

Influence of climate on malaria transmission depends on daily temperature variation

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Lets First Understand What is Malaria?

Malaria is a mosquito-borne infectious disease caused by a eukaryotic protist of the genus Plasmodium.

Widespread in tropical and subtropical regions, including parts of the Americas (22 countries), Asia, and Africa.

250 million cases of malaria/year

Major affected area : sub-Saharan Africa

Commonly associated with poverty



History Of Malaria

First described in India during **Vedic Period 1600BC** and by **Hippocrates some 2500 years ago**.

Charaka and **Sushruta** gave vivid descriptions of malaria and even associated it with the bites of the mosquitoes.

In **1640**, **Huan del Vego** first employed the **tincture of the cinchona bark for treating malaria**, although aborigines of Peru and Ecuador had been using it even earlier for treating fevers.

Morton (1696) presented the **first detailed clinical picture of malaria** and its treatment with **cinchona**.

Lancisi (1717) linked malaria with **poisonous vapours** of swamps and thus originated the name *malaria*, meaning **bad air**

Gize (1816) studied extraction of **quinine** from the **cinchona bark**.

Pelletier and Caventou (1820) extracted pure quinine alkaloids



Laveran (1880) a French physician working in Algeria, **first identified the causative agent** for human malaria while viewing blood slides under a microscope.

P.vivax and ***P.malariae*** were identified in **1885** by **Golgi**

Sakharov (1889) and **Marchiafava and Celli (1890)** identified ***P.falciparum***

Sir Ronald Ross (1897) while working as a military physician in India, **demonstrated the malarial oocysts in the gut tissue of female Anopheles mosquito**. This was reported in the **British Medical Journal**.

Paul Muller (1939) discovered the insecticidal properties of **DDT**.

Curd, Davey and Rose (1944) synthesised proguanil for treating falciparum malaria

During the World War II research into antimalarials was intensified.

Chloroquine was synthesised and studied under the name of Resochin by the Germans as early as **1934**



Short, Granham, Covell and Shute (England) identified tissue forms of *P.vivax* in the liver. Tissue stages of *P. falciparum*, *P. ovale*, and *P. malariae* were also identified later on.

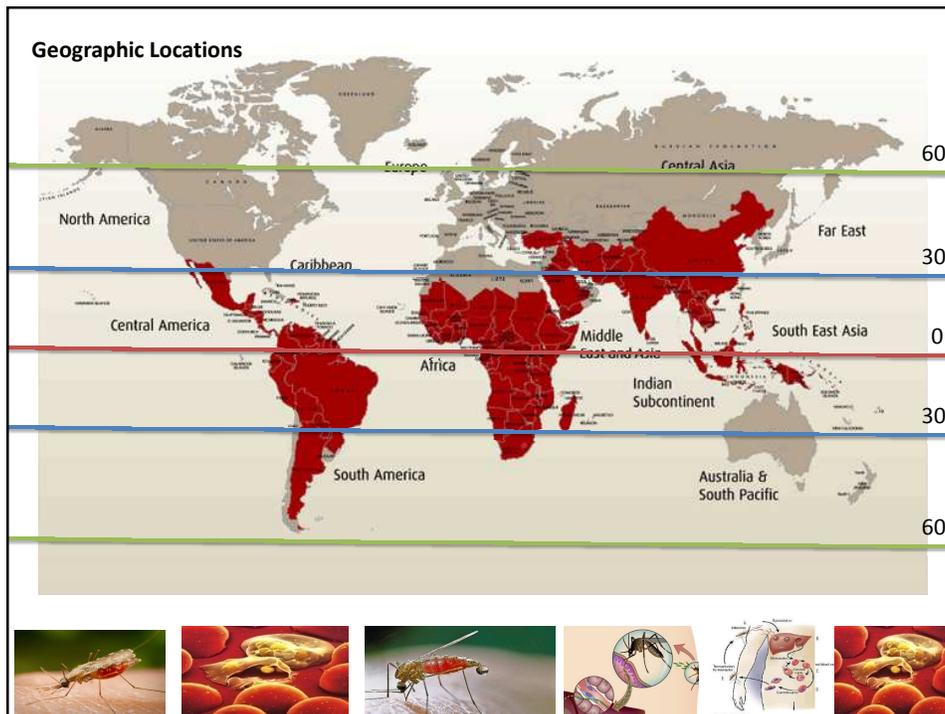
Elderfield (1950, USA) synthesised primaquine.

Lysenko (1976-78) formulated a theory on the polymorphism of *P.vivax* sporozoites.

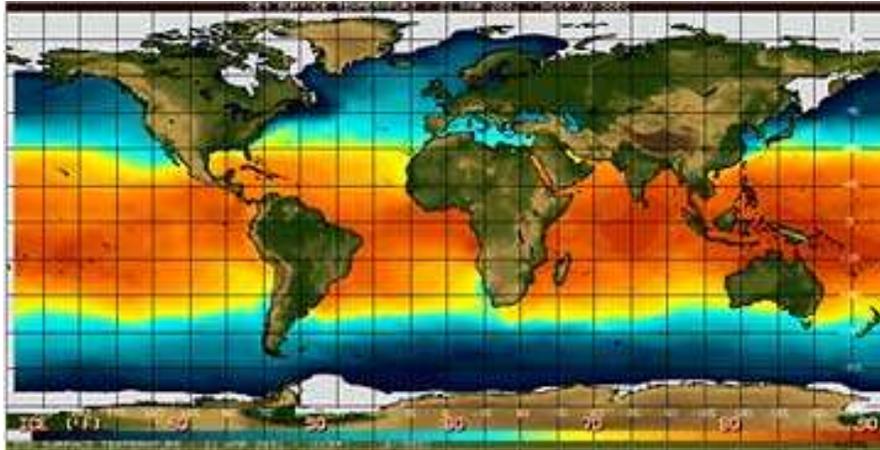
Bray and Garnham (1982) proposed that some sporozoites in the liver remain latent (hypnozoites) causing relapses later on.

Quinine has now been completely synthesized. Its synthetic analogue is called mefloquine..

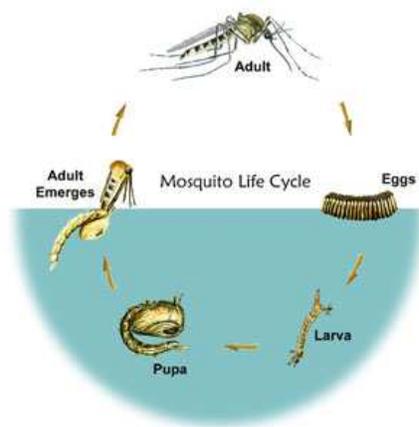
In 1967, WHO realized that the global eradication of malaria was impossible for a variety of reasons and the focus shifted to control of the disease.

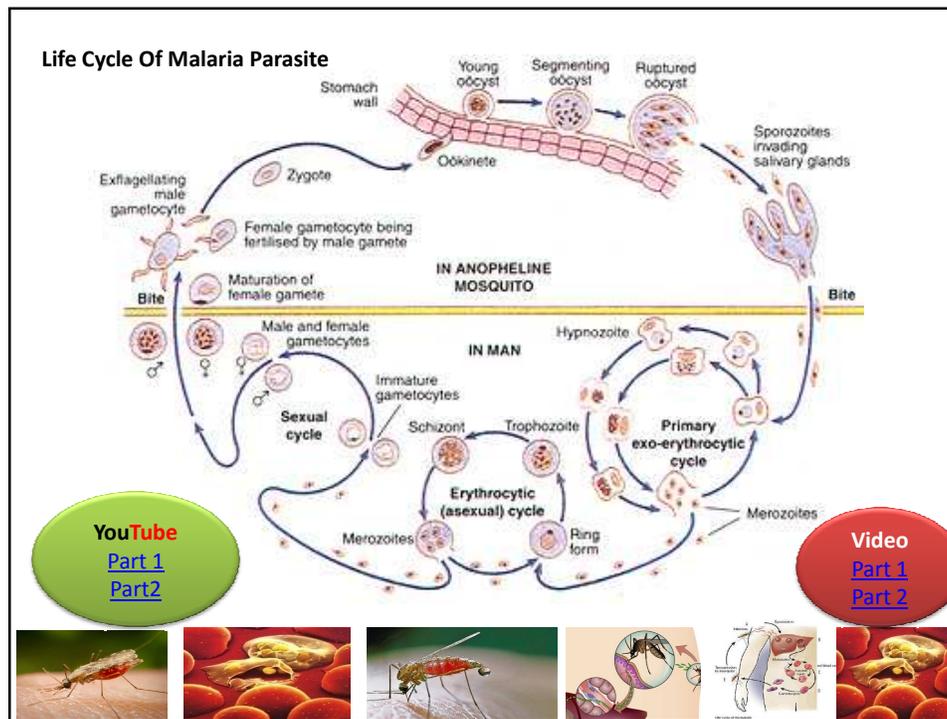


Global Temperature Map



Life cycle of Malaria Vector:





Climate and Malaria

The three main climate factors that affect malaria are **temperature**, **precipitation**, and **relative humidity** (Pampana, 1969).

Climate predicts, to a large degree, the natural distribution of malaria (Bouma and van der Kaay, 1996).

Temperature

Temperature affects many parts of the malaria life cycle.

The duration of the **extrinsic phase** depends on **temperature** and on the **species** of the parasite the **mosquito** is carrying (Pampana, 1969).

The **extrinsic cycle normally lasts nine or ten days**, but sometimes can be as short as five days (Bradley *et al.*, 1987).

As the temperature decreases, the number of days necessary to complete the extrinsic cycle increases for a given *Plasmodium* species.



P. vivax and *P. falciparum* have the shortest extrinsic incubation times and therefore are more common than *P. ovale* and *P. malariae* (Oaks *et al.*, 1991).

The extrinsic phase takes the least amount of time when the temperature is 27°C (Pampana, 1969).

The time required for development of the ookinete, the egg of the parasite, in the midgut of the Anopheline mosquito, decreases as temperature increases from 21°C to 27°C (Patz *et al.*, 1998).

Below 20°C, the life cycle of *falciparum* is limited. Malaria transmission in areas colder than 20°C can still occur because **Anophelines often live in houses, which tend to be warmer than external temperatures.**

Larval development of the mosquito also depends on temperature (Russell *et al.*, 1963). Higher temperatures increase the number of blood meals taken and the number of times eggs are laid by the mosquitoes (Martens *et al.*, 1995).



The intersections of the ranges of minimum and maximum temperature for parasite and vector development determine the impact of changes in temperature on malaria transmission.

The minimum temperature for **mosquito development is between 8-10°C**, the minimum temperatures for **parasite development are between 14-19°C** with *P. vivax* surviving at lower temperatures than *P. falciparum*.

The optimum temperature for mosquitoes is 25-27°C, and the maximum temperature for both vectors and parasites is 40°C (McMichael *et al.*, 1996). There are some areas where the climate is optimal for malaria and *Anopheles* mosquitoes are present, but there is no malaria.

This is called "**Anophelism without malaria**" which can be due to the fact that the *Anopheles* mosquitoes present do not feed primarily on humans (Bruce-Chwatt, 1985) or because malaria control techniques have eliminated the parasite .



Precipitation

Anopheline mosquitoes breed in water habitats, thus requiring just the right amount of precipitation in order for mosquito breeding to occur.

Different Anopheline mosquitoes prefer different types of water bodies in which to breed (Nagpal and Sharma, 1995).

Too much rainfall, or rainfall accompanied by storm conditions can flush away breeding larvae.

Not only the amount and intensity of precipitation, but also the time in the year, whether in the wet or dry season, affects malaria survival (Russell *et al.*, 1963).

Rainfall also affects malaria transmission because it increases relative humidity and modifies temperature, and it also affects where and how much mosquito breeding can take place (Pampana, 1969).



Relative Humidity

Relative humidity also affects malaria transmission.

Plasmodium parasites are not affected by relative humidity, but mosquitoes are.

If the average monthly relative humidity is below 60%, it is believed that the life of the mosquito is so shortened that there is no malaria transmission (Pampana, 1969).

Wind

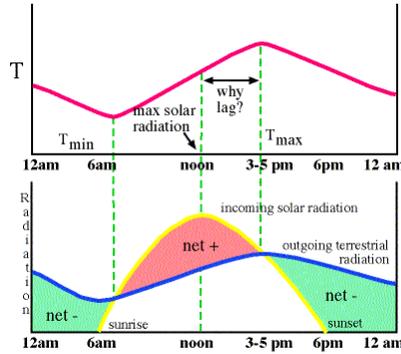
Wind may play both negative and positive roles in the malaria cycle because very strong winds can decrease biting or ovipositing by mosquitoes, while at the same time extending the length of the flight of the mosquito.

During a monsoon, wind has the potential to change the geographic distribution of mosquitoes (Russell *et al.*, 1963).



Daily Temperature Variations - Net Radiation

Diurnal temperature variation is a meteorological term that relates to the variation in temperature that occurs from the highs of the day to the cool of nights.



The *net radiation* determines whether the surface temperature rises, falls, or remains the same.

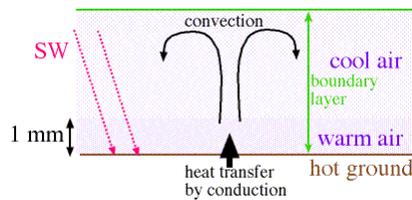
net radiation = incoming solar - outgoing IR.

If the net radiation > 0, surface warms (6 AM - 3-5 PM)

if the net radiation < 0, surface cools (3-5 PM - 6 AM)



Factors Affecting Daytime Warming - Fundamental Process.

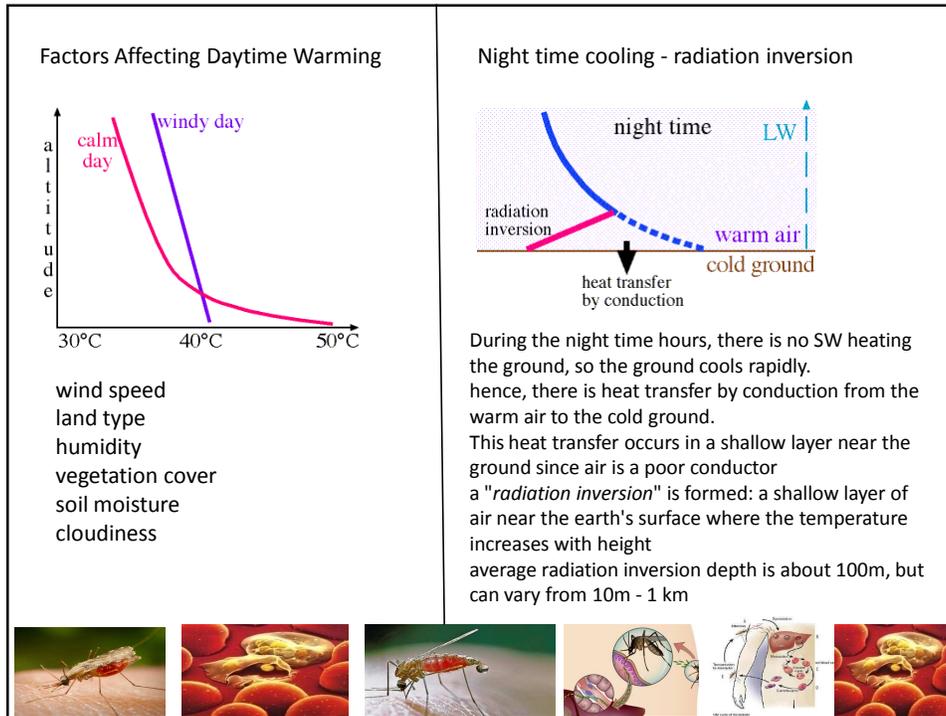


Heat is transported from the hot surface to air molecules very near the hot surface by *conduction*.

Heat is then transported further upward by *convection* - thermals of air.

The layer of air near the earth's surface where most of the daily temperature variation occurs as a result of the heating/cooling of the ground is called the *boundary layer* (1-1.5Km)





From the Paper:

Reproductive number (R_0),

$$R_0 = ma^2 bce^{-pS} / pr$$

where,

m = vector:human ratio,

a = vector biting frequency,

bc = transmission coefficients defining vector competence,

p = daily vector survival rate,

S = the extrinsic incubation or development period of the parasite within the vector, and

r = recovery rate of the vertebrate hosts from infection.

These parameters relate in some way to mosquito abundance, its biology, or physiology

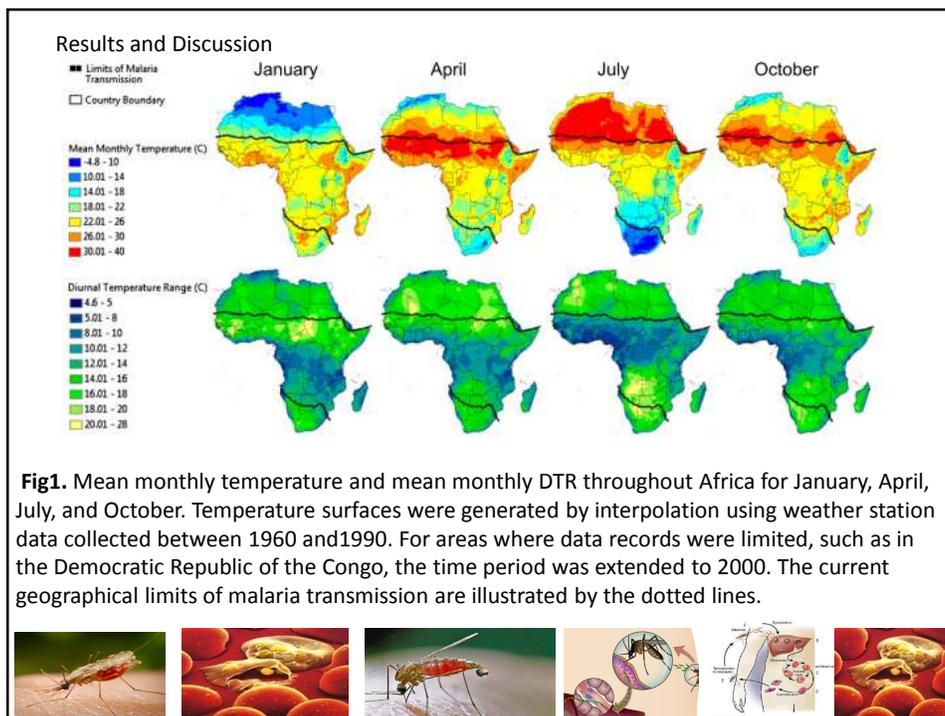


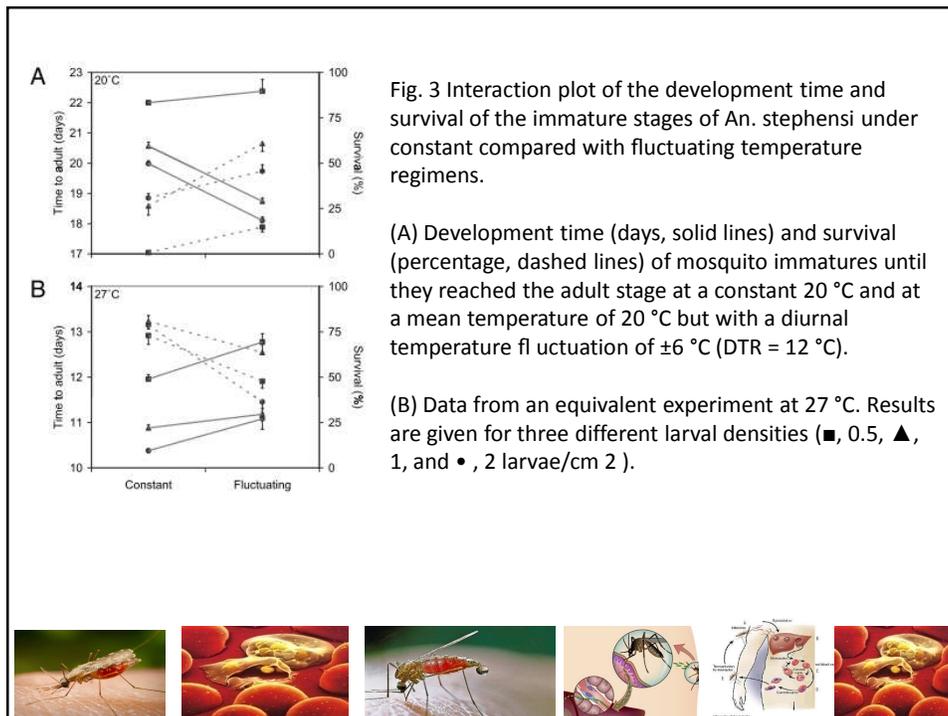
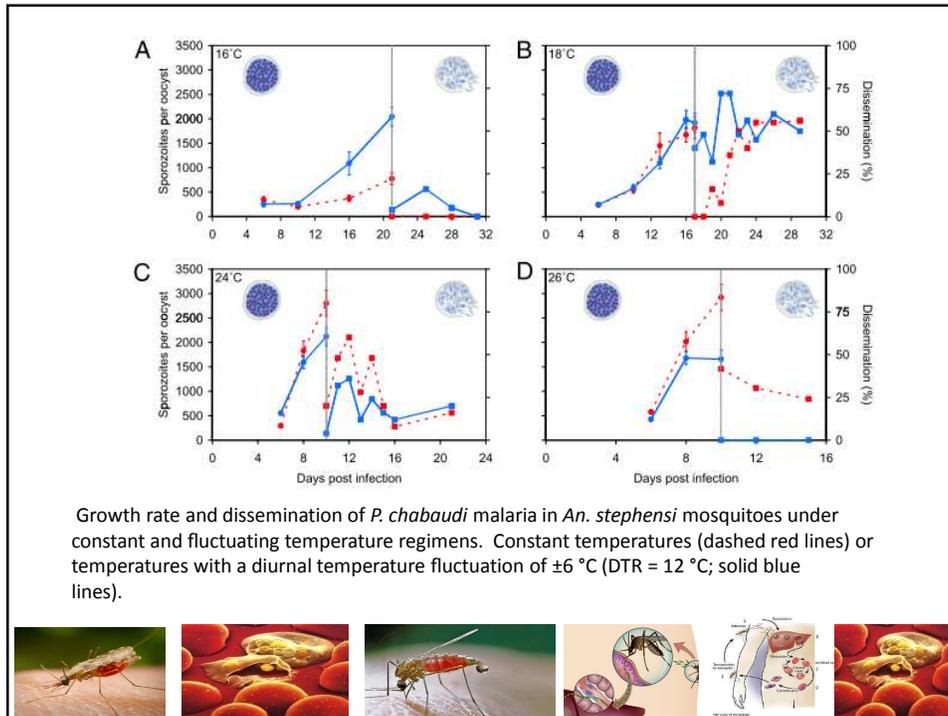
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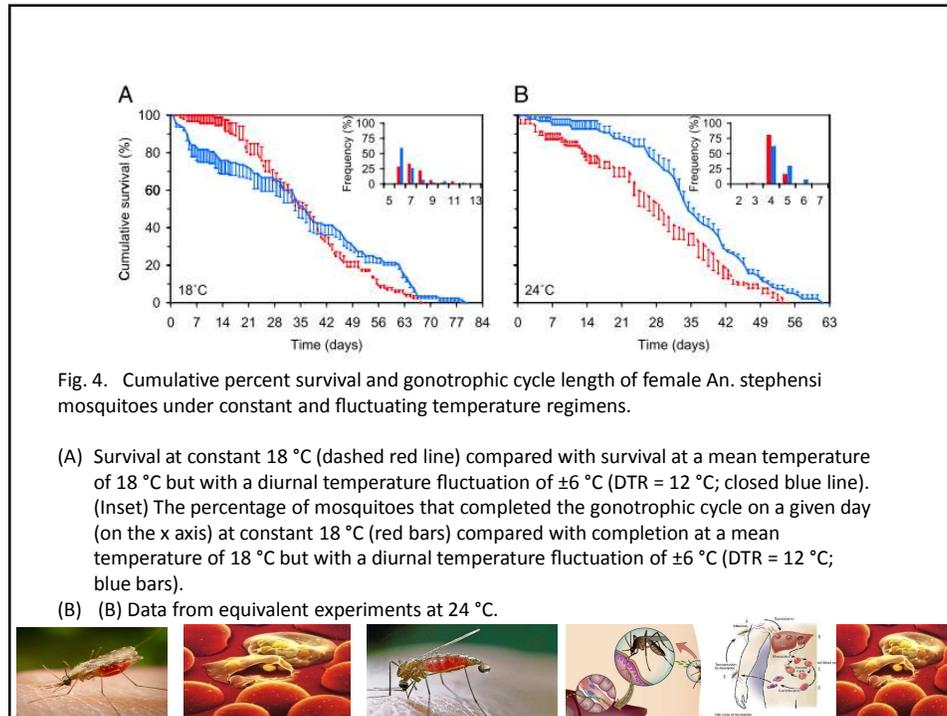
Role of temperature (constant and fluctuating) in

1. Growth and dissemination of the *P.chabuadi* inside the mosquito.
2. Survival rate of mosquito larva.
3. Gonotropic cycle * length of female mosquitoes.

* The complete cycle from time of feeding to oviposition (Covell et al 1953).







The key mosquito-related traits that combine to determine malaria transmission intensity are all sensitive to daily variation in temperature.

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1. parasite infection,
2. parasite growth and development,
3. immature mosquito development and survival,
4. Length of the gonotrophic cycle, and adult survival.

Temperature fluctuation increases relative rate processes under cool conditions and slows rate processes under warm conditions.



Limitations:

Used rodent malaria and one species of mosquito need to extend investigations to human malaria species and to other important vectors.

These findings caution against standard practice in studies estimating mosquito and/or malaria climate relations and strengthen arguments for greater ecological understanding of how infectious organisms respond to the natural environment.

What we learn?

Daily temperature fluctuation on **basic aspects of insect and parasite life histories** suggest the need to consider the role of temperature variation for many ectotherms (other insects, amphibians, reptiles, etc.) and their parasites and pathogens, both for understanding current biology and the likely impacts of climate change



Beer Consumption Increases Human Attractiveness to Malaria Mosquitoes

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Abstract

Background: Malaria and alcohol consumption both represent major public health problems. Alcohol consumption is rising in developing countries and, as efforts to manage malaria are expanded, understanding the links between malaria and alcohol consumption becomes crucial. Our aim was to ascertain the effect of beer consumption on human attractiveness to malaria mosquitoes in semi field conditions in Burkina Faso.

Methodology/Principal Findings: We used a Y tube-olfactometer designed to take advantage of the whole body odour (breath and skin emanations) as a stimulus to gauge human attractiveness to *Anopheles gambiae* (the primary African malaria vector) before and after volunteers consumed either beer (n = 25 volunteers and a total of 2500 mosquitoes tested) or water (n = 18 volunteers and a total of 1800 mosquitoes). Water consumption had no effect on human attractiveness to *An. gambiae* mosquitoes, but beer consumption increased volunteer attractiveness. Body odours of volunteers who consumed beer increased mosquito activation (proportion of mosquitoes engaging in take-off and up-wind flight) and orientation (proportion of mosquitoes flying towards volunteers' odours). The level of exhaled carbon dioxide and body temperature had no effect on human attractiveness to mosquitoes. Despite individual volunteer variation, beer consumption consistently increased attractiveness to mosquitoes.

Conclusions/Significance: These results suggest that beer consumption is a risk factor for malaria and needs to be integrated into public health policies for the design of control measures.

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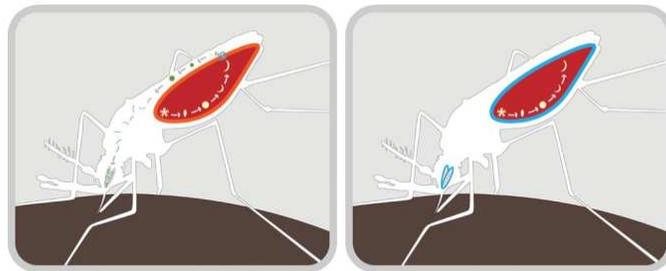
Competing Interests: The authors have declared that no competing interests exist.

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Malaria Control with Transgenic Mosquitoes

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Figure 1. Mechanism for Blocking Malaria Transmission in the Mosquito

Left: Mosquitoes become infected with the malaria parasite upon taking an infected human blood meal. This produces an oocyst in the mosquito's gut wall (light red). When the oocyst ruptures, it releases sporozoites that pass through the gut (dark red) and into the hemocoel (white). The sporozoites are then amplified and migrate through the mosquito's body to the salivary glands, ready to infect a new human. Right: The laboratory of Marcelo Jacobs-Lorena at Johns Hopkins University has identified receptor sites for proteins that are necessary for the malaria parasite to pass through the gut wall after the oocyst ruptures. The same receptors are involved with the passage of sporozoites into the salivary glands. The laboratory has produced small proteins that preferentially occupy these sites (blue), blocking transmission of sporozoites through the gut wall and into the salivary glands. The appropriate gene constructs have been introduced into *An. stephensi* mosquitoes, thus rendering them refractory to *P. berghei* (a model system for human malaria).



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ARTICLES

Odorant reception in the malaria mosquito *Anopheles gambiae*

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The mosquito *Anopheles gambiae* is the major vector of malaria in sub-Saharan Africa. It locates its human hosts primarily through olfaction, but little is known about the molecular basis of this process. Here we functionally characterize the *Anopheles gambiae* odorant receptor (AgOr) repertoire. We identify receptors that respond strongly to components of human odour and that may act in the process of human recognition. Some of these receptors are narrowly tuned, and some salient odourants elicit strong responses from only one or a few receptors, suggesting a central role for specific transmission channels in human host-seeking behaviour. This analysis of the *Anopheles gambiae* receptors permits a comparison with the corresponding *Drosophila melanogaster* odorant receptor repertoire. We find that odourants are differentially encoded by the two species in ways consistent with their ecological needs. Our analysis of the *Anopheles gambiae* repertoire identifies receptors that may be useful targets for controlling the transmission of malaria.



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Malarial Mosquitoes Are Evolving Into New Species, Say Researchers

ScienceDaily (Oct. 21, 2010) — Two strains of the type of mosquito responsible for the majority of malaria transmission in Africa have evolved such substantial genetic differences that they are becoming different species, according to researchers behind two new studies published in the journal *Science*.

Over 200 million people globally are infected with malaria, according to the World Health Organisation, and the majority of these people are in Africa. Malaria kills one child every 30 seconds.

The international research effort, co-led by scientists from Imperial College London, looks at two strains of the *Anopheles gambiae* mosquito, the type of mosquito primarily responsible for transmitting malaria in sub-Saharan Africa. These strains, known as M and S, are physically identical. However, the new research shows that their genetic differences are such that they appear to be becoming different species, so efforts to control mosquito populations may be effective against one strain of mosquito but not the other.



The scientists argue that when researchers are developing new ways of controlling malarial mosquitoes, for example by creating new insecticides or trying to interfere with their ability to reproduce, they need to make sure that they are effective in both strains.



Two strains of the *Anopheles gambiae* mosquito: the top one is from the M strain, and the bottom one is from the S strain. (Credit: Photo by James Gathany/CDC, via)



Malaria may not rise as world warms

Studies suggest that strategies to combat the disease are offsetting the impact of climate change.

Of the many climate-change catastrophes facing humankind, the anticipated spread of infectious tropical diseases is one of the most frequently cited — and most alarming. But a paper in this week's *Nature* adds to the growing voice of dissent from epidemiologists who challenge the prediction that global warming will fuel a worldwide increase in malaria.

On the surface, the connection between malaria and climate change is intuitive: higher temperatures are known to boost mosquito populations and the frequency with which they bite. And more mosquito bites mean more malaria.

Yet when epidemiologists Peter Gething and Simon Hay of the Malaria Atlas Project at the University of Oxford, UK, and their colleagues compiled data on the incidence of malaria in 1900 and 2007 (see page 342), they found the opposite: despite rising temperatures during the twentieth century, malaria has lost ground. According to the models the researchers used to tease out the factors affecting the incidence



Preventative measures such as the widespread use of bed nets have outweighed the effects of climate warming on malaria.

of malaria, the impact of public-health measures such as improved medications, widespread insecticide use and bed nets have overwhelmed the influence of climate change. "Malaria is still a huge problem," says Gething. "But climate

change per se is not something that should be central to the discussion. The risks have been overstated."

Some earlier analyses painted a dire picture of a malaria-ridden future, but these models often exclusively evaluated the impact of warmer temperatures without taking other factors into consideration, says Paul Reiter, an entomologist at the Pasteur Institute in Paris. The latest assessment of the Intergovernmental Panel on Climate Change noted these concerns: "Despite the known causal links between climate and malaria transmission dynamics, there is still much uncertainty about the potential impact of climate change on malaria at local and global scales."

Gething and colleagues' study is the first of its kind to provide a detailed statistical model of global trends over the twentieth century, but it does have limitations. For instance, the data used to generate a global map of malaria in 1900 sum up all malarial infections, including those by a malaria parasite named *Plasmodium vivax*, whereas the data in



Thank You



