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A REVIEW ON MALARIA

Dr.Aamer Quazi* Ajinkya N. Bansode[1], Pratik M. Maske[2] , Saurabh J. Mane[3].

(Professor, student[1], Student[2], Student[3].)*
ASPM'S K.T.PATIL COLLEGE OF PHARMACY, OSMANABAD M.S – 413501 India.
Corresponding Author: Dr.Aamer I. Quazi M. Pharm ,PhD (Department of Pharmaceutics)*

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ABSTRACT:A parasite of the genus Plasmodium infects people and causes malaria, an important parasitic disease that is spread by female anopheles. The majority of study has been focused on P. falciparum since it is the most dangerous infection of all the others (P. ovale, P. vivax, and P. malariae), notably in terms of morbidity and mortality.

KEYWORDS : Epidemiology, Transmission, Pathogenesis, Life cycle

I. INTRODUCTION:

The word malaria comes from the Mediaeval Italian mala aria, which means "bad air"; the disease was once known as ague or marsh fever because of its connection to swamps and marshlands. Although malaria is no longer endemic in most of Europe and North America, imported cases still happen there occasionally. Infections are caused by different Plasmodium species in some animals. Each species of mammal, bird, and reptile has a unique type of malaria.

II. HISTORY:

Malaria's distinctive periodic fevers have been discussed throughout recorded history, starting in China circa 2700 BC. Malaria was so common in Rome that it earned the nickname "Roman fever" and may have contributed to the fall of the Roman Empire.Quinine was first refined from tree bark in 1820. The ground bark had been utilised to cure malaria for many years earlier.The malaria parasite is originally identified by Charles Louis Alphonse Laveran in 1880. For the finding, he receives the 1907 Nobel Prize.Sir Ronald Ross proves that mosquitoes spread malaria in 1898. For this accomplishment, he is awarded the Nobel Prize in 1902.The anti-malarial medication chloroquine is discovered in 1934 by Hans Andersag in Germany; nevertheless, it is not utilised widely until after World War II.1939 Hermann Paul.

REASON FOR MALARIA

- Feline malaria

Plasmodium relictum, a protist that infects birds in tropical areas, is the protist most famously responsible for causing avian malaria. There are numerous other Plasmodium species that infect birds, including Plasmodium anasum.

- Placenta gallinaceum

But aside from the poultry industry on occasion, these are less significant. However, in places where avian malaria has just been introduced, like the Hawaiian Islands, it can be devastating to birds that have lost their natural resistance to it.
Four species of the Plasmodium parasites have been discovered as having the potential to infect people with illness.
Falciparum Plasmodium
Plasmodium ovale and Plasmodium vivax
Plasmodium knowlesi and Plasmodium malariae.

- Classification within science

Domain: Eukaryota Phylum: Apicomplexa
Class: Aconoidasida
Order: Haemosporida
Family: Plasmodiidae
Plasmodium species include P. relictum and others from the genus.

EPIDEMIOLOGY

Approximately 65 Plasmodiun species have been found in over 1,000 different bird species, making them one of the susceptible groups. Only a small percentage of the Plasmodium species that have been found seem to be natural parasites of domestic poultry. Numerous other Plasmodia species, which are primarily found in passerine birds, have the potential to infect domestic poultry or have already been successfully transmitted in experiments.

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- Vulnerable host:

Canaries, falcons, pigeons, domestic poultry, penguins, and ducks can all contract Plasmodium, but passerine birds are the most prevalent species to do so asymptomatically.
Humans, reptiles, other mammals, non-human primates, and others.
Age at which someone is susceptible: The majority of instances (65%) involve children under the age of 15.
Sexually active: Pregnant women are particularly at risk for infection; each year, nearly 125 million of them are at danger.

TRANSMISSION

Plasmodium may use many mosquito genera as both intermediate hosts and vectors.
The mosquitoes Culex, Anopheles, Culiceta, Mansonia, and Aedes
Mosquito bites; ii. Mechanically, such as during a mass vaccination; iii. Caponizationandinjection.

Anopheles mosquitoes are the main vectors used by malaria parasites to spread from person to person.
Blood with parasites is ingested into the mosquito's gut when it bites. The parasites go through a complicated development process over the course of ten or more days, and once they reach maturity, they settle in the salivary glands of the mosquito, where they can be transmitted to another person when it bites them again. The parasite first infects the liver of the next human host, where it engages in rapid reproduction for at least five days before infecting red blood cells.
The most severe malaria symptoms, such as cerebral malaria, which is brought on by parasitized blood cells obstructing blood capillaries in the brain, are caused by parasites in the blood.

LIFE CYCLE OF SPECIES OF PLASMODIUM

- Male Life Cycle

While consuming a blood meal, a female anopheline mosquito injects "Sporozoites," which are parasites.

- Schizophrenia pre-erythrocytic

The sporozoites enter the liver cells and transform into "Merozoites" by having tapered ends and an elongated nucleus. Pre-erythrocyticSchizogony is finished in 6 days in P. falciparum, 9 days in P. Ovale, 8 days in P. Vivax, and 15 days in P. malariae.

- Schizogony with erythrocytes

The parasite-filled hepatocytes burst, releasing merozoites that feed on red blood cells. There are no clinical symptoms or pathological harm (the blood is still sterile throughout the pre-erythrocytic stage).

The parasites infect the RBC at this stage and transform into the following forms.

- Trophozoites

These organisms have blue cytoplasmic rings, red nuclei, an unstained region that contains the "nutrient vacuole," and active amoeboid motions. Granules of pigment, which are metabolic byproducts, emerge.
A Falciparum trophozoite is affixed to the host red blood cell's periphery. The 'Maurer's dots', which are dark brown or black pigment grains, are used in paint.

Granules made by Schuffner
P. vivax, the RBC In distorts and grows to be twice as large as before. Yellow specks make up the pigment; they resemble basophillicstippling.It has a brown tint and is referred to as "Schuffner's Granules."

- Schizont

A fully developdtrophozoite is called a schizont, and in P. falciparum, the schizont's nucleus divides multiple times to produce spherical masses referred to as merozoites.
The pigmented mass Is located in the core of a rosette-shaped arrangement of merozoites that were created from schizonts in P. vivax.Schizogony with exoerythrocytes

Pre-erythrocytic phase entirely vanishes after blood infection is established in P. falciparum, but it survives in P. Vivax, P. Ovale, and P. malariae in the form of local schizogony in the liver, which is what causes relapses in these species. The 'Hypnozoites' are the merozoites that this schizogony unleashed.

- Gametocytes

The development of 'Gametocytes', which continue to develop inside the female anopheline mosquito, marks the beginning of the sexual cycle in the human host.

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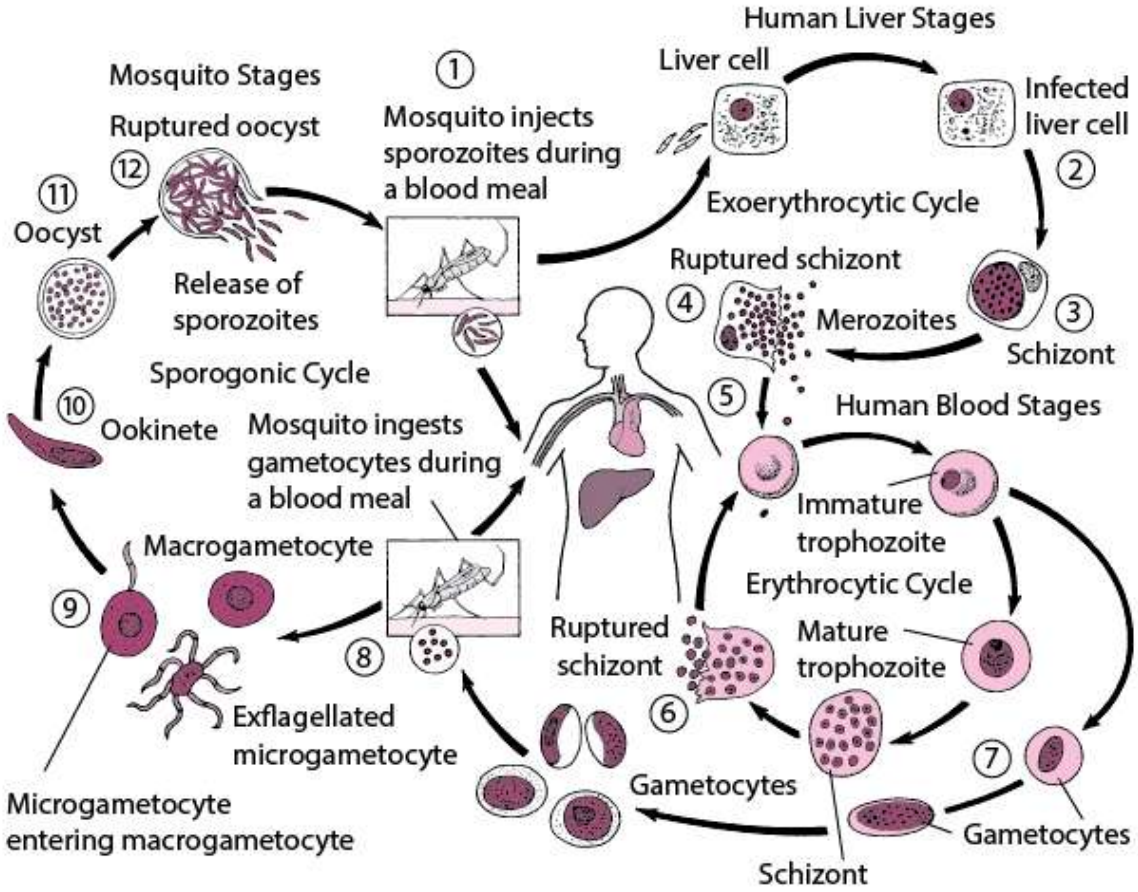
At least 12 gametocytes must be present in every millilitre of human blood, and there should be a surplus of female gametocytes.



Genetic Resistance

Malaria, particularly the P. falciparum species, is responsible for high rates of mortality and morbidity, and it has recently exerted the most selective pressure on the human genome. Sickle cell trait, thalassaemia characteristics, glucose-6-phosphate dehydrogenase deficiency, and the presence of Duffy antigens on red blood cells are among the genetic variables that contribute to some resistance to it.

Particularly intriguing is how the sickle cell trait affects immunity against malaria. Haemoglobin in the blood has a deficiency due to the sickle cell trait. The mutated haemoglobin S molecule causes the red blood cell to sickle or distort into a curved shape as opposed to maintaining the biconcave shape of a typical red blood cell. The sickle-shaped molecule makes it less efficient in absorbing or releasing oxygen, which prevents malaria parasites from finishing their life cycle in the cell. Sickle-cell disease affects people who are homozygous (having two copies of the faulty haemoglobin beta allele), whereasOli malaria resistance affects people who are heterozygous (having one abnormal allele and one normal allele.

Pathogenesis

First, by surface expression of Plasmodium falciparum erythrocyte membrane protein 1 (EMP1), parasitized red blood cells (PRBCs) cling to receptors expressed by brain microvascular endothelial cells, such as intercellular adhesion molecule 1 (ICAM1). Parasite glycosylphosphatidylinositol (GPI), which is either released into the blood or present in parasite membranes, serves as a pathogen-associated molecular pattern and toxin, eliciting an inflammatory response when merozoites are liberated from PRBCs 4 hours later.

The endothelium Is then activated, and there is local synthesis of cytokines and chemokines as a result. This causes the expression

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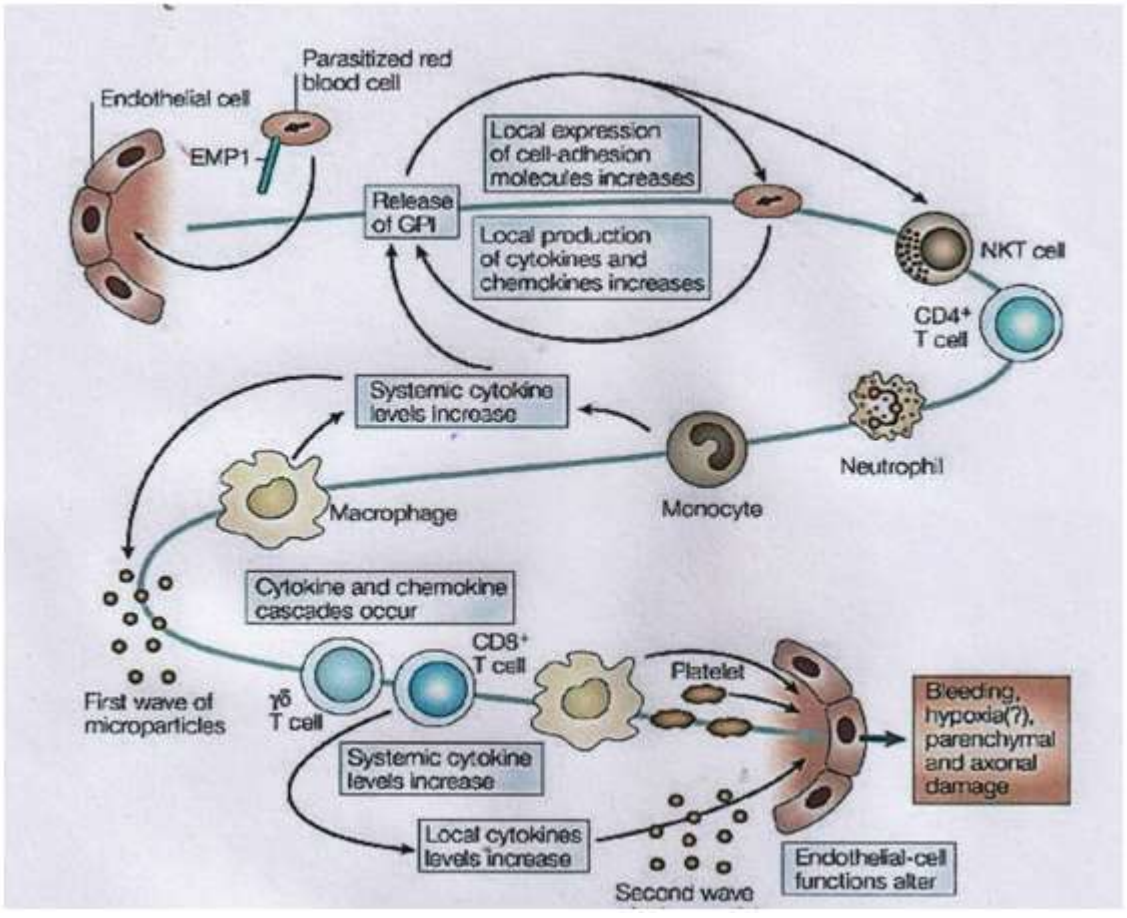
of cell-adhesion molecules by endothelial cells to be upregulated.

Due to an increase in parasite population and increased PRBC binding to endothelial cells with elevated expression of cell-adhesion molecules, this cycle is continued and made worse within the following 24 hours. For CD1d-restricted natural killer T (NKT) cells, GPI can also act as a ligand, activating them. Depending on which natural-killer-complex loci are expressed, activated NKT cells can control the development of CD4+ T cells into T helper 1 (TH1) or TH2 cells, thus activation and participation of CD4+ T cells take place.

Additionally, chemokines attract monocytes and stimulate neutrophils, though it is unknown whether neutrophils infiltrate the brain microvessels of mice or humans with cerebral malaria. Monocytes that have been attracted can later develop into macrophages and become imprisoned in brain microvessels. GPI can also activate macrophages, and interferon- amplifies this action. Infiltration of cells, sequestration of PRBCs, and release of microparticles (which are likely derived from endothelial cells) are all amplified by locally activated macrophages' increased production of chemokines, which are then released systemically. After a few more cycles, T cells and CD8+ T cells may get involved, releasing more chemokines and cytokines both locally and systemically, and perhaps causing lesions in the endothelium caused by perforin.

Platelets are sequestered and take part in modifying endothelial-cell activities along with locally halted macrophages. More platelet-, endothelial-, and monocyte-derived microparticles are released, which causes pro-inflammatory and pro-coagulant effects to spread. Finally, endothelial damage may occur, leading to perivascular haemorrhage, axonal injury, neurotransmitter alterations, and metabolic abnormalities. Whether all of these processes take place or only a few of them may affect the total disease spectrum in humans.



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SIGNS AND SYMPTOMS :

The incubation period is the amount of time between the first infection and the onset of symptoms. Generally speaking, it depends on the kind of parasite:

9 to 14 days for P. falciparum
12 to 18 days for P. vivax
12 to 18 days for P. ovale
P. malariae – between 18 and 40 days

For P. vivax and P. ovale, incubation times can range from as little as 7 days to several months. The incubation period is typically prolonged if you are taking chemoprophylaxis medicine to avoid infection.

In human:

The hallmark sign of malaria is a paroxysm, which is a cycle of sudden coldness, rigour, fever, and sweating that happens every two days in P. vivax and P. ovale infections and every three days in P. malariae infections (tertian fever). P. falciparum infection can result in either a milder, nearly constant fever or recurring fever every 36–48 hours (quartan fever).

Malaria signs and symptoms often appear 8 to 25 days after infection; they include: Reduced consciousness Significant weakness to the point that the person is unable to walk

Lack of appetite Two or more convulsions
Low blood pressure (adults: less than 70 mmHg; children: less than 50 mmHg)
Breathing difficulties
Cardiovascular shock
Haemoglobin in the urine or kidney failure
Bleeding issues or haemoglobin less than 5 g/dl
Thoracic edoema
Low blood sugar levels (less than 2.2 mmol/l / 40 mg/dl)
A parasite level in the blood of more than 2%, acidosis, or lactate levels greater than 5 mmol/l
Damage to the retina and convulsions. A normal peripheral blood leukocyte count together with hyperbilirubinemia, thrombocytopenia, splenomegaly (enlarged spleen), fever without localising symptoms, and other symptoms.
Gross lesions: Liver and spleen enlargement and blackening of the skin
The existence of watery and pale cardiac blood.
Birds that perished before 21 days after PI had a little amount of subcutaneous fat deposits and had very healthy flesh, with just slight atrophy of the pectoral muscles.
Impression smears from these tissues frequently show schizonts; emaciated carcass; large keels.
Schizonts are found throughout the body in a variety of tissues.

TREATMENT OF MALARIA

In order to treat malaria, the following conditions must be met:

1. Infection type
2. Infection severity
3. The status of the host; 4. Associated illnesses or circumstances

Infection type

The sort of infection must certainly determine the course of treatment. Patients with P. falciparum malaria should undergo a thorough evaluation due to the probable severity of the illness and potential for medication resistance.

P. vivax: just 25 mg/kg of chloroquine and 14 days of primaquine.

P. falciparum: Treatment should be based on sensitivity and severity. To stop the spread, primaquine, a gametocytocidal, is essential.

Blood schizonticides for P. falciparum and Primaquine for P. vivax are effective treatments for mixed infections.

Infection severity

Malaria sequelae should be carefully and properly evaluated in all people who have the disease. Only P. falciparum malaria is characterised by acute, life-threatening consequences. Malaria is likely the only illness of its sort that can be effectively treated in just three days, but if a patient's diagnosis and appropriate treatment are put off, it can easily and swiftly lead to death.

If there is any doubt about the drug sensitivity of the parasite, it is safer to treat these instances as chloroquine resistant malaria with medications like quinine or artemisinin. All cases of severe malaria should be assumed to be caused by P. falciparum malaria.

All severe cases of malaria should be treated, monitored, and evaluated in a hospital setting.

All cases of severe malaria should be treated with injectable antimalarials

To guarantee optimal absorption and plasma drug levels, all cases of severe malaria should be treated with injectable antimalarials (chloroquine, quinine, artemisinin). To ensure thorough treatment, it is preferable to utilise two blood schizonticidal medications—one quick acting and another delayed acting. Mefloquine and halofantrine are two more recent medications that should not be taken. It is

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important to thoroughly evaluate and treat any related conditions.

MALARIA PREVENTION AND CONTROL

Prophylactic medications, mosquito eradication, and prevention of mosquito bites are some of the techniques used to stop the spread of disease or to protect people in places where malaria is an endemic problem.

- Reducing avian malaria

Amorphous nanoporous silica molecules with hydrophobic and hydrophilic characteristics that have been surface-modified can be employed successfully as therapeutic drugs to treat chicken malaria in the poultry industry. The amorphous nanosilica was created utilising a top-down methodology employing silica from volcanic soil as a starting material.

VLDL, serum triglycerides, and other components of serum cholesterol are physically absorbed by these nanosilica molecules as part of their primary mechanism of action in the lipophilic nanopores of nanosilica. This lowers the amount of cholesterol derived by the host, which restricts the growth of the malaria parasite in vivo.

- Vector command

Prior to the development of DDT, malaria was successfully eradicated or controlled in a number of tropical regions by eliminating or poisoning mosquito breeding sites or the aquatic habitats of the larval stages, such as by draining or smearing oil into areas with standing water. In Africa, these techniques have not been widely used for more than 50 years.

Vaccines:

Malaria vaccines are currently being developed, but none of them are 100 percent effective. There are several different vaccination possibilities on the market right now.

Edward Jenner created the first smallpox vaccine in 1789, more than 200 years before the current vaccination era began. Even so, it wasn't until 1980 that the WHO pronounced small pox to be extinct. Many of these vaccines were created empirically and from either killed or attenuated whole organisms, and they were developed by renowned figures in the history of medicine whose contributions significantly aid in the control and spread of life-threatening diseases.It suffices to say that thesevaccines were not developed overnight as it took enormous time, energy, patience and resources tobe able to do that. However, it could be said that vaccines has had a more positive effect on reducing death and helping populations across the globe

The majority of research for the malaria vaccine is focused on pre-erythrocytic vaccinations (vaccines that target the parasite before it reaches the blood), particularly vaccines based on circumsporozoite protein (CSP). Other potential vaccines include those that aim to develop immunity to the blood stages of the infection, those that aim to prevent more severe malaria diseases by blocking parasite adhesion to blood venules and placenta, and others.

Vaccinations that prevent transmission that would halt the parasite's growth in the mosquito as soon as the mosquito consumed a blood meal from an infected person. The genome of P. falciparum is being sequenced in the hopes of identifying potential targets for novel medications or vaccinations.

III. CONCLUSION:

Given that it claims the lives of more than 600,000 people annually, malaria is a public health issue. Globally, it is known that more than 50% of people are at risk of malaria, and the majority of these people are children under the age of five (Citation1). Plasmodium, which has four human-infecting species (Plasmodium vivax, P. ovale, P. malariae, and P. falciparum), of which P. falciparum can be fatal if not treated immediately, causes malaria, an acute febrile illness (Citation2). Mixed species infections are frequent in endemic areas. Heymann (Citation 3) recently noted that P. vivax and P. falciparum are the two most prevalent species worldwide, and that P. falciparum is a severe public health problem due to its severity and frequently deadly consequence.

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