Are we ready for the tropics? - Tropical viruses

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3. Abstract

Arthropod-borne viruses are a threat to human health. Infections can occur after the bite by a vector, like mosquitos. The *Aedes* mosquito species are shown to be capable of transmitting tropical arbo-viruses including Zika, Dengue, Yellow Fever and the Chikungunya virus. Globalization and climate changes are increasing the spread of *Aedes* mosquito thus also the spread of arboviruses. Factors including temperature, humidity and rainfall are affecting the environment suitability, transmission potential, mosquito development, survival, reproduction rate, biting rates and the virus incubation time. In the recent years, infections are occurring in Southern Europe, whereas they were found absent before. Detection of these tropical arboviruses can be done by PCR and serological assays. The spread of the *Aedes* species is mainly caused by the demographics, trading and climate change resulting in an increase of the tropical virus threat to public health.

4. Introduction

Arthropod-borne viruses (arboviruses) are defined as viruses that are transmitted to humans after a bite of an infected arthropod, like mosquitos, ticks and midges[1]. These days over 500 different arboviruses are known worldwide[2]. Important tropical arboviruses described in this review are Dengue (DENV)[3], Zika (ZIKV)[4], Chikungunga (CHIKV)[5], and yellow fever virus (YFV)[6].

The *Aedes* mosquitos are playing an important role in the spread of these arboviruses. Therefore the geographical distribution of the arthropods needs intense research. Part of the increasing interest of the spatial spread of the *Aedes* mosquitos is relying on the fact that these mosquitos are now present in countries, where they were absent before. The presence of mosquitos results in an increased risk for human health by acquiring some of these arboviruses. The expansion of the mosquito breeding area is mainly due to climate change, urbanization and trade[7]. These factors are associated to the globally spread of arboviruses. How climate change affects human health and influences arbovirus transmission are discussed in this review.

It is necessary to understand the biology of the host, mosquito and virus. The role of climate change, trading and urbanization on the dynamics of these diseases will be explored and discussed and topics on laboratory diagnosis and preventive measures will also be described.

5. Mosquito vectors play an important role in viral infections

Viruses can be transmitted in many different ways. Transmission can occur through droplets on the body surface, like the eye, nose or mouth. Respiratory transmission is possible through e.g. sneezing, for example the Influenza virus. The residue of evaporated droplets or dust particles containing viruses can be transmitted through the air. This airborne way of transmission can cause infections in the upper or lower respiratory tract. Another transmission method occurs by faecal-oral contact that affects micro-organisms from the digestive system[2]. Sexual transmission is possible through a few viruses, including the ZIKV[8].

A vector is an organism that transmits infectious agents from one species to another. Vector-borne transmission is caused by the bite of an infected arthropod. Vector-borne diseases are responsible for over 17% of all infectious diseases. This results in 1 billion cases annually and 1 million deaths[9]. A recent estimation indicates annually 390 million DENV cases. Approximately a 100 million cases are clinically manifesting[10,11] and it is believed that DENV is the most prevalent virus[12].

Arthropods require blood meals from a host (i.e. humans or non-human primates) to feed themselves. During this process, the vector is transmitting infectious micro-organisms to the host. Also an infected host can transmit the virus to the vector. So the viral cycle is maintained between host and vector. Other examples of vectors are sandflies, black flies, fleas, ticks and mosquitos. The geographical areas where the mosquitos are developing, depends on the mosquito family and habitat[13].

The role of mosquito transmission cycles within viral infections

The different habitats and the mosquito species, results in briefly two cycles: the sylvatic and urban cycle[14]. The sylvatic cycle is mainly found in the tropical rainforest. The monkeys and mosquitos are the primary reservoir for the virus[15]. Travelers can be infected by one of these infectious mosquitos[14]. Large epidemic outbreaks occur mainly in the urban cycle. Urban areas are highly populated areas, where the transmission cycle can be maintained between mosquito and human. A virus introduced to these heavily populated areas with high mosquito density, can result in an outbreak. *Figure 1* shows the different mosquito transmission cycles[16].

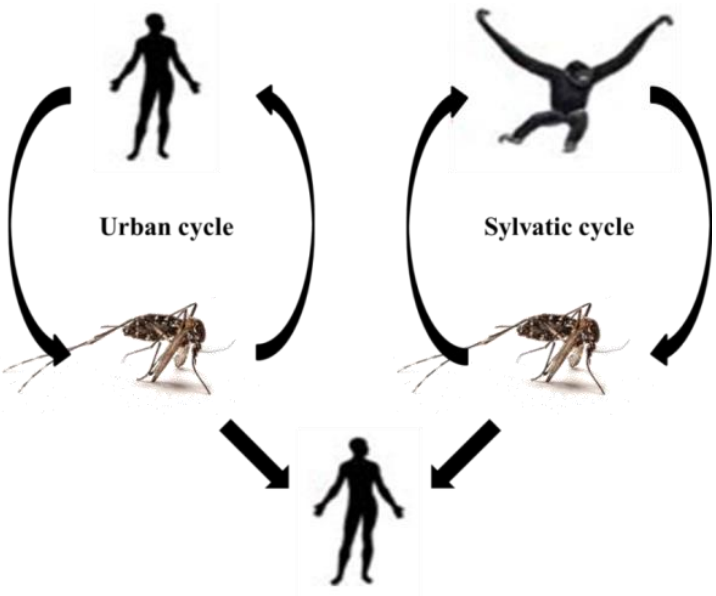

Figure 1 - Transmission cycles

The sylvatic cycle is maintained between monkeys and mosquitos Sometimes the virus is transmitted to humans. The urban cycle is maintained between humans and mosquitos. This figure is adapted from[16].

6. *Aedes* mosquito family play a major role in tropical diseases

The *Ae. aegypti* and *Ae. albopictus* mosquitos are vectors for Dengue (DENV)[3], Yellow fever (YFV)[6], Chikungunya (CHIKV)[5], and the Zika virus (ZIKV)[4]. These viruses are described in more detail in section 7. This section will elaborate on the mosquito species.

Aedes aegypti

Ae. aegypti is commonly known as the vector for yellow fever. The worldwide spread of *Ae. aegypti* is largely due to globalization. In the 15th to 18th century, slavery ships having mosquitos on board were causing a global spread from Africa to America[17], and throughout the tropical and subtropical regions [18–20]. Currently, the spread of the mosquitos are continuing through the transportation of eggs by international trade[17,21].

Ae. aegypti have evolved a preference for the most available and stable blood source which are humans [17,22,23]. The number of blood meals varies for each mosquito. The amount of blood is having an effect on the number of eggs, usually between 100 to 200 eggs[24]. These eggs can be spread by the mosquito and this can take hours to days[25].

Ae. aegypti is breeding in various places, like flower pots, spare tyres, water pools and drainage ditches[17,19,21]. The mosquitos are moving into urbanized areas and therefore they are having contact with humans. *Ae. Aegypti* is highly prevalent in settlements where no piped water systems are, so water accumulation in numerous containers and tanks is taking place. This creates suitable breeding sites for the mosquitos[26]. The larvae can remain in the larval stage for months as long as the water supply is sufficient[27]. It usually takes up to seven days for an egg to develop into a mosquito. The adult life span of the mosquito ranges from two weeks to a month[28].

Aedes albopictus

The *Ae. albopictus* is also known as the Asian tiger mosquito. The *Ae. albopictus* was first described 120 years ago by collected samples from Calcutta, India[29]. The original distribution is located in Southeast Asia, Northern China, Japan, Madagascar and on the islands of the Pacific and Indian ocean. *Ae. albopictus* spread to Northern and Southern America and Europe in the 1980s[30–32]. It is likely that the spread of *Ae. albopictus* was established by trading products, like used tyres and lucky bamboo that contained eggs[30,32–36]. The mosquitos deliver their eggs in natural and urban settlements such as places like tree holes and water-holding plants[34]. The mosquito species are active throughout the year in warmer conditions, like tropical and subtropical areas.

The *Ae. albopictus* species are more aggressive biters with a larger variety of hosts[19,32], and are having a larger distribution worldwide[37] and they are less susceptible for lower temperatures than *Ae. aegypti*[38]. *Ae. albopictus* are primarily forest species adapted to the rural, suburban and urban environment. The *Ae*. *aegypti* species are more domestic[33].

7. Different types of tropical viruses

The virus family Togaviridae (genus Alphavirus) and Flaviviridae (genus Flavivirus)[39] are associated with some diseases. The word "flavi" means yellow, which is associated with the Yellow Fever virus. The genome of a flavivirus consists of a single stranded positive sense RNA, linear non-segmented which is approximately 11 kb long[37,40]. The virus is icosahedral shaped viral capsid[40], approximately 40-50nm in diameter and composed of a single type of capsid protein[40]. Members of the flavivirus family includes ZIKV, YFV and DENV[41].

Yellow Fever virus

The YFV is mainly found in tropical and subtropical areas of Africa and Southern America[20]. The virus requires an incubation period of approximately 3 to 6 days and in most cases, the symptoms disappear within 3 to 4 days[14]. The infection can cause symptoms including fever, jaundice and hemorrhagic manifestations. The name "yellow" in yellow fever is linked to jaundice, where the skin and eyes of patients appear yellow, caused by liver cell degradation[14]. The symptoms look similar to that of hepatitis. The World Health Organization (WHO) estimates 200.000 cases and 30.000 deaths each year[42,43].

Human species living in endemic areas were able to develop protective immunity against the virus. The symptoms look similar to that of an influenza infection[44]. Most Europeans and Americans in these endemic areas died because of lack of immunity against the YFV. The first reported outbreak of the YFV was on the island of Barbados in 1647[44]. In 1881 people thought that yellow fever was transmitted from human to human[45,46]. Two centuries later, scientist Carlos Finlay had a theory that yellow fever was caused by the transmission of infected mosquitos. During the Spanish- American war in Cuba many people died of yellow fever. In 1901, a research team led by Walter Reed, confirmed Finlay's theory on the cause of yellow fever. This was obtained through the study of several volunteers, which were bitten by YFV infected mosquitos and developed yellow fever within days[47].

The key for preventing outbreaks in countries at risk is routine vaccination and it also protects travelers who are visiting YFV endemic areas to become infected[48]. YF-17D is a live attenuated vaccine, providing a long lasting immunity[39]. The YF-17D vaccine introduces life-threatening diseases in rare cases[49], such as multiple organ dysfunction and severe hypersensitivity reactions[50]. Despite the fact that these risks are very low, a vaccination is recommended for people who are at risk.

Dengue

DENV is a mosquito-borne viral disease, also known as break-bone fever[20]. The virus spreads rapidly worldwide in the recent years due to globalization and urbanization[51]. It mainly effects Asian and Latin American countries[10]. In terms of geographical distribution, morbidity and mortality, DENV is

considered as the most important arboviral disease[12,10]. Accordingly to recent estimations 3.9 billion people in 128 countries are at risk for DENV infections.[14] Approximately 390 million people are becoming infected each year[52]

20% of the DENV infection cases develop symptoms like fever, headache, skin rash, muscle and joint pain[53]. The DENV family consists of four serologically distinct serotypes (DENV-1 to -4). All serotypes can cause dengue-related disease symptoms from the unapparent to the severe forms[54]. Recently, a fifth DENV serotype was found[55]. Nowadays there is very little known about this serotype.

People, recovering from a primary DENV infection, are producing antibodies against the virus. A re-infection of a homologous serotype is prevented by the immune system. A secondary infection with a heterologous serotype can result in cross-reaction of the antibodies of the distinct serotypes. This can help the DENV spread, increasing the number of virus particles[56,57]. Dengue hemorrhagic fever (DHF), also known as severe Dengue, is widely associated with the secondary heterologous infection[58]. Severe Dengue can result in death[59], mainly in Asian and Latin American countries who are affected due to the presence of multiple serotypes[10].

Currently, a vaccine is available against DENV called Dengvaxia (CYD-TDV)[60], developed by Sanofi Pasteur and is covering the DENV 1-4 serotypes. Parts of the population in endemic areas are vaccinated to reduce future disease burdens[61]. The vaccination efficacy varies by serotype: 55% for serotype 1, 43% for serotype 2, 72% for serotype 3 and 77% for serotype 4. The vaccination of a child has a lower efficacy[47]. There are 5 more vaccines in clinical trials[14].

Zika virus

The ZIKV is named after the place of its discovery, the "Zika forest", located in Uganda. The first ZIKV identification was obtained from a rhesus monkey who lived in 1947 in the South of Uganda. The virus was identified in the *Ae. africanus* mosquito species caught in the Zika forest[62]. The ZIKV was identified in humans in 1948. A ZIKV infection results in 30% of the cases in symptoms that includes fever, skin rash, conjunctivitis, headaches, and arthralgia[41,63]. So far, there are no reported deaths associated with the ZIKV[64].

The first reported ZIKV outbreak was located in the Western Pacific island of Yap, Federated States of Micronesia in 2007[65]. The virus have spread fast on the island. 73% of the population became infected through the *Ae. hensilli* mosquito species within 4 months[66]. Recently, the largest ZIKV outbreak has occurred in French Polynesia with 31.000 suspected cases (over 60% of the population) during 2013-2014[41,51,67]. Another ZIKV outbreak during 2015-2016 with over 4.000 cases within 4 months has

occurred in Brazil. Studies associated microcephaly in neonates within a pregnant women who is infected with ZIKV. The chance of microcephaly in neonates increases by 20-fold after an infection[68–71]. Another disorder called Guillain Barré is also widely associated with a ZIKV infection[72]. Guillain Barré is a disorder that attacks the immune system. Both disorders introduce a risk for public health.

There is currently no vaccine available[73]. Nevertheless, a vaccine called VCR 705 is in phase 2 of clinical trials. The production of the vaccine is led by the National Institute of Allergy and Infectious Diseases (NIAID)[49].

Chikungunya virus

Chikungunya is written in the Makonde language, which means "that which contorts or bends up". This refers to severe arthritis and joint pain that is caused by this disease. 85% of the cases develop symptoms, like high fever, headache, skin rash, photophobia and severe joint pain. Chronic joint pain is the most common symptom that can last for months to years[74–76]. In elderly people and patients with comorbidities this disease can cause death[77].

Phylogenetic analysis is suggesting of African origin approximately 500 years ago, with spread to Asia within the last century[20]. The *Ae. aegypti* mosquito species caused a CHIKV outbreak in Southern Tanzania in 1952[77,78]. CHIKV was spread to la Réunion, a French island in the Indian Ocean during 2005-2006. Over 40% of the population became infected, resulting in 273 deaths. The outbreak was caused by the *Ae. albopictus* mosquito species[74]. Furthermore, 1.5 million cases were the cause of an outbreak in India and some cases in Europe including Italy[79] and France[80,81].

Currently CHIKV is identified in over 60 countries in Asia, Africa, Europe, Northern and Southern America[77]. A spread and an outbreak of CHIKV occurred in 9 Latin American and 28 Caribbean countries during 2013-2014[82–84]. Despite efforts to develop vaccines, there are no licensed vaccines for CHIKV available[84].

8. Changes of the environment in mosquito and virus spread

The climate plays a major role in thriving tropical virus transmission. Climate factors including temperature, humidity and rainfall patterns are affecting the environmental suitability and transmission potential of the *Aedes* mosquitos and arboviruses[85–92]. The worldwide climate change is mainly due to human activities. The atmospheric concentrations of different gases increases. These gases include carbon-dioxide, methane and nitrous oxide. They cause an increase of global temperature[93], resulting in the melting of the polar and alpine ice[94]. Change of precipitation patterns, increase of extreme weather, rise of the sea level[95], increases risks for wildlife[96] and loss of biodiversity[95].

The climate change broadens the range of *Aedes* mosquito distribution. Changes in local climates are related to the occurrence of disease outbreaks[97]. The changes in the temperature can interact synergistically with both infectious and chronic diseases occurrence[98]. Mosquitos are ectotherms, their body temperature depends on the temperature of the environment. The minimal threshold of the development of *Ae. albopictus* is at 10°C[99]. The optimal temperature for mosquito development is found at 30°C[99]. The time between an infected human and the onset of symptoms is called the intrinsic incubation period. The extrinsic incubation period is the viral incubation period, this is viremic blood meal until the mosquito becomes infectious[100]. Both periods are highly temperature affected. Higher temperatures increases the DENV replication rate and shortens the extrinsic incubation period[101–103]. The extrinsic incubation period was 12 days at 30°C and is reduced to 7 days at 32°C[101]. The hatching process of the mosquitos is also highly influenced by temperature. An optimal temperature is approximately 24-25°C, resulting in a 95% hatch within 24 hours. Temperatures between 29-30°C result in a significant decrease in a 10% hatch within 24 hours[104]. These results reveal that temperatures above 25°C, result in decreased hatching. Mosquito development is also significantly decreasing in body size[105] and wing length[104]. Rates of multiple blood meals are increasing with higher temperatures[106].

The warming up of cooler areas in the world, brings the optimal temperature of vectors closer[107–109]. A rise of temperature in warm areas, are removing the optimal temperature of the vectors.. *Aedes* mosquitos are domestic and they will find a cooler environment inside homes. Arboviruses transmitted by mosquitos in temperate regions, cause disease in summer during periods of increased vector activity. Arboviral infections usually occur during the wet season in tropical areas, providing more mosquito breeding sites. This results in an increased number of mosquitos. Nevertheless, less proper water supplies are occurring in poor countries. Water accumulation creates a suitable environment for mosquito reproduction throughout the year. The effects of climate change and environment in arbovirus transmission are shown in *Figure 2*.

Urbanization plays also an important role in the climate change. Many urban areas in the tropics are growing. Bigger cities are turning into megacities[110]. The globally urban population will increase from

34% to 54% between 1960-2014, [111]. It is expected that the population in tropical climates within Asia and Africa will increase by 1.1-1.5 % per year by 2050[112]. Urbanization changes the habitat and climate throughout a city, by turning it into a warmer region[7]. These warmer regions cause shifts in the temperature distribution. The occurrence of Socio-economic variables influences arboviral disease. Poor areas lack proper settlements and public services, such as garbage collection or water supply, which reinforces the establishment of mosquito breeding sites[26].

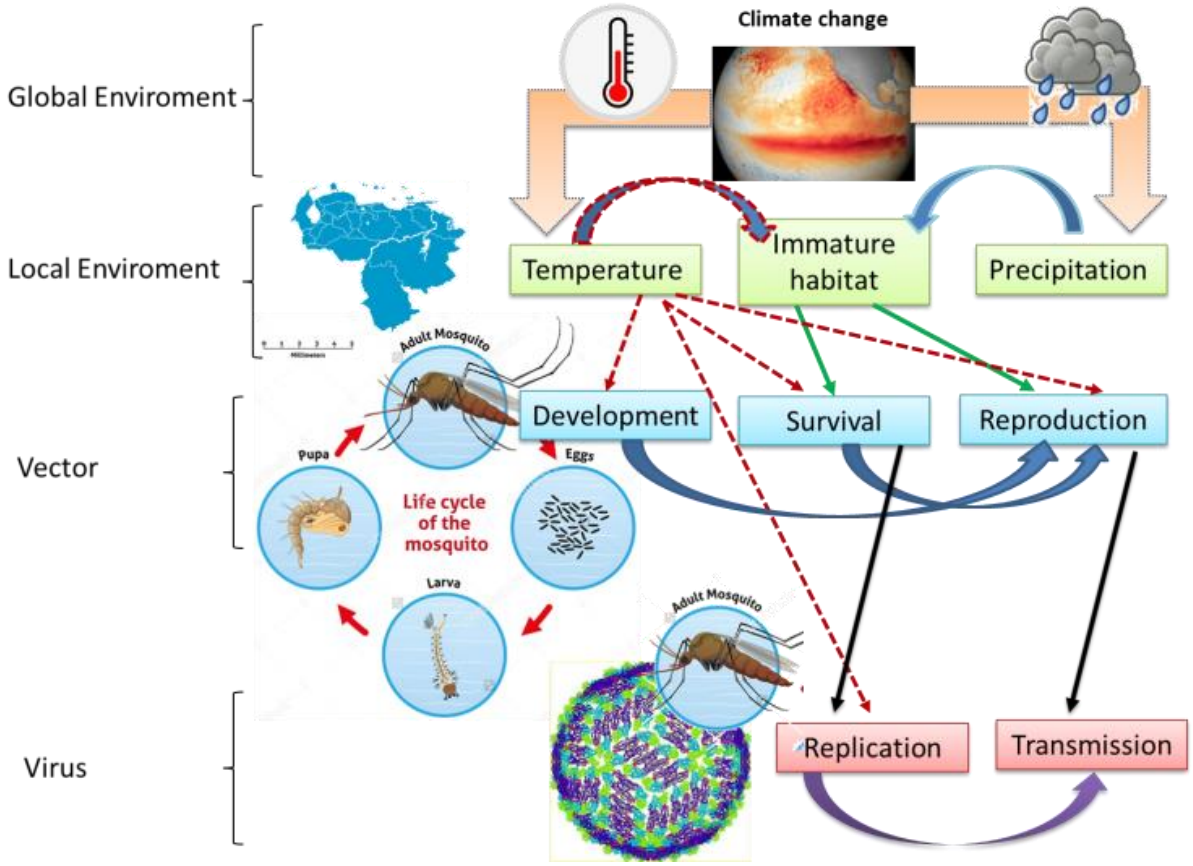

Figure 2 - Schematic overview of environmental affects in virus transmission

Global and local environment are both affected by the climate change. Temperature and precipitation affect the immature habitat. Temperature is playing a major role in the development, survival and reproduction of the Aedes mosquitos This affect the replication and transmission. This figure is adapted from Morin et al, 2013.

9. Mosquito prevention and control

The risk of infection by mosquitos can be reduced and controlled in different ways. To prevent mosquito bites it is recommended to use repellents, like DEET, Picardin, IR353, lemon eucalyptus, paramenthane-diol or 2-undecanone. Wearing long-sleeved shirts and pants and the use of a mosquito net at night provides also protection[113]. When a larger number of mosquitos are found or when people in a large area get infected by the arbovirus through mosquitos, airplanes with insecticides can be used. This is an effective and quick way, called aerial spraying. Aerial spraying is also affecting other stages of the mosquito, like the larvae. The efficacy of the insecticide can be increased by using multiple aerial sprayings. Aerial spraying can also be conducted by using Naled, which has already been used in many populated areas of the United States. Naled is a molecule that easily can be degraded into 2,2-dichlorovinyl dimethyl phosphate (DDVP) in sunlight, water and on the surface. Low concentrations of DDVP don't cause any health problems for humans[113,114].

A biological enemy of the mosquito larvae is the bacteria *Bacillus thuringiensis israelensis* (Bti), first discovered in Israel in 1976. It was found in soil and is capable of killing larvae of mosquitos within 24 hours[115]. Bti is safe for humans and other animals. The efficiency of Bti depends on mosquito species. Bti is less susceptible for the *Ae.* species[116].

Another biological enemy of mosquitos is the bacterial symbiont *Wolbachia. Wolbachia* are proteobacteria that can infect a wide range of vectors, including *Aedes* mosquito species[16]. Through RNA interference can *Wolbachia* provide resistance against viruses, like the DENV in *Ae. aegypti* mosquitos [114,117]. Researchers genetically modified *Ae. aegypti* to express *Wolbachia*. The modified mosquitos were used in the field to suppress the spread of the arboviruses with success[118,119]. These trials indicate that high *Wolbachia* infection frequencies can be established across large urban areas through local releases[119].

10. Laboratory detection of arboviral infections

Due to the threat of the arboviruses the detection of the arboviruses is important in controlling and preventing outbreaks. After an arboviral infection, the virus multiplies in local tissue and regional lymph nodes and activates the early immune response[39]. The viral RNA can be detected within 5 days post infection[120]. Molecular diagnostics for arboviral RNA detection can be done on different body fluids including whole blood, EDTA (ethylenediaminetetraacetic acid) plasma, saliva, eye moisture and urine. For the detection of the viral RNA is a real-time polymerase chain reaction (RT-PCR) and a universal PCR a suitable assay. This assay method is based on the amplification of the N-terminal of the NS-1 and NS-5 gene[120–124].

The innate immune response is activated within 4 to 7 days post infection. IgM antibodies appear in the first days after illness onset, IgG antibodies are produced within 7 to 14 days. The IgM antibodies are present for many months, characteristic for an arboviral infection[125]. IgM antibodies are only a reliable indicator of a primary infection when no IgG levels are found. The recovery of an arbovirus infection results in usually a life-long immunity against a reinfection with the homologous virus. A good indication of protective immunity is the presence of IgG antibodies[39].

Enzyme-linked immune sorbent assay (ELISA) can be used in antibody detection. Antigens are coated on the well plate, serving as a binding place for the antibody of interest. A labeled secondary antibody can be used to indicate the presence of the antibody of interest. Asides the ELISA techniques immuno-fluorescence assays (IFA) are also widely used. Both ELISA and IFA techniques are used for IgG and IgM detection[39]. Alphavirus RNA can be detected by PCR of the E1 and E2 genes[126,127]. *Figure 3* shows the *Flavivirus* and *Alphavirus* genome.

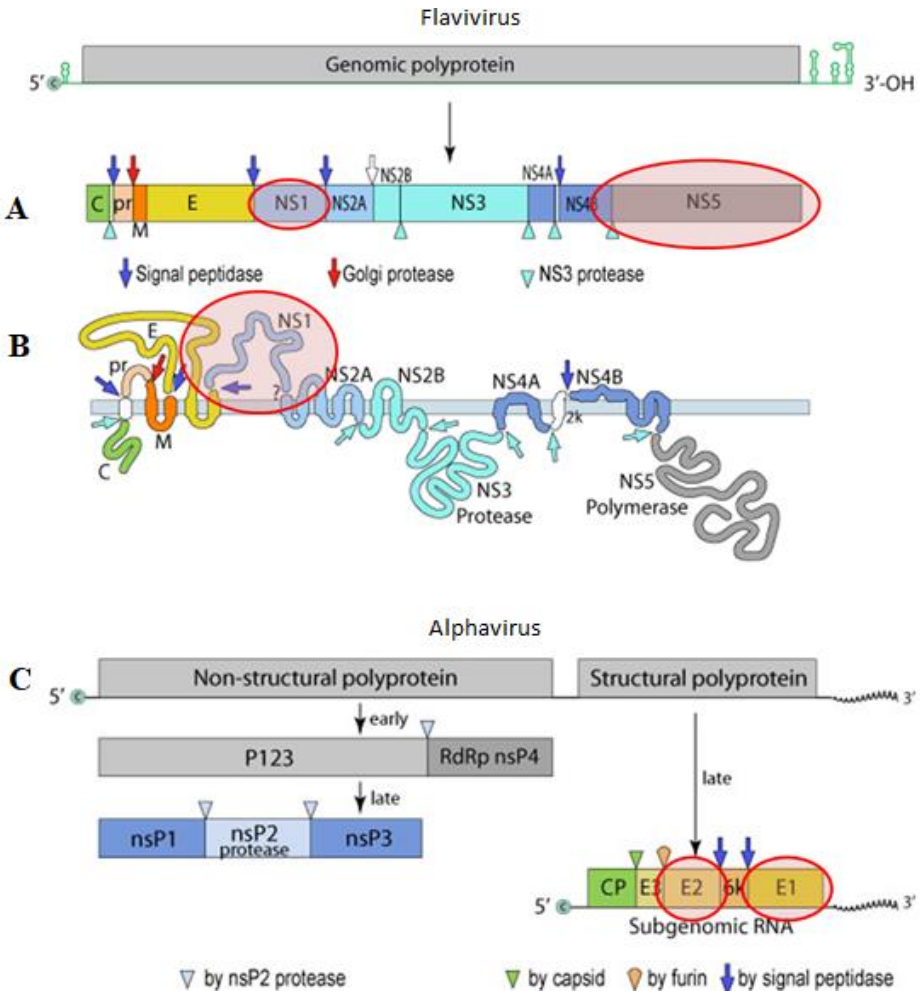

Figure 3 - Flavivirus and Alphavirus genomes

The NS1 and the NS5 genes are located on the flavivirus genome (A). For the Flavivirus detection, techniques like PCR can be performed. Produced antibodies against the NS1 protein (B) can be detected by serological assays, widely used techniques are ELISA and IFA. PCR can also be used for the detection of the E1 and E2 genes, located on the subgenomic RNA of the Alphavirus. This figure is adapted from ViralZone.

11. Conclusion & Discussion

Arboviruses can be transmitted to humans through mosquitos[1]. The *Ae. aegypti* and *albopictus* mosquitos has been shown to transmit tropical viruses, including DENV, ZIKV, CHIKV and YFV[3–6,128,129]. Nowadays increase of global trading and population influences the spread of the *Aedes* mosquitos[17,21]. The habitat of the mosquitos is important for their survival and settlement. A major reason for the expansion of the living areas of the *Aedes* mosquitos occur is climate change. Temperature, humidity and rainfall affect environmental suitability and transmission potential[85–92]. The climate change broadens the *Aedes* mosquito distribution range. The *Aedes* mosquitos are now found all over the world, across all continents. The risk of arboviral infections in these areas can be assessed by determining the *Aedes* mosquito global distribution,. Arboviruses transmitted by mosquitos in temperate regions can cause disease in summer during periods of increased vector activity. In the tropical areas is an increased vector activity during the wet season.

If the climate change trend continues, it will increase the number of vectors and new areas will become suitable for transmission. The rainfall patterns are less predictable, likely the winters become more wet and the summers more dry. The consequences of these changes are hardly to predict, there may be fewer potential breeding sites in the dryer areas. An increase of temperature results in a decreased body size and wing length of the mosquito[104,105]. The number of blood meals is also increased by higher temperatures[106]. This has a negative effect on the mosquitos by making it more difficult to survive. Not just arboviruses cover the increased risk to public health by increasing temperature and urbanization. These factors enhances also air pollution which increases the number of respiratory[130], chronic and cardiovascular diseases[131].

Humanity is creating better circumstances for larval development, habitat and shelter for mosquitos. When the environmental conditions turn bad, the mosquitos can rest indoors. Poverty can result in an improper waste management, sanitation[132] and a lack of piped water systems, which causes the practice of water accumulation[26]. These factors provide proper breeding sites for the mosquitos and contributes to a higher chance of an outbreak after the introduction of an arbovirus. The different factors that play a role in virus behavior are shown in *Figure 4*, and factors that are effected by temperature are shown in *Figure 5*. Investments to install e.g. piped water systems and sanitation can help in mosquito control.

Low concentrations of the insecticide Naled used for mosquito control, has shown not causing any humans health problems[113,114]. Other wildlife, for example bees and wasps may be harmed by the insecticide. More information is necessary, because negative impacts on the ecosystem can be prevented.

Arboviruses (ZIKV, YFV, DENV) are often grouped together according to antigenic similarity. Recovery of one flavivirus may result in protection of other flaviviruses, within the same antigenic complex[39]. Approximately 2% to 4% of patients who have a secondary infection with a heterologous type of DENV, develop more severe illness[16].

Investigation of the distribution of vector and arbovirus are important in control. Therefore, detection methods for viruses are necessary. Multiple assays can be conducted for virus identification, including RT-PCR and sequencing[120–124]. With these methods, virus identification can be done within 5 days after illness onset[120]. Alphavirus (CHIKV) antibodies show limited cross-reactivity and standard tests are usually sufficient to identify the infecting virus, depending on the Alphavirus. Flaviviruses are known to cross-react in antibody responses, which is a major problem in the diagnose of an arbovirus. The IgM and IgG detection does not give a definite evidence of an infection. Specific assays are needed for arbovirus detection and to bypass cross-reactions. The epidemiology is important for the accurate interpretation of arbovirus serology.

The recently developed CYD-TDV DENV vaccine, covers DENV1- to -4 serotypes[60]. The interesting discovery of a fifth DENV serotype in October 2013, introduces a new public health dilemma. The occurrence of the new serotype may lead to new challenges in DENV control. A primary DENV infection, result in a long lasting immunity for that particular serotype. A secondary heterotypic infection is associated with an increase of Dengue hemorrhagic fever and dengue shock syndrome[32]. To reduce DENV infections to prevent the risks of these disorders, a vaccine development is necessary[133].

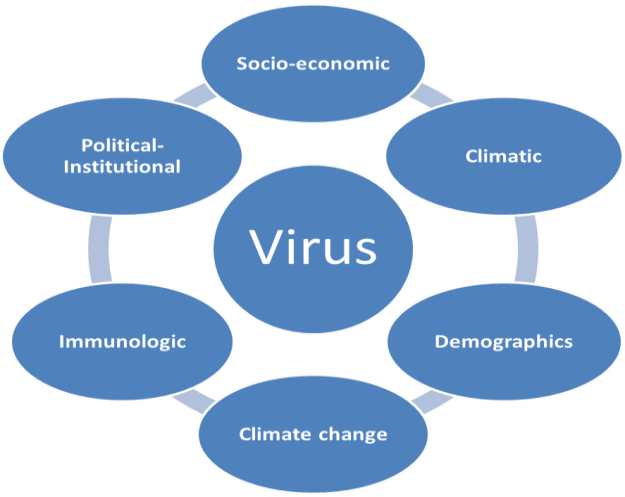

Figure 4 - Factors that play a role in virus behaviour

An arboviral disease is multifactorial. The factors responsible for dramatic resurgence and emergence of arboviruses are not fully understood yet. By demographics we include population growth, unplanned and uncontrolled urbanization[7]*. Socio-economic is linked to the poverty, deterioration in water, sewer and waste management. The climate factors precipitation, temperature and humidity*[77]*. Herd immunity is important in the way of vaccine to prevent arboviral infection. Political-Institutional: decay in public health infrastructures, lack of resources, shortage of trained specialists. Wrong public health policy that applies control and contain the arbovirus rather than prevent and predict.*

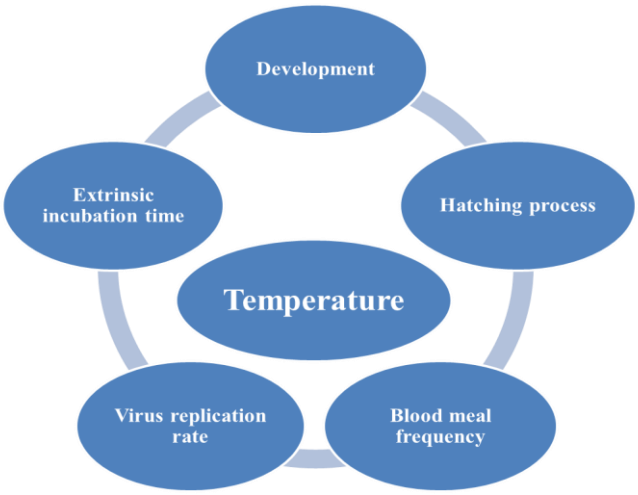

Figure 5 - Increased temperature affect vector and virus.

An increase of temperature shortens the Extrinsic incubation time, alter the development which result is a smaller body size[105]*, increases the blood meal frequency of the mosquito*[106]*. The hatching process has an optimum temperature of approximate 25 ℃ and the hatching process decreases by higher temperatures*[104]*. The virus replication rate is increased by higher temperatures*[101–103]*.*

12. Acknowledgement

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