



Faculty of Science Zoology Department Entomology Section



EN 4208 _ Essay and Research

Anopheles Mosquito as vector of human diseases

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1.Introduction:

The Anopheles mosquito is a critical vector in the transmission of several debilitating human diseases, most notably malaria. Belonging to the Culicidae family, these mosquitoes are primarily known for their role in spreading the Plasmodium parasites, which are responsible for millions of infections and significant mortality rates annually, particularly in tropical and subtropical regions.

Besides malaria, Anopheles mosquitoes also contribute to the transmission of other diseases such as lymphatic filariasis and certain arboviruses. Understanding the biology, behavior, and ecological preferences of Anopheles mosquitoes is essential for developing effective control strategies and mitigating the public health impacts of the diseases they spread. [1,2]

2. Anopheles Mosquito

2.1. Taxonomy:

Mosquitoes belong to the family Culicidae, order Diptera, class Insecta (Hexapoda), and phylum Arthropoda. There are two recognized subfamilies, the Anophelinae and Culicinae this. [3]

There are two families of Nematocera, the Chaoboridae and the Dixidae, which are closely related to the Culicidae. The blood sucking habit is found only in the Culicidae. [4]

The family *Culicidae* is divided into three subfamilies: *Toxorhynchitinae, Anophelinae* and *Culicinae,* within which only subfamilies *Anophelinae* and *Culicinae* have medically important. [5]

classification of Anopheles mosquito		
Kingdom	Animalia	
Phylum	Arthropoda	
Order	Diptera	
Family	Culicidae	
Genus	Anopheles	

2.2. Morphology:

have slender bodies with 3 sections: head, thorax and abdomen. The head - is specialized for acquiring sensory information and for feeding. The head contains the eyes and a pair of long, manysegmented antennae. The antennae are important for detecting host odors as well as odors of breeding sites where females lay eggs. The head also has an elongate, forward-projecting proboscis used for feeding, and two sensory palps (organ near the mouthpart). [6]



Fig. (1) Anopheles mosquitoes

2.2.1. difference between male and female mosquitoes:

Male mosquitoes have more flagella or fine hairs on their antennae, so many so that it appears noticeably bushy to the naked eye. These flagella are important to a male mosquito's hearing, which comes in handy when the male is looking for female mosquitoes. A female mosquito's antennae are less bushy and contain several odor receptors that help her target blood sources so that she can feed and reproduce. Only female mosquitoes bite and transmit malaria. The thorax is specialized for locomotion.

Three pairs of legs and a pair of wings are attached to the thorax. The abdomen is specialized for food digestion and egg development. This segmented body part expands considerably when a female takes a blood meal. The blood is digested over time serving as a source of protein for the production of eggs, which gradually fill the abdomen. Anopheles mosquitoes can be distinguished from other mosquitoes by the palps (sensory organ near the mouthpart), which are as long as the proboscis, and by the presence of discrete blocks of black and white scales on the wings. Adult Anopheles can also be identified by their typical resting position: males and females rest with their abdomens sticking up in the air rather than parallel to the surface on which they are resting. [7]



Fig. (2): difference between male and female mosquitoes

2.3. Life Cycle:

Like all mosquitoes, anophelines go through two phases. The first is aquatic and lasts 5-14 days depending on the species and the ambient temperature, and comprises the egg, larval and pupa stages. The second is aerial and involves the adult. The adult females can live up to a month (or more in a laboratory setting) but the majority live 2 weeks or less in nature. [8]

• Life Cycle:





Fig. (3): Life Cycle of Anopheles mosquitoes

• Life stages of Anopheles species:

1) Eggs:

- Anopheles, the mosquitoes that spread malaria, like to lay their eggs in marshy areas or near the banks of shallow creeks and streams.
- Adult, female mosquitoes lay eggs one at a time directly on water. The eggs float on the surface of the water.
- Adult, female mosquitoes lay 50–200 eggs at a time.
- Eggs do not tolerate drying out.[9]



Fig. (4): Eggs of Anopheles mosquitoes

2) Larvae:

- Larvae live in the water. They hatch from mosquito eggs.
- Anopheles larvae breathe by using special organs (called spiracles) located on their abdomen.
- Larvae shed their skin (molt) four times during this stage before becoming pupae. [9]



Fig. (5): larvae of Anopheles mosquitoes

3) Pupae:

- Pupae live in water. Pupae do not have external mouthparts, so they do not eat during this stage.
- An adult mosquito emerges from a pupa and flies away. [9]



Fig. (5): Pupa of Anopheles mosquitoes

4) Adult:

- Adult, female Anopheles mosquitoes prefer to feed on people or animals, such as cattle. Female Anopheles bite people and animals, usually late in the evening or at night. Female mosquitoes need blood to produce eggs.
- Some Anopheles male mosquitoes fly in large swarms, usually around dusk, and the females fly in the swarms to mate.
- After blood feeding, a female mosquito rests for a few days while the blood digests and the eggs develop. After the eggs develop, the female lays them in water sources. [9]





2.4. Feeding:

1.Feeding Times:

Anopheles mosquitoes are predominantly nocturnal feeders, with peak activity during the early hours of dusk and dawn. This pattern minimizes exposure to predators and harsh environmental conditions.[10]

2.Host Seeking and Selection:

Female Anopheles mosquitoes utilize a combination of sensory cues to locate hosts. They are particularly sensitive to carbon dioxide, body heat, and specific odors emitted by humans and animals. These sensory inputs are detected by receptors on their antennae and maxillary palps. [11]

3.Blood Feeding:

Blood meals are essential for female Anopheles mosquitoes as they provide the necessary proteins and iron for egg development. The feeding process involves piercing the host's skin with their proboscis and injecting saliva that contains anticoagulants, which prevent blood clotting and facilitate smooth feeding. [10]

4.Sugar Feeding:

Both male and female mosquitoes feed on plant nectar and other sugar sources to fulfill their energy requirements. Females, however, alternate between sugar feeding and blood feeding depending on their reproductive stage. [12]

5.Feeding Frequency:

Female Anopheles mosquitoes generally seek blood meals every 2-3 days. The frequency of feeding is influenced by environmental factors such as temperature and humidity, as well as the mosquito's reproductive cycle. After consuming a blood meal, females typically rest to digest the blood and develop their eggs. [10]

6.Impact on Disease Transmission:

The feeding behavior of Anopheles mosquitoes is integral to the transmission of malaria. When a mosquito feeds on an infected individual, it ingests malaria parasites (Plasmodium spp.). These parasites develop within the mosquito and can be transmitted to other humans during subsequent blood meals. [13]

3. Diseases caused by Anopheles mosquitoes:

Anopheles mosquitoes, notorious for their role as vectors of disease, pose significant public health challenges worldwide. Among the numerous diseases transmitted by these mosquitoes, malaria stands out as one of the most devastating, affecting millions of people annually, particularly in tropical and subtropical regions.

However, Anopheles mosquitoes are also responsible for transmitting other pathogens, contributing to a diverse array of diseases with varying degrees of morbidity and mortality. [14]

There are examples of diseases caused by Anopheles mosquitoes:

1.Malaria: The most well-known disease transmitted by Anopheles mosquitoes is malaria. It is caused by Plasmodium parasites, which are injected into the bloodstream during mosquito feeding. Malaria can lead to: fever, chills, anemia and in severe cases organ failure and death if not treated promptly.[15]

2.Lymphatic Filariasis: Anopheles mosquitoes can also transmit lymphatic filariasis, a parasitic disease caused by microscopic worms. The larvae are transmitted through mosquito bites, leading to the obstruction and inflammation of the lymphatic system, often resulting in swelling of the limbs and genitalia.[15]

3.Arboviral Diseases: Some species of Anopheles mosquitoes can transmit arboviruses such as Rift Valley fever virus and O'nyong'nyong virus. These viruses can cause febrile illnesses characterized by fever, joint pain, and in severe cases, hemorrhagic fever or neurological complications. [15]

3.1. Malaria Diseases:

Malaria continues to be one of the most debilitating mosquito-borne diseases. According to the WHO World Malaria Report in 2011, 216 million cases of malaria were reported in the year 2010, resulting in 655,000 deaths, of which 86% were children below five years of age. A total of 41 different species of Anopheles mosquitoes act as vectors for transmission of human malaria. Around 19 of them have been found to play a major role in disease-transmission across Asia-Pacific. Increasing instances of pathogens gaining resistance to the first-line of drugs and replacement anti-malarial have complicated the scenario of disease control in endemic areas. [16]

Malaria is a life-threatening disease caused by parasites that are transmitted to humans through the bites of infected female Anopheles mosquitoes. The primary causative agents of malaria are five species of the Plasmodium parasite: P. falciparum, P. vivax, P. malaria, P. oval, and P. Knowles. Among these, P. falciparum and P. vivax are the most common and pose significant health risks. P. falciparum is the most deadly, responsible for the majority of malaria-related deaths globally. [17]



Fig. (6): graph shows number of cases infected with malaria (2000_2018)

3.1.1. Malaria History:

Malaria is an age-long disease whose initial occurrence predates human history. In 2700 BC, malaria symptoms were recorded in the Chinese Canon of Medicine, the so-called Nei Ching. Egyptian papyri also mention malaria symptoms in around 1550 BC. In the 6th century BC, malaria-like fever affecting Mesopotamia was listed under Cuneiform. Hippocrates was the first to describe malaria paroxysm (intermittent fever) as a disease in the century of 4th BC.

In the 2nd century BC, Artemisia annua (the Qinghao plant) was described in the China medical treatise. The use of the Peruvian bark of the Cinchona tree (a source of quinine) to treat fever was recognized during the early 17th Century. [18]

3.1.2. Life Cycle of Malaria Diseases:

Parasites of the genus Plasmodium are protozoans which invade and multiply within erythrocytes of vertebrates, and are transmitted by mosquitoes.

classification of Plasmodium malaria		
Kingdom	Protozoa	
Subkingdom	Biciliata	
Phylum	Myzozoa	
Subphylum	Apicomplexa	
Class	Aconoidasida	
Order	Haemosporina	
Genus	Plasmodium	
species	Malaria	

The motile invasive stages (merozoite, ookinete and sporozoite) are elongate, uninucleate cells able to enter cells or pass through tissues, using specialized secretory and locomotory organelles. Intracellular stages live in a membrane-lined cavity (parasitophorous vacuole) within the host cell cytoplasm.

The subphylum Apicomplexa comprises nearly 5000 described species, all parasitic including several genera of medical and economic importance including, Plasmodium and other. [19]

All types of Plasmodium species have a similar and complex life cycle. The life cycle of every malaria parasite infecting human is distinguished by: (<u>1) an exogenous sexual phase (sporogony)</u>, in which replication takes place in many Anopheles mosquito species, and (<u>2</u>) an endogenous asexual phase (schizogony), which occurs in the vertebrate hosts.[20]



Fig. (7): the life cycle of malaria parasites

1. exogenous sexual phase (sporogony):

The sexual cycle is taking place in the gut and abdominal walls of some species of the female mosquito. The life cycle within the mosquito takes about eight to thirty-five days, after which the Plasmodium is infective. When the insect bites the skin, the sporozoite (motile infectious form) will be injected into the human's dermis and then searches for a blood vessel to feed on.

The mosquito discharges various vasodilators to raise the likelihood of finding a vessel. It also salivates into our blood to prevent blood clotting. The fate of these sporozoites is not clearly illustrated. However, they can take 1- 2 hours to exit from the dermis. The TRAPlike protein (TLP) of the sporozoites plays a role in this cell transversal program using gliding motility.

Those sporozoites that remained in the skin could be killed and drained by the lymphatics, where a host immune response is activated. After thirty to sixty minutes of the injection, the sporozoites (with the thread-like shape) will be transported to the liver through the vascular system. One single sporozoite in one liver cell multiplies into tens of thousands of exoerythrocytic merozoites.

Within seven to twelve days, the sporozoites develop into schizonts and then grow up to 30,000 merozoites, which burst the hepatocytes. Alternatively, some sporozoites of vivax and ovale species turn into dormant forms (hypnozoites) in the liver for months/years and can cause relapsed malaria. Uncommonly, the recurrence of falciparum malaria was observed in patient's years after the departure of an endemic area. This indicates that P. falciparum has a dormant stage although occurs occasionally. [20]

2. endogenous asexual phase (schizogony):

The asexual cycle that causes the disease manifestations is taking place in the liver and RBCs of humans. The asexual erythrocytic cycle begins with the invasion of the RBCs by the merozoites where they are furnished with the hemoglobin of the host. The parasites then multiply ten times every two days, destroying erythrocytes and infecting new cells throughout the body. Inside the host RBC, the parasite continues its maturity from the early ring stage to the late trophozoite. Following mitotic divisions, the trophozoite undergoes the schizont stage, which upon rupture, can produce about 6-32 merozoites depending on the parasite species.

The prepatent period (period from acquiring infection through a mosquito bite and the first appearance of the trophozoites in erythrocytes) is the characteristic of every Plasmodium species. It lasts nine days in falciparum, eleven up to thirteen days in vivax, ten up to fourteen days in oval, fifteen days in malaria and nine up to twelve days in Knowles.

When the blood schizont bursts, the discharged merozoites maintain the life cycle by invading the neighbor erythrocytes until it is brought under control. The rupture of schizonts is accompanied by the manifestation of the malaria febrile paroxysm typically lasting eight to twelve hours ("Golgi cycle") and characterized by three stages:

1. The first stage:

which is known as the cold stage, is manifested by the quick rise in body temperature together with a sensation of extreme cold (chills). The patient desires to cover with the blankets.

2. The second stage:

(hot stage) is with the temperature peak (may rise to 410C), skin vasodilatation, myalgia, and very severe headache. Patients feel too burning hot and cast their clothes.

3. The third stage:

(sweating stage), the patients have profuse sweating and their fever become drops. Then, the patients may go to sleep due to tiredness.

At the time of blood meal, the erythrocytic gametocytes migrate to the mosquito gut. In the mosquito midgut, matured gametocytes egress from the host cell and differentiate into male and female gametes.

Fall in temperature, rise in pH, and increase in xanthurenic acid concentration are the triggering factors for this differentiation. Then, undergo gametogenesis (the flagellated forms of microgametes/male gametocytes formed by exflagellation penetrate/fertilize the macrogametes/female gametocytes) to form a diploid zygote.

The zygote develops into motile ookinetes, which penetrate the mosquito midgut and develop into round oocysts. The oocyst development (the only extracellular portion of the Plasmodium life cycle) is the longest developmental phase (takes 3 - 30 days). only 25 percent of those released from oocyst travel through the hemocoel fluid to the acinar cells of salivary glands, where after about a day of residence, they became highly infective. [20]



Fig. (8): Life Cycle of Malaria Diseases

***** Summary Life Cycle of Malaria Diseases:

1. Infection of Mosquito:

When an Anopheles mosquito bites an infected person, it ingests Plasmodium gametocytes along with the blood. [21,22]

2. Parasite Development:

Inside the mosquito, gametocytes develop into sporozoites, which migrate to the mosquito's salivary glands. [21,22]

3. Human Infection:

The mosquito transmits sporozoites to a new human host during subsequent blood meals. The sporozoites travel to the liver, where they mature and multiply. [21,22]

4. Red Blood Cell Invasion:

Mature parasites are released into the bloodstream, where they invade red blood cells, causing symptoms of malaria. [21,22]





3.1.3. Signs and Symptoms of Malaria Diseases:

- Fever, Chills, and General feeling of discomfort.
- Headache, Nausea and vomiting, and Diarrhea.
- Abdominal pain, Muscle or joint pain, and Fatigue.
- Rapid breathing, Rapid heart rate, and Cough.
- Some people who have malaria experience cycles of malaria "Attacks." An attack usually starts with shivering and chills, followed by a high fever, followed by sweating and a return to normal temperature.
- Malaria signs and symptoms typically begin within a few weeks after being bitten by an infected mosquito. However, some types of malaria parasites can lie dormant in your body for up to a year.[23]





3.1.4. Diagnosis and Treatment:

1. Diagnosis:

Typically involves microscopic examination of blood smears or rapid diagnostic tests to detect Plasmodium antigens. There are two ways of diagnosing malaria:

1. blood is taken and tested for malaria through Rapid Diagnostic Test (RDT) and Microscopy Test.

2. blood is taken and tested for malaria through Rapid Diagnostic Test (RDT) and Microscopy Test. [23]

2. Treatment:

• Malaria is treated with prescription drugs to kill the parasite. The types of drugs and the length of treatment will vary, depending on:

1. type of malaria parasite.

2. The severity of symptoms.

3. age.

- The most common antimalarial drugs include:
 - Chloroquine phosphate.
 - Artemisinin-based combination therapies (ACTs).
 - Atovaquone-proguanil (Malarone).
 - Quinine sulfate (Qualaquin) with doxycycline (Oracea,
 - Vibramycin, others).
 - Primaquine phosphate. [24]

3.2. Lymphatic Filariasis Diseases:

Lymphatic filariasis (LF) is the second most common mosquito borne disease globally. LF infection occurs by exposure to mosquito bites. [25]

Lymphatic filariasis, commonly known as elephantiasis, is a neglected tropical disease. Infection occurs when filarial parasites are transmitted to humans through mosquitoes. Infection is usually acquired in childhood and causes hidden damage to the lymphatic system. The painful and profoundly disfiguring visible manifestations of the disease lymphoedema, elephantiasis and scrotal swelling occur later in life and can lead to permanent disability. These patients are not only physically disabled, but suffer mental, social and financial losses contributing to stigma and poverty. [26]

3.2.1. Lymphatic Filariasis History:

About 600 B.C., a singular symptom of bancroftian filariasis (elephantiasis arabum) was described by ancient Hindus and Persian doctors. However, there is an indication that lymphatic filariasis existed as early as 1500 B.C. [27]

Although there are no manuscripts about LF before the 16th century, but the historical evidence of LF can be ratified through ancient artifacts which suggested that the disease may have been found about 2000 BC such as a statue of Pharaoh Mentuhotep depicting swollen limbs, also the replicas of illustrations which were found on the wall tomb of Tutankhamen depicting the prince of Punt and his wife who suffer from elephantiasis. [25]

3.2.2. Life Cycle of Lymphatic Filariasis Diseases:

The filariases are a group of arthropod-borne nematode infections that are endemic mostly in tropical areas of the world. Instead of residing in the intestine, mature adult filarial worms characteristically live in the lymphatics or in connective tissue Eight filarial species infect humans: *Wuchereria bancrofti, Brugia malayi, Onchocerca volvulus, Brugia timori, Loa loa, Mansonella streptocerca, Mansonella perstans,* and *Mansonella ozzardi.* The first three are the most common filariases worldwide. Although not usually fatal, these infections can result in significant disability and disfigurement, such as irreversible limb lymphedema in the case of *W. bancrofti* and other.[28]

classification of Wuchereria bancrofti		
Kingdom	Animalia	
Phylum	Nematoda	
Class	Phasmida	
Order	Filaroidea	
Family	Filariidae	
Geuns	Wuchereria	

Wuchereria bancrofti pass through 2 hosts during their life cycle, the definitive host is humans and intermediate host is female mosquito. Culex quinquefasciatus considered is the major vector in India and most other parts of Asia. When the mosquito feeds on an infected person, the microfilariae are taken with the blood meal and reach the mosquito's stomach within 2-6 hours, the microfilariae release the sheaths and penetrate the wall of the stomach then migrate to the thoracic muscles to complement its growth.

The extrinsic incubation period is the time it takes from enter the microfilaria into the mosquito until it reaches to infective stage larva, its period is 10-20 days, its period varies according to environmental factors such as humidity, temperature and the vector species.

When an infected mosquito bites a healthy person, the larvae is injecting into the host's body and migrates into the lymphatic vessels and grows into adult worms that later produce microfilaria. The time between infection and the production of adult worms for microfilaria was about 12 months. Microfilariae move outside and inside peripheral blood according to a daily cycle. In some species microfilaria move through the night between 10 pm- 4 am. [29]



Fig. (11): life cycle of Lymphatic Filariasis Diseases

Summary Life Cycle of Lymphatic Filariasis Diseases:

Life-cycle of filarial parasites, demonstrated with W. bacncrofti. Both a vector and a host are important for the completion of the life-cycle of filarial nematodes:

(1) The infected vector transmits the infective-stage larvae into the human host during a blood meal.

(2) The L3-stage larvae mature into adult worms.

(3) The parasites develop into adults and then produce microfilariae (MF), which migrate to the lymphatics and blood for circulation.

(4) The vector once again ingests the microfilariae during a blood meal on an infected host.

(5) The microfilariae then migrate to the thoracic muscles of the vector through the midgut.

(6) The microfilariae develop into the L1 stage.

(7) then subsequently into the L3 larvae.

(8) The L3 larvae migrate to the vector's proboscis via the hemocel. [30]



Fig. (12): Wuchereria bancrofti

3.2.3. Symptoms of Lymphatic Filariasis Diseases:

Lymphatic filariasis infection involves asymptomatic, acute and chronic conditions:

The majority of infections are asymptomatic, showing no external signs of infection while contributing the transmission of the parasite. These asymptomatic infections still cause damage to the lymphatic system and the kidneys and alter the body's immune system. When lymphatic filariasis develops into chronic conditions it leads to lymphoedema (tissue swelling) or elephantiasis (skin/tissue thickening) of limbs and hydrocele (scrotal swelling). Involvement of breasts and genital organs is common.

Such body deformities often lead to social stigma and sub-optimal mental health, loss of income-earning opportunities and increased medical expenses for patients and their caretakers. The socioeconomic burdens of isolation and poverty are immense.

Acute episodes of local inflammation involving skin, lymph nodes and lymphatic vessels often accompany chronic lymphoedema or elephantiasis. Some of these episodes are caused by the body's immune response to the parasite. Most are the result of secondary

bacterial skin infection where normal defenses have been partially lost due to underlying lymphatic damage. These acute attacks are debilitating, may last for weeks and are the primary cause of lost wages among people suffering with lymphatic filariasis. [26]



Fig. (13): Symptoms of Lymphatic Filariasis Diseases

3.2.4. Diagnosis and Treatment:

1. Diagnosis:

There are many laboratory tests to diagnosis of lymphatic filariasis:

1. Basic serology testing: this test used to detection for microfilariae in peripheral blood.

2. Askin biopsy: this test is to diagnose nematode infections that live in tissues.

3. Ultrasonography: used to locate and visualize the movement of living adult worms of W.bancrofti in the scrotal lymphatics.

4. PCR tests: this test used to detect parasite DNA in humans and vectors in brugian and bancroftian filariasis, this test are high specificity and sensitivity

5. lymphoscintigraphy: it has been shown up early, clinically asymptomatic stage of the disease, there are lymphatic deformities in the infected limb of human with microfilaria.

6. Immunochromatographic: it's a test used to diagnose the W.bancrofti infection and is considered assays a high sensitive and specific to filarial antigen detection. [29]

2. Treatment:

Elimination of lymphatic filariasis is possible by stopping the spread of the infection through preventive chemotherapy. [26]

1. Diethylcarbamazine (DEC):

is an effective drug against microfilariae and adult worms DEC lowers the microfilaria levels in the blood. This effect was observed at 50% only of patients although DEC kills the adult worms.

2. Ivermectin (IVM):

this drug effects directly on microfilaria in single doses and lowers the level of microfilaria in the blood even after one year such as DEC.

3. Albendazole (ALB): Antihelmintic drug is used to destroy the adult worms. [29]

4. control of Anopheles mosquitoes:

controlling mosquito-borne diseases include long-lasting insecticidetreated nets (LLINs), indoor residual spraying (IRS), peridomestic space spraying, and the use of mosquito repellents among others [31]:

- Environmental clean-up: eliminate or destroy all mosquito breeding places and conduct general clean-up of bushes and tall grasses where they live.
- Insecticide-treated mosquito nets and house screening: prevent adult mosquito biting in the house.
- Indoor residual spraying: killing of adult mosquitoes in the house.
- Presumptive treatment: killing of malaria parasite in the blood before they cause malaria.
- Mosquito repellents: mosquito coils and local remedies.
- Individual protection: wearing long sleeve and trousers. [23]

Summary Research

The research focuses on the Anopheles mosquito, a key vector of human diseases such as malaria, lymphatic filariasis, and certain arboviruses. Anopheles mosquitoes belong to the Culicidae family and are primarily nocturnal feeders.it is a vector of many diseases, through the bite of, with significant mortality rates globally.

The study highlights the mosquitoes' feeding behavior, hostseeking strategies, and the development of malaria & lymphatic filariasis parasites within them. Effective control measures include the use of insecticide-treated nets, indoor spraying, and environmental clean-up.

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