

Review on Malaria Disease

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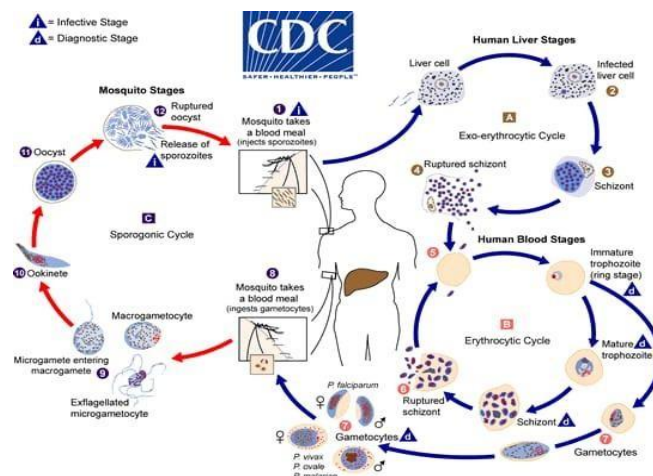
Abstract: Malaria continues to be the main community health problem in numerous nations. Six species of Plasmodium are documented as the cause of human malaria infection. Among others, Plasmodium falciparum and Plasmodium vivax parasites produce an immense challenge in the public health. Anopheles funestus and Anopheles gambiae are the major transmitters of the disease (malaria) from one person to another. The disease parasite has a complicated cycle of life that occurs in human and mosquitoes. In general, malaria diagnosis is divided into parasitological and clinical diagnosis. Internationally, the death rate of malaria becomes reduced although few records from Ethiopia describe the presence of raised prevalence of malaria in certain areas. Apart from reduction in incidence and prevalence, transmission of malaria is continued throughout the globe. Hence, its control needs a combined approach comprising treatment with effective antimalarial agents. A lot of novel compounds are under pre-clinical and clinical studies that are triggered by the occurrence of resistance among commonly used antimalarial drugs. In addition to the already known new compounds and targets for drug discovery, scientists from all corners of the world are in search of novel targets and chemical entities.

Keywords: Malaria, Plasmodium, antimalarial drugs, resistance, clinical trials, novel compounds

I. INTRODUCTION

Malaria itself or a disease looks like malaria has been distinguished before 4,000 years. The term malaria was derived from two Italian words “mala aria” meaning foul or bad air [1]. This name is originated from the observation that malaria cases were prevalent in areas where there is bad air associated with the accumulation of pools [2]. Malaria is caused by the genus Plasmodium (mosquito-borne apicomplexan parasite). At the time of bite by infected female Anopheline mosquitoes, this protozoal blood infection becomes conveying from one person to the next person [3, 4]. According to Miller et al. [5], malaria is expressed as a disease caused by repeated life cycle of the Plasmodium in the red blood cell. It is also defined as an illness brought by a parasite that lives some of the life in humans and some in mosquitoes [6].

II. THE PARASITE LIFE CYCLE



Life cycle of malaria parasites [40]. The malaria parasite life cycle involves two hosts. During a blood meal, a malaria-infected female Anopheles mosquito inoculates sporozoites into the human host. Sporozoites infect liver cells and

mature into schizonts, which rupture and release merozoites. After this initial replication in the liver (exo-erythrocytic schizogony), the parasites undergo asexual multiplication in the erythrocytes (erythrocytic schizogony). Merozoites infect red blood cells. The ring stage trophozoites mature into schizonts, which rupture releasing merozoites. Some parasites differentiate into sexual erythrocytic stages (gametocytes). The gametocytes, male (microgametocytes) and female (macrogametocytes), are ingested by an Anopheles mosquito during a blood meal. The parasites' multiplication in the mosquito is known as the sporogonic cycle. While in the mosquito's stomach, the microgametes penetrate the macrogametes generating zygotes. The zygotes in turn become motile and elongated (ookinetes) which invade the midgut wall of the mosquito where they develop into oocysts. The oocysts grow, rupture, and release sporozoites, which make their way to the mosquito's salivary glands. Inoculation of the sporozoites into a new human host perpetuates the malaria life cycle [41].

III. CONVENTIONAL MEDICINES

- **Chloroquine** - the prototype anti-malarial drug, is the drug of choice for both treatment and chemoprophylaxis of all malaria parasites except for chloroquine-resistant Plasmodium strains.
- **Amodiaquine** - Amodiaquine is closely related to chloroquine and it probably shares mechanisms of action and resistance with chloroquine. Amodiaquine has been widely used to treat malaria (10 mg base/kg/day for 3 days) because of its low cost, limited toxicity, and, in some areas, effectiveness against chloroquine-resistant strains of falciparum.
- **Primaquine** - Primaquine (the prototype drug in 8-aminoquinolines) is indicated for radical cure of vivax or ovale malaria; for presumptive anti-relapse therapy (terminal prophylaxis- use after the completion of travel to an endemic area to markedly diminish the hypnozoite stages).
- **Quinine** - Quinine is one of the four antimalarial cinchona alkaloids and has rapid schizonticidal activity against intraerythrocytic malaria parasites.
- **Mefloquine** - Mefloquine was first used to treat chloroquine-resistant falciparum malaria in Thailand. However, the slow elimination of mefloquine fostered the emergence of drug-resistant parasites [63].
- **Halofantrine** - Halofantrine hydrochloride is a phenanthrene methanol structurally related to quinine. It is effective against erythrocytic (but not other) stages of all four human malaria species.
- **Atovaquone** - Atovaquone, a highly lipophilic analogue of ubiquinone, is active against all Plasmodium species, Pneumocystis jirovecii and Toxoplasma gondii. It is highly active against asexual blood stage (erythrocytic schizonts) of falciparum malaria. This drug (only administered orally) is also effective against liver stages.
- **Artemisinins** - Artemisinins (endoperoxide sesquiterpene lactone) is a potent and fast acting blood schizonticidal killing all parasite stages, inducing more rapid parasite clearance and fever resolution than any other currently licensed antimalarial drug.

Symptoms :-

- Signs and symptoms of malaria may include:
- Fever
- Chills
- General feeling of discomfort
- Headache
- Nausea and vomiting
- Diarrhea
- Abdominal pain
- Muscle or joint pain
- Fatigue
- Rapid breathing
- Rapid heart rate
- 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.

Diagnosis

To diagnose malaria, your doctor will likely review your medical history and recent travel, conduct a physical exam, and order blood tests. Blood tests can indicate:

- The presence of the parasite in the blood, to confirm that you have malaria.
- Which type of malaria parasite is causing your symptoms.
- If your infection is caused by a parasite resistant to certain drugs.
- Whether the disease is causing any serious complications.

Treatment :

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

- Which type of malaria parasite you have
- The severity of your symptoms
- Your age
- Whether you're pregnant

Medications :

The most common antimalarial drugs include :

- **Chloroquine phosphate** : Chloroquine is the preferred treatment for any parasite that is sensitive to the drug. But in many parts of the world, parasites are resistant to chloroquine, and the drug is no longer an effective treatment.
- **Risk factors**: The greatest risk factor for developing malaria is to live in or to visit areas where the disease is common. These include the tropical and subtropical regions of:

Sub-Saharan Africa

South and Southeast Asia

Pacific Islands

Central America and northern South America

The degree of risk depends on local malaria control, seasonal changes in malaria rates and the precautions you take to prevent mosquito bites.

Risks of more-severe disease

People at increased risk of serious disease include :

- Young children and infants
- Older adults
- Travelers coming from areas with no malaria
- Pregnant women and their unborn children

Complications :-

- **Cerebral malaria** : If parasite-filled blood cells block small blood vessels to your brain (cerebral malaria), swelling of your brain or brain damage may occur. Cerebral malaria may cause seizures and coma.
- **Breathing problems** : Accumulated fluid in your lungs (pulmonary edema) can make it difficult to breathe.
- **Organ failure** : Malaria can damage the kidneys or liver or cause the spleen to rupture. Any of these conditions can be life-threatening.
- **Anemia** : Malaria may result in not having enough red blood cells for an adequate supply of oxygen to your body's tissues (anemia).

- Low blood sugar : Severe forms of malaria can cause low blood sugar (hypoglycemia), as can quinine — a common medication used to combat malaria. Very low blood sugar can result in coma or death.

Prevention :

If you live in or are traveling to an area where malaria is common, take steps to avoid mosquito bites. Mosquitoes are most active between dusk and dawn. To protect yourself from mosquito bites, you should :

- **Cover your skin :** Wear pants and long-sleeved shirts. Tuck in your shirt, and tuck pant legs into socks.
- **Apply insect repellent to skin :** Use an insect repellent registered with the Environmental Protection Agency on any exposed skin. These include repellents that contain DEET, picaridin, IR3535, oil of lemon eucalyptus (OLE), para-menthane-3,8-diol (PMD) or 2-undecanone. Do not use a spray directly on your face. Do not use products with oil of lemon eucalyptus (OLE) or p-Menthane-3,8-diol (PMD) on children under age 3.
- **Apply repellent to clothing.** Sprays containing permethrin are safe to apply to clothing.
- **Sleep under a net.** Bed nets, particularly those treated with insecticides, such as permethrin, help prevent mosquito bites while you are sleeping.

Preventive medicine

If you'll be traveling to a location where malaria is common, talk to your doctor a few months ahead of time about whether you should take drugs before, during and after your trip to help protect you from malaria parasites.

Vaccine

The World Health Organization has recommended a malaria vaccine for use in children who live in countries with high numbers of malaria cases. Researchers are continuing to develop and study malaria vaccines to prevent infection.

IV. CONCLUSION

Malaria is one of the ancient human diseases and remains an important cause of illness and death among adults as well as children in the world. However, an increasing resistance toward currently available antimalarial drugs is a big obstacle in the fight against malaria. The past instances indicate that resistance to the conventional antimalarial medicines will spread to Africa including Ethiopia. As a result, we are in an urgent need of novel, safe, and effective drugs. Some of the newer compounds possess multi-stage activity and are highly potent in inhibiting the parasite multiplication. Those novel agents that have different structure and new mechanism of action than older drugs could be the game changer in combating malaria. The current breakthroughs will still require long-term financial investments, political will, and scientific endeavor to ensure sustainability and translate to more reduction in global burden of malaria

REFERENCES

- [1]. Service W, Townson H. The anopheles vector, in Essential Malariology, 4th edition. Gilles H, Warrell D (Ed.). London: Arnold, 2002, 59-84
- [2]. Amorosa F, Corbellini G, Coluzzi M. Lessons learned from malaria: Italy's past and sub-Saharan's future. Health and Place, 2005, 11: 65-73
- [3]. Carter R, Mendis K. Evolutionary and historical aspects of the burden of malaria. Clin Microbiol Rev., 2002, 15(4):564-594
- [4]. Greenwood B, Bojang K, Whitty C, Targett GA. Malaria. Lancet, 2005, 365(9469):1487- 1498
- [5]. Miller L, Good M, Milon G. Malaria pathogenesis. Science, 1994, 264(5167):1878-1883
- [6]. NIAID. Understanding Malaria. Fighting an ancient scourge. No. 07-7139; 2007
- [7]. Bhowmik D, Chiranjib B, Navinkanth S, et al. Recent advances in prevention, Treatment and Medication of Malaria. J Chem Pharm Res., 2010, 2(1):83-90
- [8]. CDC. Human factors and Malaria. Center for disease prevention and control. Global Health-division of parasitic diseases and Malaria. USA, 2016.
- [9]. Katzung. Basic and Clinical Pharmacology, 12th edition. The McGraw-Hill Companies, Inc; 2012.

- [10]. Goodman, Gilman's. Chemotherapy of Malaria, in the Pharmacological Basis of Therapeutics, 12th Edition; 2010.
- [11]. Krungkrai J, Burat D, Kudan S, et al. Mitochondrial oxygen consumption in asexual and sexual blood stages of the human malaria parasite, Plasmodium falciparum. Southeast Asian J Trop Med Public Health, 1999, 30:636-642
- [12]. Achan J, Talisuna A, Erhart A, et al. Quinine, an old anti-malarial drug in a modern world: Role in the treatment of malaria. Malaria J., 2011, 10:144.
- [13]. White N, Pukrittayakamee S, Hien T, et al. Malaria. Lancet, 2013, 383:723-735.
- [14]. AskMayoExpert. Malaria. Rochester, Minn.: Mayo Foundation for Medical Education and Research; 2018.
- [15]. Jameson JL, et al., eds. Malaria. In: Harrison's Principles of Internal Medicine. 20th ed. New York, N.Y.: The McGraw-Hill Companies; 2018. <https://accessmedicine.mhmedical.com>. Accessed Oct. 9, 2018.
- [16]. Tintinalli JE, et al., eds. Malaria. In: Tintinalli's Emergency Medicine: A Comprehensive Study Guide. 8th ed. New York, N.Y.: McGraw-Hill Education; 2016. <http://www.accessmedicine.mhmedical.com>. Accessed Oct. 9, 2018.
- [17]. Malaria. Merck Manual Professional Version. <http://www.merckmanuals.com/professional/infectious-diseases/extraintestinal-protozoa/malaria>. Accessed Oct. 9, 2018.
- [18]. Malaria. Centers for Disease Control and Prevention. <http://wwwnc.cdc.gov/travel/diseases/malaria>. Accessed Nov. 6, 2015.
- [19]. Breman JG. Clinical manifestations of malaria in nonpregnant adults and children. <https://www.uptodate.com/contents/search>. Accessed Oct. 9, 2018.
- [20]. Daily J. Treatment of uncomplicated falciparum malaria in nonpregnant adults and children. <https://www.uptodate.com/contents/search>. Accessed Oct. 9, 2018.
- [21]. Key points: World malaria report 2017. World Health Organization. <https://www.who.int/malaria/media/world-malaria-report-2017/en/>. Accessed Oct. 9, 2018.
- [22]. Malaria. World Health Organization. <https://www.who.int/malaria/en/>. Accessed Oct. 9, 2018.
- [23]. Mutebi JP, et al. Protection against mosquitoes, ticks, & other arthropods. In: CDC Yellow Book 2018: Health Information for International Travelers.