within this host. Biological transmission occurs by far more often than mechanical transmission (Kuno and Chang 2005). As this article focuses on a possible transmission of HIV by mosquitoes, the following passages concentrate on the mechanisms of vector-based and HIV transmission, respectively.

3.2.1 Vector-Based Transmission

As a non-taxonomic clade, arboviruses represent an exceptional group of viruses. Belonging to different taxonomic clusters, the members only share the arthropod-borne mode of transmission. It is commonly accepted that arboviruses primarily originate from arthropod-specific viruses and that this host switch has arisen several independent times during evolution (Halbach et al. 2017). The vast majority of arboviruses are RNA viruses with double-stranded or single-stranded RNA genomes of either positive or negative polarity (Gubler 2001). Members of the taxa alphavirus, flavivirus, bunyavirus, phlebovirus, orbivirus, vesiculovirus, and thogotovirus belong to the group of arboviruses (Weaver and Reisen 2010). In fact, only one arbovirus harboring a DNA genome is known till today: the African swine fever virus. This is probably due to the lower mutation frequency of DNA compared to RNA viruses. DNA viruses simply do not explore the genetic diversity and thus not the possibility to adapt to a new host. Actually, increasing the replication fidelity

and thus minimizing the genetic variability of RNA arboviruses reduces their infectivity in mosquitoes and mice, indicating the absolute need of a certain genetic flexibility (Pfeiffer and Kirkegaard 2005; Coffey et al. 2011).

Importantly, many arboviruses are zoonotic (transmittable from animals to humans), representing a severe danger for public health (Kuno and Chang 2005; Weaver and Reisen 2010). About 300 types of mosquitoes are able to transmit arboviruses, which only represents less than 10% of all mosquitoes living worldwide. Representatives of the species Aedes and Culex transmit the highest number of different viruses. Thus, only a minority of mosquitoes can even serve as a viral vector. Besides the horizontal transmission between two hosts (from vertebrate to vertebrate), arboviruses can also be transmitted vertically to the arthropods' offspring.

The spatial distribution of arboviruses is absolutely connected to the habitat of the arthropod vector, while the temporal distribution depends on the seasons—e.g., arthropods are most active during warm periods. The spread in human populations, on the other hand, depends on several other factors: urbanization, growth of the population, using new ecosystems, increased traveling, climatic changes, and resistance against biocides.

As viruses do not possess genes encoding proteins necessary to execute their own life cycle, they are classified as obligatory intracellular parasites that depend on a host cell to replicate. This genome limitation forces them to adapt perfectly to the host cell conditions (Diehl and Schaal 2013). Replicating in two completely different hosts—like vertebrates and arthropods—however, puts even more adaptive pressure on a virus (Turner et al. 2010; Forrester et al. 2014). But what are the requirements for a virus to be transmitted by arthropods?

In case of biological transmission, the lifecycle of arboviruses within the mosquito begins with the blood meal, whereby they are taken up and initiate the infection in the midgut. They then disseminate to secondary tissue, where further amplification takes place. This is followed by infection of salivary glands and the release of viruses into salivary ducts. When the infected mosquito then sucks blood from a new vertebrate host, a fresh virus generation gets transmitted within the saliva (Hardy et al. 1983). Within the mosquito, the escape from the midgut seems to be a critical bottleneck for many viruses. To leave, they need to infect the epithelial cells (Franz et al. 2015), of which only a few cells seem to be permissive (about 20–30% of cells get infected) even with a high virus dose (Smith et al. 2008). Thus, very high viral titers are required for efficient arbovirus infection.

Besides these tissue barriers in mosquitoes to overcome, arboviruses are faced with the two different immune responses of their arthropod and vertebrate host, respectively. Though arthropods do not possess the powerful immune system and the humoral antiviral response of vertebrates, they also react to an infection and are capable to produce antiviral factors (Fragkoudis et al. 2009; Cheng et al. 2016). However, our knowledge of the insect antiviral response is very poor compared to our knowledge of the vertebrate system. But due to whole genome sequencing, many advances have been made during the last years (Nene et al. 2007; Arensburger et al. 2010).

An essential and best studied antiviral mechanism in arthropods is the RNA interference (RNAi) pathway (Wang et al. 2006; Sanchez-Vargas et al. 2009), though signaling of evolutionary conserved innate immune response pathways like Toll, Imd, and Jak-Stat also exists (Xi et al. 2008; Fragkoudis et al. 2009; Merkling and van Rij 2013). The RNAi pathway senses and cleaves viral RNA to inhibit the virus spread. Most of the studies elucidating the mechanism of RNAi in insects have been performed in the fruit fly *Drosophila* (Wang et al. 2006). Even though the existence of orthologues of core components of the pathway in genomes of mosquitoes indicate conserved structure (Christophides et al. 2002; Waterhouse et al. 2007), we have to keep in mind that *Drosophila* doesn't serve as a viral vector and consequently differences in the molecular biology cannot be excluded.

In principal, the RNAi pathway processes as follows: The infiltrated viral RNA is cleaved into 21-nucleotide-long RNAs by the cellular endonuclease Dicer-2, and the RNA molecules then associate with proteins into an RNA-induced silencing complex (RISC) to guide cleavage of further viral target sequences and thus minimize virus spread (Galiana-Arnoux et al. 2006; van Rij et al. 2006). RNAi is an important antiviral mechanism in arthropods—when RNAi genes are silenced, higher infection rates and severe course of disease are observed (Campbell et al. 2008; Samuel et al. 2016). Beside this well -studied RNAi pathway, recent analyses suggest that the PIWI-interacting RNA (piRNA) pathway also plays a critical role in antiviral strategies as piRNAs are newly synthesized in vector mosquitoes as a response to viral sequences (Miesen et al. 2015, 2016). However, as the pathway was primary only thought to function in genome integrity of germ cells, this illustrates our lack of knowledge about the immune system of arthropods. Though some viral strategies to escape the mosquitoes' immune responses exist (Fragkoudis et al. 2009; Bronkhorst and van Rij 2014), there seems to be a well-balanced trade-off between the immune response and the viral spread (Kang et al. 2008). This is illustrated by the fact that arboviruses do not cause clinical symptoms or influence the behavior or the life span of mosquitoes (Liang et al. 2015; Xiao et al. 2015). Thereby, it is guaranteed that the host remains infectious through its entire life. Suppressing the immune response in *Aedes aegypti* cell cultures or in living mosquitoes results in higher infection rates of the alphavirus Sindbis virus (SINV) and increased mortality (Cirimotich et al. 2009), which would be detrimental to the virus.

On the other hand, vertebrate host can suffer severe diseases, clear the arbovirus infection or die from it. Within the human host, the virus is faced with two defense mechanisms: the innate and the more specialized adaptive immune response. The dengue virus, for instance, is injected from the mosquitoes' salvia into the bloodstream of the vertebrate host. The virus then infects nearby keratinocytes (the most common type of skin cells) and dendritic cells, which then migrate to the lymph nodes (Diamond 2003), where the virus is counteracted by the IFN-dependent innate immune response and later also by neutralizing antibodies. This leads in most cases to the recovery of the patient. The virus, however, has evolved strategies to counteract the immune response in and prolong the infection of its vertebrate host (Morrison et al. 2012). Probably, this is because the virus needs to remain at least as long in the host till it generates titers in the blood high enough to infect new hosts.

The other mode of vector-based transmission is mechanically via contaminated mouthparts of the mosquito. In this scenario, no viral replication in the arthropod takes place. This mode of transmission is quite rare and actually prevalently a veterinary problem (Carn 1996; Chihota et al. 2001; Kuno and Chang 2005). However, at least in laboratory experiments, mechanical transmission has been observed. One prerequisite for mechanical transmission is a high virus titer in the blood, because only small amounts of blood can contaminate the mosquito mouthparts (less than 20 nL) (Hoch et al. 1985). Additionally, the virus must resist the environmental conditions outside the host body like temperature or acidity.

3.3 HIV Transmission

HIV-1 is an enveloped virus with two copies of a positive-sensed single-stranded RNA genome. It belongs to the family of retroviruses (subfamily, *Orthoretrovirinae*; genus, *Lentivirus*), which replicate by using a DNA intermediate (Fig. 3.1). HIV infects cells of the immune system expressing the CD4 receptor on their cell surface. This includes T-cells, macrophages, and dendritic cells (Clapham and McKnight 2001). The attachment to the CD4 receptor leads to conformational changes and exposing of the obligate co-receptor. If the co-receptor is the chemokine receptor CXCR4 or CCR5 is determined by the envelope of the particular HIV strain (Berger et al. 1999). The virus then fuses completely to the host cell membrane to unload the viral genome, which is then translated into double-stranded DNA by the viral transcriptase, which had been incorporated in the viral capsid. The DNA is then imported into the nucleus where it gets integrated in to the host cell genome. This stable integration in to the host genome is the reason, why the infection with HIV persist a lifelong. To produce 18 protein isoforms form only a 9 kb genome, the virus highly relies on pre-mRNA splicing, a process during which intronic sequences are removed and exonic sequences are ligated to build the mature mRNA. Through alternative splicing, which enables differential usage of splice sites, various transcript isoforms originating from one genetic template and thus potentially different proteins are generated (Nilsen and Graveley 2010), enriching the proteomic diversity. To produce the different proteins, HIV completely relies on the cellular spicing machinery (Purcell and Martin 1993). After the translations of these mRNAs into proteins, they get along with two copies of the viral genome enclosed into nascent capsids. Finally the mature virions are released and able to infect further cells.

After initial infection, patients may not suffer from severe symptoms expect flu-like illness. This phase is followed by an asymptomatic stage with an average length of 8 years. Meanwhile, the patients stay infectious. Over time, more and more CD4+ immune cells get irritated by the virus and the constitution of patients' declines. The weakened immune system makes them susceptible for opportunistic infections, which eventually cause their death.

In principal, the transmission of HIV-1 by mosquitoes could take place via the two already descripted ways: biologically or mechanically. These possibilities are discussed below.

3.3.1 *Biological Transmission of HIV by Mosquitoes: Possible?*

For biological transmission by mosquitoes, the respective virus has to successfully replicate within the arthropod host. Having a closer look at the first step during HIV replication, the possibility of a transmission by mosquitoes already becomes highly questionable. As already mentioned, to enter a host cell, the CD4 and either the CXCR4 or CCR5 receptors have to be expressed on the cell surface, which is only true for certain cells of the immune system in higher eukaryotes. Mosquitoes lack cells harboring any of these receptors. As a consequence, absorbed HI viruses cannot enter any cells within the arthropod and thus disappear about 1–2 days after the uptake, which is exactly the amount of time mosquitoes need to digest their blood meal (Bockarie and Paru 1996). In comparison with HIV, arboviruses have a relatively broad cell tropism. Dengue virus, for example, seems able to use many different molecules for the cell entry such as sulfated glycosaminoglycans, lectins, laminin-binding proteins, and glycosphingolipids, both in the vertebrate and arthropod host (Table 3.1) (Hidari and Suzuki 2011).

Imagining that the virus somehow overcomes this hurdle and enters epithelia cells within the arthropods gut, another bunch of barriers is waiting. Several studies showed that hundreds host cell proteins, referred to as dependency factors, are necessary for an efficient HIV replication (Brass et al. 2008; Konig et al. 2008; Zhou et al. 2008; Murali et al. 2011). These proteins are involved in RNA metabolism, protein translation, intracellular transport, or DNA replication. To gain control over the regulation of these cellular processes, virally encoded proteins tackle a spectrum of host cell signaling pathways, which control these activities (Diehl and Schaal 2013). Many of these human proteins involved in HIV replication only have an orthologous gene product with rare similarities in mosquitoes. Considering the genetic differences between humans and *Aedes* species, for instance (*Aedes*, 12,000 genes; humans, 23,000 genes), it becomes obvious that these organisms differ a lot in their molecular biology.

Having a closer look at one essential cellular mechanism for the virus, splicing is only one example of the fine-tuned adaption of the virus to its mammalian host: as already mentioned HIV encodes for 18 protein isoforms, which are all generated from its relatively small 9 kb genome (Jager et al. 2011). To produce several different transcripts ordered and balanced from a single primary transcript, the virus uses extensive alternative splicing (Karn and Stoltzfus 2012). Thereby, not only the specific amount of each mRNA but also its timely expression is critical to the success of the viral life cycle (Klotman et al. 1991; Purcell and Martin 1993). To perform and

coordinate alternative splicing, HIV uses the cellular splicing machinery. This does not only include the host spliceosome, the multi-protein complex that performs the splicing reaction, but also a network of different splicing regulatory proteins. Already minor changes in the amount or the activation status of these proteins are detrimental for the viral replication. Hence, this precisely adjusted system is quite sensitive and unresisting to modifications and perfectly adapted to the human host.

Aside from these molecular requirements of HIV, there are other factors within a mosquito making the life cycle or even the survivor of the virus nearly impossible. As an enveloped virus with a quite instable envelope composed of viral glycoproteins and lipid bilayers taken from the host cell membrane, HIV isn't able to exist for a long time outside a cell (Tjotta et al. 1991; Abdala et al. 1999, 2000). The virus is very sensitive to changes in pH values: below a pH of 5.7, the virus gets destroyed within hours, and also values above 8 are deadly for the virus (Ongradi et al. 1990; Tjotta et al. 1991). Within the mosquito gut pH values between 8.5 and 9.5. were measured (del Pilar Corena et al. 2005), representing a destructive viral environment. Taking together, HIV is not able to enter mosquitoes' cells because of the lack of the respective receptor. Despite that, factors that would be necessary for the viral replication within in the host cell are partially missing in insects. As a consequence, HIV is destroyed in the mosquitoes gut, and thus the biological transmission can technically be excluded.

3.3.2 Mechanical Transmission of HIV by Mosquitoes: Possible?

Having now agreed that biological transmission of HIV by mosquitoes is virtually impossible, what is about mechanical transmission?

Besides the sexual and mother to child transmission, needle sharing among drug users is an increasingly important cause of HIV transmission worldwide. Thereby, contaminated blood in needles, syringes, and paraphernalia are the main sources. During every injection, blood from the user gets inserted into the needle and syringe. If this user is HIV positive and another uninfected drug users utilizes the same paraphernalia without cleaning, the potential virus contaminated blood directly gets injected into the bloodstream, where the virus immediately can infect its target cells without having the hurdle of tissue barriers. Nowadays, people who inject drugs account for 30% of new HIV infections outside the sub-Saharan Africa. Yet, a single incident of shared needle or syringe will not necessarily lead to an HIV infection. The estimation of the infection risk from one injection ranges from 0.6 to 2.4% (Baggaley et al. 2006). The high numbers of newly infected persons who inject drugs can probably be explained with the frequency of contaminated needle usage.

The question is: is there a difference between a needle and a mosquito?

The process of blood sucking by mosquitoes and the injection of drugs with needles highly differ in the mechanism: during blood sucking, mosquitoes send salvia via one tube into the host and suck the host's blood via another tube. The

salvia is composed of substances that prevent blood clotting and platelet aggregation along with vasodilatory substances (Ribeiro and Francischetti 2003). In addition, the salvia contains ant-inflammatory and immunosuppressing proteins, which seem to facilitate viral infections (Edwards et al. 1998; Schneider et al. 2010; Surasombatpattana et al. 2012). Consequently, no blood of the previous host gets injected into the new host. Hence, infection could only appear from blood that glues on the mosquitoes mouthparts. However, this could only be possible for very little amount of blood and thus viral particles. Calculations estimated that more than ten million bites of a mosquito with HIV contaminated mouthparts would be necessary for a HIV-free person to receive a single unit of the virus (Bockarie and Paru 1996).

In sum, mechanical transmission of viruses by arthropod vectors depends on the amount of blood (and the respective virus load) and the way an HIV-free person gets "injected." While shared needles contain considerably higher amounts of blood that directly get injected into the blood stream, potential amounts of HIV-containing blood on mosquito mouthparts can be neglected. Moreover, no blood gets injected into the host during blood sucking.

3.4 Summary

Taken together, we can answer the question asked within the title with a clear "not possible." For biological transmission the virus would need to replicate within the arthropods host, which we have seen can be excluded for the highly specialized HI virus. For mechanical transmission, however, the amount of blood with which the mosquito mouthpart could be contaminated with is by far too low for an infection. In addition, HIV is a quite sensitive virus and thus gets destroyed quite soon outside a host cell. The fact that arthropod-specific viruses are ancestral to arbovirus and that no host change in the other direction has been reported yet makes a mosquito transmission of HIV even more unlikely. Yet, a scenario, in which an arthropod-specific virus, we only don't know, undertakes a host-switch in the future and causes symptoms comparable to HIV, may not be excluded.

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