Climate, environment and transmission of malaria

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SUMMARY

Malaria, the most common parasitic disease in the world, is transmitted to the human host by mosquitoes of the genus *Anopheles*. The transmission of malaria requires the interaction between the host, the vector and the parasite. The four species of parasites responsible for human malaria are *Plasmodium falciparum*, *Plasmodium ovale*, *Plasmodium malariae* and *Plasmodium vivax*. Occasionally humans can be infected by several simian species, like *Plasmodium knowlesi, recognised as a* major cause of human malaria in South-East Asia since 2004. While *P. falciparum* is responsible for most malaria cases, about 8% of estimated cases globally are caused by *P. vivax*. The different *Plasmodia* are not uniformly distributed although there are areas of species overlap. The life cycle of all species of human malaria parasites is characterised by an exogenous sexual phase in which multiplication occurs in several species of *Anopheles* mosquitoes, and an endogenous asexual phase in the vertebrate host. The time span required for mature oocyst development in the salivary glands is quite variable (7-30 days), characteristic of each species and influenced by ambient temperature. The vector *Anopheles* includes 465 formally recognised species. Approximately 70 of these species have the capacity to transmit *Plasmodium* spp. to humans and 41 are considered as dominant vector capable of transmitting malaria. The intensity of transmission is dependent on the vectorial capacity and competence of local mosquitoes. An efficient system for malaria transmission needs strong interaction between humans, the ecosystem and infected vectors.
Global warming induced by human activities has increased the risk of vector-borne diseases such as malaria. Recent decades have witnessed changes in the ecosystem and climate without precedent in human history although the emphasis in the role of temperature on the epidemiology of malaria has given way to predisposing conditions such as ecosystem changes, political instability and health policies that have reduced the funds for vector control, combined with the presence of migratory flows from endemic countries.

Keywords: malaria, climate changes, vector borne diseases.

INTRODUCTION

Malaria is the most common parasitic disease in the world. The parasite is transmitted to the human host by mosquitoes of the genus *Anopheles*.
The WHO reported in 2013 an estimated 198 million of cases of malaria occurred worldwide. Most of these cases (82%) were in the WHO African Region, followed by the WHO South-East Asia Region (12%) and the WHO Eastern Mediterranean Region (5%). *Plasmodium falciparum* is responsible for most of the cases of malaria, but about 8% of estimated cases globally are caused by *Plasmodium vivax*. Outside of the African continent this proportion increases to 47% [1].
Although only *P. falciparum* is considered life-threatening, the lack of severe complications associated with *P. vivax* infection has been recently questioned in several reports [2].
Indeed, it is an important cause of early pregnancy loss, reduced birth weight, severe disease and death in pregnant women and small children [3-6].
Vector borne diseases such malaria are highly influenced by climatic factors, which enhance their

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transmission rate and extend their geographic presence. However to understand the epidemiology of malaria others factors must be considered, like human activities and their impact on local ecology. Climatic factors, especially temperature, play a crucial role on the survival of mosquitoes and their longevity, but they also exert an influence on the rate of multiplication of the parasite into the vector. In cold countries, mosquitoes and parasite have developed strategies to survive during the winter, and on the other extreme, to survive during the dry season [7].
Temperature, rainfall, and humidity are important, as well as the wind and the duration of daylight. The circadian rhythm affects other behaviours of the vector, such as feeding, resting, and oviposition which are restricted to optimum times, regardless of ambient temperature.
Every single element that influences the climate and with it the entire ecosystem, is strongly altered by humans and their activities.
Although forest ecosystems are well known to support transmission of malaria, significantly contributing to the global disease burden, the forest clearance can provide favourable conditions to mosquitoes. Vectors that prefer temporary ground pools exposed to full sunlight like *Anopheles* can find a better condition to larval development, and the proximity of vegetation near human habitation can increases the population of forest vectors of malaria [8].
Additional factors come from behaviour and cultural traits of the exposed population: daily activity patterns, the location of homes in relation to mosquito breeding sites, the kind of housing, the availability of bed nets and the access to the health care system. A crucial role is played by the water employed for agriculture and livestock. Drainage of wetlands can eliminate the breeding sites of the vector. Forest clearance provides a new habitat for vectors of malaria and changes the local microclimates by reducing the shade, altering the rainfall patterns, augmenting air movement. Humidity changes and proximity of cattle to human habitation can shift the behaviours of the anophelines vectors from feeding on animals to feeding on human host.
Moreover, migration, urbanization, degradation of the health infrastructure, war, civil strife, and natural disasters can highly impact on malaria transmission by moving infected people from high endemic countries to areas where the transmission is lower or absent.
Occasional focal outbreaks might occur when malaria transmission extends from the forest shade (nidus) to peri-urban and urban areas, where the much higher density of human population and presence of vectors could fuel large epidemics [9, 10].

The Parasite

Plasmodium species

Approximately 250 species of *Plasmodium* are presently believed to be parasites of mammals, birds, and reptiles. More than 30 species of *Plasmodium* have been reported in non-human primates, including apes, gibbons, and New and Old World monkeys. It is believed that all kind of malaria in the primates are transmitted only by *Anopheles* mosquitoes [11].
Traditionally the four restricted or adapted species recognized as responsible of human malaria are *P. falciparum*, *P. ovale, P. malariae* and *P. vivax*. Occasionally humans can be infected by several simian species such as *P. cynomolgi cynomolgi, P. cynomolgi bastianelli, P. simiovale, P. brasilianum, P. schwetzi, P. inui* and *P. knowlesi* that emerged as an important cause of human malaria in South-East Asia, especially the Malaysian Borneo since 2004. The life cycle of all species of human malaria parasites is characterized by an exogenous sexual phase (named sporogony) in which multiplication occurs in several species of *Anopheles* mosquitoes, and an endogenous asexual phase (named schizogony) which takes place in the vertebrate host [12].

Distribution of plasmodia

The different *Plasmodia* are not uniformly distributed, although there are areas of overlap of the species.

Plasmodium falciparum

Eighty-five countries are actually classified as endemic for *P. falciparum* malaria with 2.57 billion people living in area at risk for transmission of this infection. Of these, 1.44 billion people lives in area of stable transmission, mainly in Africa (52% of the global total) and Central, South and East Asia (46%) [13, 14].
Once considered strictly human specific, *P. falciparum* can infect bonobos, chimpanzees and gorillas and thus these African apes might serve also

as possible reservoir for the malignant form of human malaria [15, 16].

Plasmodium vivax

Of all malaria species that infect humans, *P. vivax* is the most geographically widespread. Compared with the more virulent *P. falciparum*, *P. vivax* tolerates a wide range of temperature environmental (minimum: 16°C vs. 21°C for *P. falciparum*), which may explain its broader distribution. Alternatively, this distribution may reflect a longer historical association with humans. According with phylogenetic analysis of Mu et al., *P. vivax* became a human parasite via a host switch from Asian macaques [17].

In endemic areas of Asia, Oceania, Central and South America, and in the horn of Africa *P. vivax* malaria remain a major cause of morbidity [18]. *It* is present throughout the tropics with low rate of infection in western and central sub-Saharan Africa. The high proportion of Duffy-negative people in West and Central Africa has long be viewed as the most plausible explanation of the rarity of *P. vivax* malaria in those geographical areas [12].

It is more difficult to control and eliminate *P. vivax* than *P. falciparum* because of its tendency to relapse after resolution of the primary infection.

There is significant geographical variation in the rate at which a "strain" of *P. vivax* relapses.

Temperate and subtropical strains often exhibit either a long incubation or latent period of around eight to ten months. Tropical strains are characterized by short incubation times and short latency (approximately three to six weeks). Tropical strains relapse more rapidly than temperate strains and New World strains vary from those in the Old World.

Relapse periodicity varies according with geographic region and is categorized in nine global regions with similar malaria transmission dynamics.

How hypnozoite relapse is triggered, and the source of this phenotypic variation, is unresolved. One theory is that the mechanism is an adaptive trait of the parasite to sequester or "hibernate" during times when climatic conditions would be inhospitable to the parasite's anopheline vectors. This potential for long-term latency provides the obvious advantage of safe harbour during cold winter months and this theory would explain the presence of malaria in northern Europe and Russia, where *P. vivax hibernans was present* (in Finland the last case of malaria was reported in 1954) [19]. Another hypothesis explaining the relapse periodicity is that latent hypnozoites are activated by a systemic febrile illness, thus interpreting the large number of *P. vivax* relapses that follow *P. falciparum* infections in tropical areas [20].

Plasmodium ovale

Humans are the only natural hosts of *P. ovale*. Their natural distribution is in Sub Saharan Africa and in the islands of the western Pacific. *Anopheles gambiae* and *A. funestus* are the likely natural vectors. Infection to anopheline mosquitoes outside its geographic distribution is possible, and thus the reasons for geographic isolation are not due to vector incompetence [21]. Previous infection with *P. ovale* did not prevent reinfection but resulted in reduced levels of parasitemia and fever. Previous infection by other *Plasmodium spp.* did not prevent infection; there was some reduction in the frequency and intensity of fever and parasite counts. It has been estimated that the global burden of *P. ovale* in Africa might exceed 15 million cases annually [22].

Plasmodium malariae

P. malariae has developmental cycles in the mosquito and in the primate host. *P. malariae* infection has been observed in all major malaria-endemic regions of the world where *P. falciparum* is also present. In the recent past, it was prevalent in Europe and in southern parts of the United States. Actually it is widespread throughout sub-Saharan Africa, much of southeast Asia, into Indonesia, and on many of the islands of the western Pacific. It is also reported in areas of the Amazon Basin of South America, along with *Plasmodium brasilianum*, a parasite commonly found in New World monkeys. This parasite is apparently the same species as *P. malariae* that has naturally adapted to grow in monkeys following human settlement of South America within the last 500 years. The ready passage of *P. brasilianum* to humans and the passage of *P. malariae* to New World monkeys indicate that such interspecies transmission between primates and humans is both feasible and probable [23].

P. malariae has been characterized to exhibit opposing seasonal fluctuation with *P. falciparum*, with prevalence of *P. malariae* and/or parasite

densities increasing in the dry season. Outside Africa there has been no report of opposing seasonal fluctuation in the prevalence of *P. malariae* and *P. falciparum* infections [19].

Plasmodium knowlesi

P. knowlesi, a simian plasmodium that infects forest macaque monkeys (*Macaca fascicularis*, *Macaca nemestrina*, *Trachypithecus obscurus*, *Presbytis-melalophus*), is now recognized as an important cause of human malaria not only in the Peninsular Malaysian Borneo but also in other parts of South-East Asia.

The first case of a naturally acquired *P. knowlesi* infection was described in 1965, but it was not identified until 2004 when Singh et al. have detected 120 individuals with malaria as single or mixed *P. knowlesi* infections [24].

Furthermore, although they are not epidemiologically important, some plasmodia of monkeys can infect humans. Thuy et al. first have described a woman with naturally acquired human infection by *Plasmodium cynomolgi* [25].

The vector

In nearly all mosquito species, the female obtains the protein she needs for the development of her eggs by feeding on vertebrate blood. During this meal, an infected anopheline vector can transmit the parasite to a host.

The life cycle of all species of human malaria parasites is characterized by an exogenous sexual phase (named sporogony), occurring in several species of *Anopheles* mosquitoes, and an endogenous asexual phase (named schizogony) which take place in the vertebrate host.

The sexual development of malaria parasite (sporogonic cycle) will be completed only when mature female and male gametocytes of *Plasmodium spp*. will be ingested by a biologically suitable species of female *Anopheles* mosquito during a blood meal.

The genus *Anopheles* includes 465 formally recognised species and more than 50 unnamed members of species complexes. Approximately 70 of these species have the capacity to transmit human malaria parasites and 41 are considered

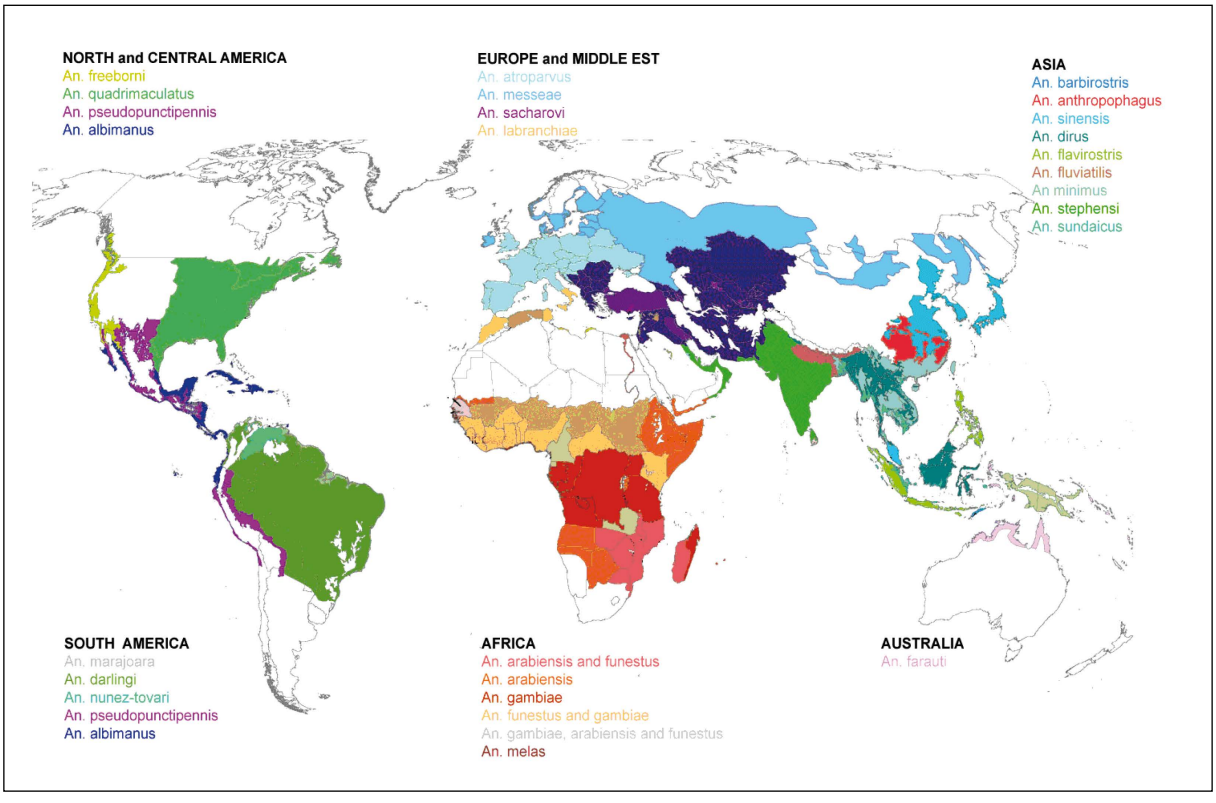

Figure 1 - Distribution of predominant malaria vectors.

Table 1 - The 41 dominant vector species/species complexes (DVS) per region.

Anopheline species or species complex
AMERICAS
An. freeborni An. pseudopunctipennis An. quadrimaculatus An. albimanus An. albitarsis An. aquasalis An. darlingi An. marajoara An. nuneztovari
Total DVS: 9
EUROPE AND MIDDLE-EST
An. atroparvus An. labranchiae An. messeae An. sacharovi An. sergentii An. superpictus
Total DVS: 6
AFRICA
An. arabiensis An. funestus An. gambiae An. melas An. merus An. moucheti An. nili
Total DVS: 7
ASIA
An. barbirostris An. lesteri An. sinensis An. aconitus An. annularis An. balabacensis An. culicifacies An. dirus An. farauti An. flavirostris An. fluviatilis An. koliensis An. leucosphyrus An. maculatus group An. minimus An. punctulatus An. stephensi An. subpictus An. sundaicus
Total DVS: 19
TOTAL: 41

Table 2 - Time required to development of mature oocyst and temperature

	Sporogonic cycle at 28°C	*Sporogonic cycle at 20°C*
P. falciparum	9-10 days	22 days
P. vivax	8-10 days	16 days
P. malariae	14 days	30-35 days
P. ovale	12-14 days	–

as dominant vector species/species complexes (DVS), capable of transmitting malaria at a level of major concern to public health (Figure 1 and Table 1) [26].

A mosquito blood meal is, on average, 2 to 3 µL, and should contain at least one male and one female gametocyte to be infective. Host location by the mosquito is mediated by physical (heat, moisture, visual) and chemical cues that play a role during orientation and landing. It is known that skin bacteria play an important role in the production of human body odour and that they convert non-volatile compounds into volatile compounds with characteristic smells [27].

The time span required to development of mature oocyst in the salivary glands is quite variable (7-30 days), characteristic of each species and influenced by ambient temperature (Table 2) [12-28,29,30].

The temperature influence the cycle of Plasmodium because it affects the duration of the sporogonic cycle and the longevity of the vector. For P. falciparum, the development stops at 16°C, but transmission below 18°C is unlikely because few adult mosquitoes survive the 56 days required to complete sporogony at 16°C and because mosquito abundance is limited by long larval duration.

Although the sporogonic cycle takes less than a week above 32°C, the vector population turnover and mortality are high. At 40°C the daily survival of mosquitoes is not possible. The higher development threshold for the parasite is of 32°C for *P. falciparum* and of 33°C for *P. vivax* [31].

Vectorial capacity

In human malaria, the intensity of transmission is highly dependent on the vectorial capacity and competence of local mosquitoes. Most mosquitoes are dead ends for the parasite, and only a limited number of *Anopheles* is able to transmit plasmodium to humans.

The major aspects of vectorial capacity and competence in *Anopheles* are: the vector longevity, the duration of sporogonic development, the contact between the mosquito and vertebrate host suitable for the parasite and the susceptibility/resistance of the vector to the parasite.
Vectorial capacity and competence also present quantitative features in the sense that some species have a major role in malaria transmission than others. Even at the species level, some populations or individual mosquitoes can have different impacts on transmission.
Plasmodium infection can reduce the vectorial longevity of *Anopheles* but this effect is balanced when the vector live enough to become infectious [32].

Entomological parameters
Distribution, abundance, feeding behaviour, host preference, parity status and human-biting, and infection rates are among the medical entomological parameters essential factors in determining the vectorial competence of natural populations.
An efficient system for malaria transmission needs a strong interaction between human and infected vectors. In Africa the principal malaria vectors belong to the *Anopheles gambiae complex* and to the *Anopheles funestus* group. Humans, mosquitoes and *Plasmodium* coexist from thousands of years and have therefore developed and efficient system for malaria transmission. These vectors feed almost exclusively indoors at night, on sleeping humans. Changes in mosquito biting behaviour have been shown to be immediately and directly induced by vector control tools, especially when excito-repellent insecticides are used.
The propensity to bite indoors is referred to as endophagy, the propensity to bite during the night when people usually sleep is referred to as nocturnality and the propensity to bite human host is referred to as anthropophagy [33].
Parity status is a proxy of the survival time of adult female mosquitoes and determines whether a parasite has sufficient time to complete its life cycle within the mosquito, thus determining whether the mosquito will serve as an effective vector.

The human host-epidemiology
The determination of the spleen rate to quantify malaria endemicity was first introduced in India in 1848. Spleen rate is defined as proportion of a sampled population with palpable enlargement of the spleen, reflecting the prevalence of the infection, found during a malariometric survey. If splenomegaly in the 2-9 year-old age-group is found in more than 75% of the subjects examined malaria is holoendemic, between 51-75% is hyperendemic, 11-50% is mesoendemic and less than 10% is hypoendemic.
Another classification was developed by Macdonald. He showed that the stability of malaria was determined by the average number of feeds that a mosquito takes on a human being during its life. This vector-based index distinguish stable malaria (insensitive to natural and man-made perturbations, with values more than 2,5) from unstable malaria (very sensitive to climate and very amenable to control, with values less than 0,5). Between these extremes is intermediate stability [34].
The stable endemic malaria occurs in regions where the anophelines are anthropophilic and have a high survival rate. Temperature and humidity are generally high and with relatively little seasonal variation.
The great efficiency of the transmission makes hard to control the spread of malaria. The transmission rate is high but severe and fatal illness are generally limited to children and people coming from non immune countries because older inhabitants who survived multiple infections maintain a high degree of immunity.
From the other side, unstable malaria occurs in regions where the anopheles are less anthropophilic and prefer to bite animals. Transmission rates can vary greatly and when an epidemic occurs the lack of immunity in the population is responsible of more severe disease.

Entomological inoculation rate
The most direct way of detecting human exposure to infectious bites and mosquito population monitoring are the entomological inoculation rates (EIR), defined as the product of man biting rates (Ma) and the sporozoite rate (SR, proportion of mosquitoes carrying sporozoites):

$$EIR = Ma \times SR$$

Unfortunately, under conditions of very low malaria transmission the EIR suffers from well recognized limitations [35-37].

The environment

Malaria in urban setting

The process of urbanization includes physical landscape modification and transformation. Moreover, urbanization involves significant socio-economic change that generally improves health, housing and increase wealth. These factors, common to urban areas, cause marked entomological, parasitological and behavioural effects and reduce malaria transmission both within the urban core and surrounding peri-urban areas [38].

The need of clear water for the breeding site of *Anopheles* mosquito is believed to be a major factor that generally reduces the development of anopheline larvae in urban setting. Although there is an evidence of decreasing from rural to urban areas, and transmission intensity is on the average eight times greater in African rural areas than in urban centres, malaria transmission still occurs in most urban settings. Where the urbanisation is rapid and unplanned, poverty, deteriorating infrastructure and overcrowding are some of the factors that contribute to the development of anopheline breeding sites. *Anopheles gambiae spp.* can adapt to a wide range of polluted water. Anopheline larvae can survive under conditions that modify their habitat, like water contaminated with human faeces and oil from petrol tanks [39]. *Anopheles gambiae spp.* have developed tolerance to increasing levels of heavy metal such cadmium, copper and lead, but this resistance has a significant biological cost.

Although pollution can adversely affect the mosquito's ecological performance and fitness, growing evidence suggests that *A. gambiae* is expanding its ecological niche into polluted habitats and adaptation of this mosquito to the urban environment is now a real threat [40].

Change in land use

Land use has been investigated as a driver of changes in mosquito population dynamics. Different studies in Kenya have shown a local increase in temperature and humidity, altering the development and densities of local vector populations as a consequence of deforestation [41-43].

In Uganda higher temperatures, higher mosquito densities, and higher malaria transmission were observed in cultivated than in natural swamps [44].

Changes in land cover affect land surface energy and water balances, by altering physical parameters that influence small-scale hydrology and microclimate.

Vegetation has a critical role in determining rainfall partitioning and is one of the primary determinants of runoff because water availability in temporary pools creates a breeding habitat for the mosquitoes.

Variable amounts of shading, temperature, and evaporation are mechanisms by which land use affects the surface microclimates that can influence malaria transmission.

Not only land use type, but also spatial relations between land use and breeding habitats may have an important influence on runoff, reaching malaria vector breeding habitats in water-limited environments.

Vegetation and landscape characteristics are critical environmental components that contribute to dynamic spatial variability in host, vector, and pathogen populations, by altering feeding patterns, habitat availability, dispersal and dispersion, and microclimates [45-47].

To answer the need of food in the African continent, many governments have sought ways of improving agricultural production by initiating large-scale irrigation projects. The irrigation has often been blamed for aggravating malaria transmission in local communities, but available evidence suggests that this happens only in areas of unstable transmission. This apparent paradox is explained by a number of factors, including the previous immunity of the population and widespread use of bednets and antimalarial drugs in villages where the residents become wealthier due to income generated from agricultural production. On the other hand, availability of water increase the number of vectors and lead to increased cases of malaria in areas of unstable transmission, where people have little or no immunity to malaria parasites [48].

Climate

Among five major factors characterizing *Anopheles* population dynamics (temperature, moisture, nutrient competition, predation and diseases, dispersal), two are strictly connected with climate.

Temperature is a critical regulator of growth and development within each stage, in determining the end of one stage and the beginning of the next and in regulating the length of the gonotrophic cycle [49].

Temperature affects the mosquitoes at each stage of their life-cycle. If the temperature of the water where mosquitoes lay their eggs is too hot or cold, then fewer eggs hatch. After the egg stage, mosquitoes develop into larvae and then pupae. The temperature has also been shown to affect the time it takes to transition between these stages with the optimum water temperature for survival and shortest transition between larvae and pupae being between 22°C and 26°C [50]. In the range of 18°C to 26°C, a change of only 1°C in temperature can change a mosquito's life span by more than a week [51].

Specific temperature ranges are also important for the development of the parasite in the mosquito. It has been shown that the optimum range for parasite development is between 25°C and 30°C. The minimum temperature observed for survival for *P. falciparum* is 18°C and the maximum has been reported at 40°C [52].

However, while the temperature is a variable that affects the development of both the vector population and the parasite within the vector, because the parasite develops inside the mosquito's salivary glands, only the temperature is a factor limiting or favoring the growth of the parasite. The life cycle of the parasite is therefore independent of the availability of water and moisture.

Temperature close to 40°C recorded in small pools exceeds thermal death point of many species, including *A. funestus.* This may help to explain why these species are rarely found in small pools and if the temperature of water is above 40°C [53].

The cut-off of survival for *Anopheles* eggs in dry soil is of 15 days, but some African regions where malaria is endemic experience drought periods longer than two months. Here the survival of *Anopheles* seems to be allowed by adult aestivation [54]. Survival rate may also be reduced when hot weather is accompanied by low humidity, but in areas where such conditions are normal, local species have adapted to cope with them [55].

Global warming

Climate changes induced by human activities have focused the risk of increasing burden of vector-borne diseases, and especially on malaria.

Climate based models have predicted that increases in temperature and changes in rainfall patterns will result in a longer malaria season for many sub-Saharan African regions [56].

Because lower temperatures have a limiting effect on transmission of malaria, highland areas where average temperature is below a threshold are often malaria free. Although vectors such as *A. gambiae* have been reported at altitudes up to 3,000 m above sea level, endemic malaria disappears above 1,800-2,000 m and human populations living in these areas have low degree of acquired immunity. These populations experience high rates of morbidity and mortality as a result of epidemics, and clinical picture of severe disease [57].

The International Panel on Climate Change has concluded that there is likely to be a net extension in the distribution of malaria in areas of high altitude where *P. falciparum* transmission is limited by low temperature.

In recent decades, outbreaks of malaria have been reported from many mountain regions of Kenya, Uganda and Rwanda, but a high degree of temporal and spatial variation in the climate of East Africa suggests further that claimed associations between local malaria resurgence and regional changes in climate are overly simplistic [58-60]. Increases in malaria have been attributed to migration, breakdown in both health service provision and vector control operations and to deforestation. Economic, social and political factors can therefore explain recent resurgence in malaria rather to climate change [61].

Existing models will tend to underestimate mosquito population growth under current conditions, and may overestimate relative increases in population growth under future climate change. Paaijmans et al., suggest that although widely used, air temperature alone does not provide an appropriate variable for estimating immature mosquito development or for setting threshold temperatures. Mean water temperature in typical mosquito breeding sites was 4-6°C higher than the mean temperature of the adjacent air, resulting in larval development rates, and hence population growth rates, that are much higher than predicted based on air temperature. A temperature-dependent population dynamic model demonstrate that a small change in mean ambient air temperature of just 0.5°C could translate into a 30-100% increase in mosquito abundance. The use of air temperature rather than water temperature will tend to underestimate current mosquitoes growth rates, while strongly overestimating the impact of warming on population growth rates [62].

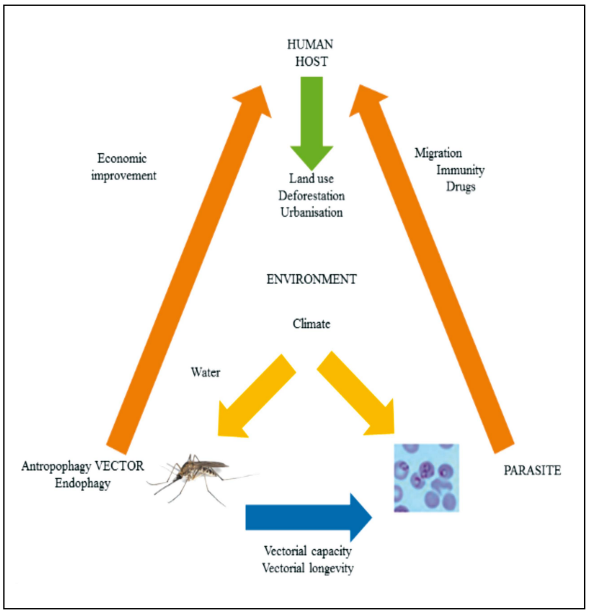

Figure 2 - Interactions between human host, vector and parasite.

Models considering *A. gambiae* vector complex species estimate that climate change effects on African malaria vectors shift their distributional potential from west to east and south. Although is likely a reduction of the malaria burden, these epidemiological changes will pose novel public health problems in areas where it has not previously been common (Figure 2) [63].

DISCUSSION

Last decades have witnessed changes in the ecosystem and climate without precedent in human history. The implications of these changes on human health have been widely investigated and especial emphasis has been placed on a potential increase in distribution of vector-borne diseases such as malaria [64].
The transmission of malaria requires the interaction between the host, the vector and the parasite. The parasite, which completes the sporogonic cycle inside the mosquito and asexual cycle in the human host, cannot complete their development outside of a range of temperatures which are different depending on the different *Plasmodium* species. *P. vivax* has developed strategies that allow him to survive the winter in cold climates. The external temperature, the presence of vectors suitable for the transmission and susceptible hosts are the elements required by the parasite to complete its life cycle.
Instead several are the factors required to ensure the survival of mosquitoes in the environment and the outdoor temperature is only one of many. The third actor, humans suffer only the indirect consequences of climate change in the case of vector-borne diseases.
Extreme weather events such as floods and dryness can trigger migration of populations, but without the vector and the parasite, there will be no changes in transmission of the disease. Where malaria has been eradicated in the last century, the improvement of living conditions, the ability to clean up the environment, the access to drugs and the stability of borders have been crucial [65-68]. The reintroduction of malaria in already declared malaria-free countries has been indeed the result of political instability (countries of the former USSR) or the consequence of health policies that have reduced the funds for the vectors control joined to the presence of migratory flows from endemic countries [69-73]. In contrast, the distribution of mosquito nets, the wide availability of highly effective antimalarial drugs such as artemisinin derivatives has led to the reduction of malaria cases and mortality [74].

CONCLUSION

The emphasis about the role of temperature on the epidemiology of malaria has been reduced in light of other conditions directly or indirectly linked to other aspects of climate, to changes of the ecosystem, and to the improvement of sanitary and economic conditions. If it is not possible to say in absolute terms that rising temperatures will cause an increase in cases of malaria it must be noted that it would lead to ideal conditions for malaria transmission also in regions where the disease is not reported. In tropical regions the temperature increase might even be unfavorable to the survival of the vector. To predict the future epidemiological scenarios we need more complex models than those based merely on the temperature and above all it will be necessary ensure access to treatment and health facilities to the people affected.

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