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A BRIEF REVIEW ON MALARIA AND ITS PREVENTIVE MEDICINE

Kirti [*] Rohit [*] Dr. Shailesh Kumar Ghatuary[**] Sarika Chaturvedi[***]Mamta Dubey[***]Deeksha shakya[***] Surendra[***]

Undergraduate Student[*] Principal[**] Lecturer [***]Assistant Professor[****]

Shri RLT Institute of Pharmaceutical Science and Technology affiliated to PCI and AKTU, Etawah, Uttar Pradesh, India

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Abstract:

Malaria has been a major global health problem of humans from history and is a leading cause of death and disease across many tropical and subtropical countries. Over the last 15 years renewed efforts at control have decrease the prevalence of malaria by over half, raising the prospect that reduce and perhaps eradication may be a long-term possibility. Achievement of this goal requires the development of new tools including novel anti malarial drugs and more efficacious vaccines as well as araise understanding of the disease and biology of the parasite. This has catalyzed a major effort resulting in development and regulatory approval of the first vaccine against malaria (RTS, S/AS01) as well as identification of novel drug targets and anti malarial compounds, some of which are in human clinical trials.

Corresponding author:

Kirti

Undergraduate Student,

Shri RLT Institute of Pharmaceutical Science and Technology, Etawah

Email.id- kirti80tiwari@gmail.com

QR code

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INTRODUCTION

Malaria is a severe disease caused by parasite of the genus plasmodium which is transmitted to the human by a bite of an infected female mosquito of the species Anopheles.Malaria is the most common disease in Africa and some countries in Asia with the highest number of indigenous cases. The malaria mortality rate globally ranges from 0.3-2.2%, and in cases of severe form of malaria in region with tropical climate from 11-30%. The causative agent of malaria is belonging to the group of plasmodium species. Some of the plasmodium species caused disease in human [1]. Five species can infect human these are P. malariae, P.falciparum, P. vivax, P. ovale, & P. Knowlesi. is recorded. Other species rarely infect human. Malaria is a disease caused by a parasite. The parasite is spread to humans through the bites of infected mosquitoes. People who have malaria usually feel very sick with a high fever and shaking chills.While the disease is uncommon in temperate climates, malaria is still common in tropical and subtropical countries. Each year nearly 290 million people are infected with malaria, and more than 400,000 people die of the disease.To reduce malaria infections, world health programs distribute preventive drugs and insecticide-treated bed nets to protect people from mosquito bites. The World Health Organization has recommended a malaria vaccine for use in children who live in countries with high numbers of malaria cases[2].

CAUSES OF MALARIA

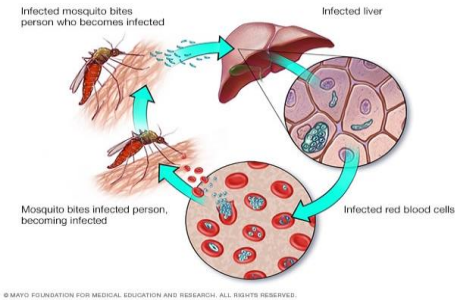
Malaria is an acute febrile illness caused by *Plasmodium* parasites, which are spread to people through the bites of infected female *Anopheles* mosquitoes. There are 5 parasite species that cause malaria in humans, and 2 of these species – *P. falciparum* and *P. vivax* – pose the greatest threat. *P. falciparum* is the deadliest malaria parasite and the most prevalent on the African continent. *P. vivax* is the dominant malaria parasite in most countries outside of sub-Saharan Africa[20].

MALARIA TRANSMISSION CYCLE

Malaria is caused by a single-celled parasite of the genus plasmodium. The parasite is transmitted to humans most commonly through mosquito bites.

Mosquito transmission cycle

- **Uninfected mosquito.** A mosquito becomes infected by feeding on a person who has malaria.



- **Transmission of parasite.** If this mosquito bites you in the future, it can transmit malaria parasites to you.

- **In the liver.** Once the parasites enter your body, they travel to your liver — where some types can lie dormant for as long as a year.**Fig: 1Malaria transmission**

- **Into the bloodstream.** When the parasites mature, they leave the liver and infect your red blood cells. This is when people typically develop malaria symptoms.

- **On to the next person.** If an uninfected mosquito bites you at this point in the cycle, it will become infected with your malaria parasites and can spread them to the other people it bites.

Other modes of transmission

Because the parasites that cause malaria affect red blood cells, people can also catch malaria from exposure to infected blood, including:

- From mother to unborn child
- Through blood transfusions
- By sharing needles used to inject drugs[24]

HISTORY OF MALARIA CONTROL IN INDIA[23]

Prior to 1940	No organized National Malaria Control Programme
1945	-Insecticide properties of DDT identified
Prior to 1953	-Estimated malaria cases in India- 75 million -estimated Deaths due to malaria-1 million
1953	-Launching of National Malaria Control Programme
1958	-Launching of National Malaria Eradication Programme
Early 70's	-Resurgence of malaria
1976	Malaria cases 6.46 million highest in post DDT era (one of the reasons for resurgence was insecticide resistance in malaria vectors)
1977	Modified Plan of Operations Implemented
1997	World Bank Assisted Enhanced Malaria Control Project (EMCP)
1999	Renaming of programme to National Anti Malaria Programme (NAMP)
2002	Renaming of NAMP to National Vector Borne Disease Control Programme
2005	The NVBDCP became an integral part of the NRHM Global Fund assisted Intensified Malaria ControlProject(IMCP) launched

Prior to the launching of the National Malaria Control Programme (NMCP) in 1953, malaria was a major scourge in India contributing 75 million cases with about 0.8 million deaths annually. The widespread DDT indoor residual spray (IRS) in the country under the NMCP resulted in a sharp decline in malaria cases and as a result the GOI converted the NMCP into the National Malaria Eradication Programme (NMEP) in 1958. The NMEP was initially a great success with the malaria incidence dropping to a 0.1 million cases and no deaths due to malaria reported in 1965. The Urban Malaria Scheme (UMS) was also launched in 1971-72 covering 131 cities and towns[3, 4]

1. DIAGNOSTIC TESTING

Prompt malaria diagnosis either by microscopy or rapid diagnostic tests (RDTs) is recommended by WHO for all patients with suspected malaria before they are given treatment. Early and accurate diagnosis is essential both for effective management of the disease and for strong malaria surveillance.

Parasite-based diagnostic testing significantly reduces illness and death by enabling health providers to swiftly distinguish between malarial and non-malarial fevers and select the most appropriate treatment. It improves the overall management of patients with febrile illnesses and may also help reduce the emergence and spread of drug resistance test negative should be assessed for other causes of fever[5, 6]

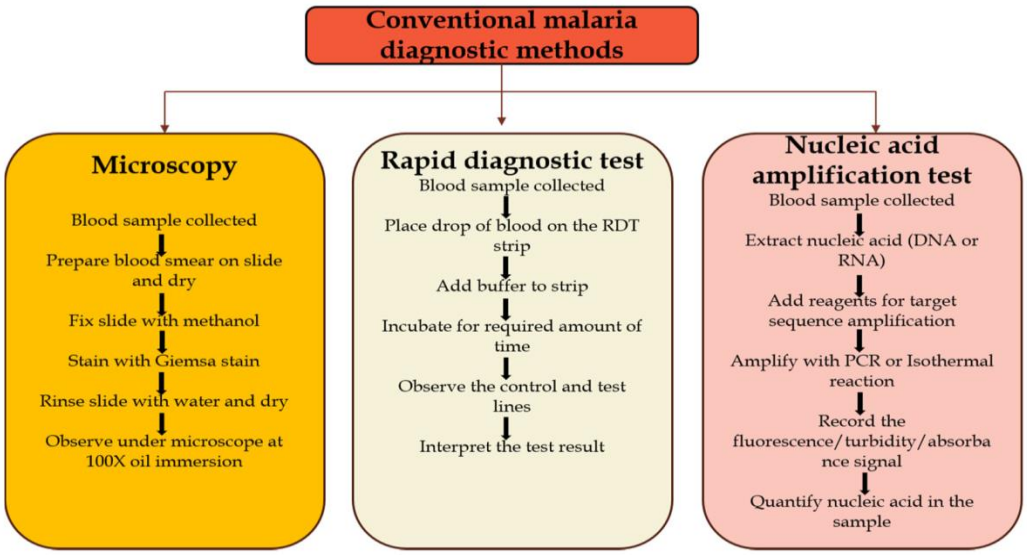


Fig: no. 2

MICROSCOPY

The microscopic examination of thick and thin blood films is a "gold standard" test that is used to detect parasitemia in the blood and guiding appropriate treatment. A drop of blood is collected from a patient via a finger stick or venipuncture. When a venipuncture is used for blood collection, it is suggested that the blood is spread onto a slide immediately after collection to prevent prolonged exposure to anticoagulants in the collection tube that may alter parasite morphology. Thick smears are more sensitive and involve placing one to two drops of blood on a slide in a circle. The red blood cells are lyses and the various malaria parasite blood-stages, trophozoites, gametocytes and schizonts are released. Thin smears are used to detect the morphology of the parasite species and are prepared by spreading a drop of blood across a slide to create a feathered edge that contains a single layer of cells. The slide was stained with the Giemsa stain and examined using an Olympus bright-field microscope. The sensitivity and specificity for this method is 95% and 98. The limit of detection for this method is approximately 50-200 parasites per µL of blood .A skilled laboratory personnel is able to quantify parasitemia in a blood smear in about 60 min.

RAPID DIAGNOSTIC TEST

Rapid Diagnostic Tests are based on the detection of circulating parasite antigens. Several types of RDTs are available[7].RDTs are produced by different companies, so there may be differences in the contents and in the manner in which the test is done. The user's manual should always be read properly and instructions followed meticulously. The results should be read at the specified time. It is the responsibility of the clinician or technician doing a rapid test for malaria to ensure that the kit is within its expiry date and has been transported and stored under recommended conditions. Failure to observe these criteria can lead to false/negative results. It should be noted that Pf HRP2 based kits may show positive result up to three weeks of successful treatment[8]

Some of them can only detect P. falciparum, while others can detect other parasite species also. The latter kits are expensive and temperature sensitive. Presently, NVBDCP supplies RDT kits for detection of P. falciparum at locations where microscopy results are not obtainable within 24 hours of sample collection[9]

NUCLEIC ACID SEQUENCE-BASED AMPLIFICATION (NASBA)

NASBA is a diagnostic method that involves the use of three enzymes, reverse transcriptase, T7 RNA polymerase and RNase , to amplify RNA targets in a double-stranded DNA background. The RNA target, such as 18S RNA, is copied into complementary DNA (cDNA) using reverse transcriptase and then the cDNA is amplified

using T7 RNA polymerase. It does not require the use of a thermocycler because the reaction can be carried out at 41◦C resulting in more than 10^8-fold amplification of the target RNA sequence. The sensitivity of the method when compared to microscopy ranges from 97.40% to 100% while the specificity ranges from 80.90% to 94%.The limit of detection is 0.01–0.1 parasites per µL of blood. The test is estimated to take about one hour.

EPIDEMIOLOGY

The malaria parasite is transmitted via the bite of a female *Anopheles* spp mosquito, which occurs mainly between dusk and dawn. Other rare mechanisms for transmission include congenitally acquired disease, blood transfusion, sharing of contaminated needles, organ transplantation, and nosocomial transmission[10]

Malaria is widely distributed in subtropics and tropic of Asia, Latin America and Africa. Malaria affecting 300 million people worldwide[16]

IMMUNOGLOBULINS

Malaria infections are accompanied by marked changes in serum immunoglobulin levels. Induced malaria in non immune adults leads to increases in the IgG and IgM fractions[11]

Field studies consistently show that IgG and IgM levels are especially elevated in tropical areas where malaria in endemic[12]and there is frequently a strong correlation between total IgM levels and malaria antibody levels, suggesting that malaria is implicated in the excessive IgM response[13,]

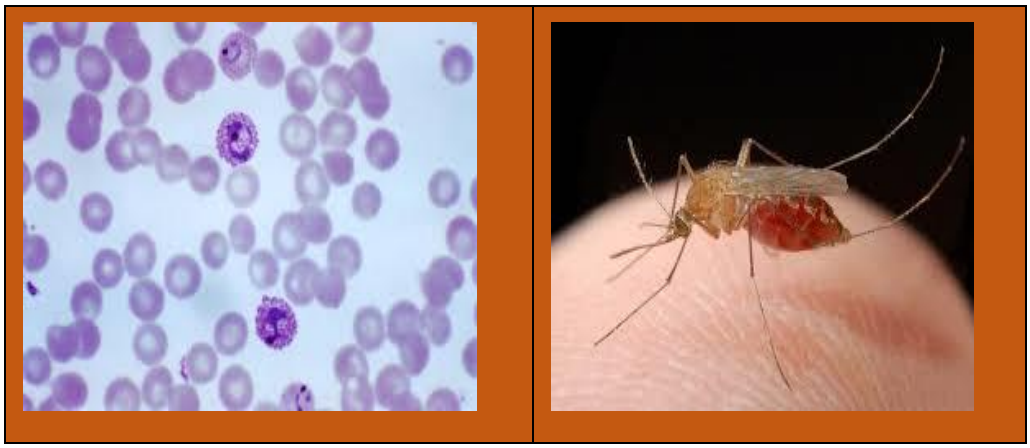


Fig: no 3 malaria parasite *plasmodium vivax* inside a red blood cell& Mosquito anopheles feeding on a human

INCUBATION PERIOD OF THE PARASITE[16]

SPECIES	INCUBATION PERIOD
P. falciparum	7-14 days
P.vivax	12-17 days
P. ovale	9-18 days
P.malaria	13-20 days

PATHOPHYSIOLOGY

Malaria is caused by protozoan parasites of the genus *Plasmodium* (phylum Apicomplexa).In humans, malaria is caused by P. falciparum, P malariae, P ovale, P. vivax and Plasmodium knowlesiP. vivax is the most common cause of infection, responsible for about 80% of all malaria cases P. falciparum, the mostsignificant cause of disease, is responsible for about 15% of infections and 90% of deaths [17] [18]

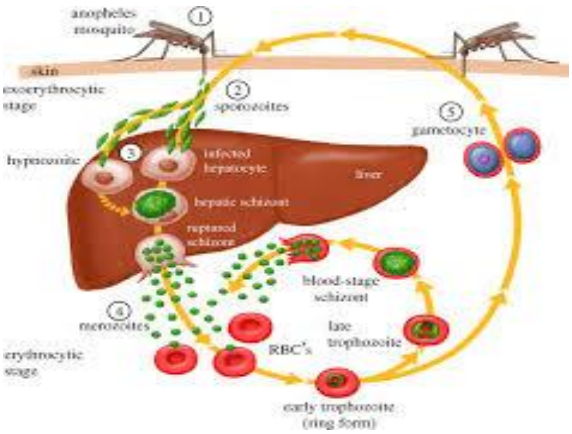


Fig: no.4 Life cycle of malaria parasite

DISEASE MANAGEMENT

Some herbal bark used in the treatment of malaria such as cinchona. Traditionally, herbal medicine remains the backbone for the treatment of malaria for over thousands of years. The first antimalarial drug (quinine) was isolated from the bark of the *Cinchona* tree, in the family of Rubiaceae, an herbal medicine. In the early 1632, an infusion of the Cinchona bark was used for the treatment of human malaria.[29]

Fig: no 5 World health organisation workers distributing mosquito nets in village & Cinchona tree bark

LOW RISK AREA

PT comprises of a single dose of chloroquine phosphate 10 mg/kg. Body weight to all fever / suspected malaria cases.

Age in Year	Chloroquine Phosphate	
	Mg. Base	No. of Tablets (150 mg)
< 1	75	½
1-4	150	1
5-8	300	2
9-14	450	3
15 & above	600	4

HIGH RISK AREA:

As per revised policy of NVBDCP presumptive treatment of all suspected malaria cases, up to sub-centre level only, in "high risk areas" (as defined in the MAP 95), is as follows:

Chloroquine Base	Day 1	10 mg/kg (600 mg adult)
Primaquine	Day 1	0.75 mg/kg (45 mg adult)
Chloroquine base	Day 2	10 mg/ kg (600 mg adult)
Chloroquine base	Day 3	5 mg/kg (300 mg adult)

TREATMENT OF SEVERE AND COMPLICATED MALARIA

Semiconscious or comatose patients of severe *Falciparum* infection should be treated with Quinine. It is the drug of choice also for pregnant women and infants.

DOSAGE AS PER AGE GROUPS:

AGE IN YEARS	DAY 1		DAY 2	DAY 3
	TAB CHLOROQUINE (150 MG BASE)	PRIMAQUINE (7.5 MG)	TAB CHLOROQUINE (150 MG BASE)	TAB CHLOROQUINE (150 MG BASE)
< 1	½	0	½	¼
1-4	1	1	1	½
5-8	2	2	2	1
8-14	3	4	3	1 ½
>14	4	6	4	2

PLASMODIUM VIVAX

AGE IN YEAR	CHLOROQUINE PHOSPHATE 150 MG BASE SINGLE DOSE		PRIMAQUINE 2.5 MG BASE DAILY DOSE FOR 5 DAYS	
	MG BASE	NO. OF TABLETS	MG BASE	NO. OF TABLETS
< 1	75	1/2	Nil	Nil
1-4	150	1	2.5	1
5-8	300	2	5.0	2
9-14	450	3	10.0	4
15 & above	600	4	15.0	6

DOSE FREQUENCY

- **QUININE**

I.V. 10mg/kg body wt. (600 mg.) 8 hourly, (total 24-hour intake should not exceed 1.8 gms in an adult) till the patient regains consciousness and is able to take drugs orally. Oral Quinine 600 mg TDS is to be continued for seven to ten days. When adequate facilities for management of complications arising out of Quinine toxicity are available a loading dose of Quinine dihydrochloride 20 mg per kg body weight

as infusion is given, and it should be well diluted with 500 ml of 5 per cent glucose. Infusion is given over a period of 5 hours (2 ml per minute). If no I.V. facility is available, deep intramuscular dose of 10 mg per kg body wt. is given 8 hourly. I.M. injections produce complications which, sometimes in the long run, are crippling if proper precautions are not taken.

- **INJECTION ARTEETHER:**

It is available in 2 ml ampoules containing 150 mg. The recommended regimen is 150 mg /day once daily by intramuscular route for three days for adults. The dosage for children is 3 mg/kg per day IM for three days.

- **CHLOROQUINE INJECTION**

Chloroquine is not well tolerated specially by infants or young children. In a patient of any age it may produce low blood pressure, sudden collapse with high mortality. Parenteral administration of Chloroquine is more hazardous than parenteral administration of quinine.It should be used only when quinine or arteether injections are not available. It is given in doses of 3.5 mg/kg body wt 8 hourly slowly in isotonic fluid. Total 24-hour dose should not exceed 600 mg base (up to 10 mg/kg body weight). Dose of Chloroquine I.M. is 5 mg per kg body wt. [26]

CLASSIFICATION OF THE CURRENTLY USED ANTI-MALARIALS

A. aminoquinolines,	eg. Chloroquine, Hydroxychloroquine, Amodiaquine
B. 8- aminoquinolines,	eg. Primaquine, Tafenoquine, Bulaquine
C. Arylamino alcohols,	eg. Quinine
D. Methanols i. 4 quinoline methanol ii. 9- phenanthrene methanol	 eg. Mefloquine eg. Halofantrine, Lumefantrine
E. Biguanides	eg. Proguanil
F. Diaminopyrimidines	eg. Pyrimethamine
G. Antimalarial endoperoxidases i. First generation endoperoxidases (Artemisinin derivatives) ii. Second generation endoperoxidases a. Trioxanes b. Tetroxanes	eg. Artesunate, Artemether, Arteether
H. Hydroxynaphthoquinone	eg. Atovaquone
I. Benzonaphthyridinederiative	eg. Pyronaridine
J. Antibiotics	eg.Sulfonamides, Tetracycline, Doxycycline, Clindamycin, Azithromycin

CONCLUSION:

Malaria has had a profound effect on human lives for thousands of years and remains one of the most serious, life-threatening infectious diseases. It is concluded that malaria is serious life-threatening disease that leads to millions of death yearly. Lets takes stand and educate individual properly on this public health issue and eradicate this completely.

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