Malaria, a disease of antiquity, has proved to be a formidable deterrent to the cultural and socio-economic progress of man in the tropical, sub-tropical and monsoon prone zones of the world. History is replete with instances of devastation caused by this disease. Wide distribution and its intensity of transmission in India were important factors for slow economic, scientific and industrial progress in the country during last two centuries. However, towards the end of the last century, when the biological characteristics of vector-borne diseases began to be unravelled through pioneering research initiated by Sir Ronald Ross, the mechanism of transmission of human malaria began to be revealed.

Malaria is one of the major public health problems in the developing countries. Recent estimates indicate that between 300-500 million clinical cases and between 1.5-2.7 million deaths due to it, occur worldwide annually, 90% of which occur in tropical Africa. It is estimated that 1.2 billion people out of the 1.4 billion people of SE Region live in Malarious areas. In 1995, malaria cases in the region were estimated at 21.9 million, with almost 32,000 deaths. India accounts around 85% of the total reported cases in the region in the same year. During 1996 also, India contributed 83% of total malaria cases in SE Region. Thus around 80% of reported cases in the region are being contributed by India.

Malaria is a complex disease and various factors influenced by human activities and natural calamity like excessive rainfall, flood, drought and other disasters have great bearing on mosquitogenic conditions leading to increased potential for malaria transmission. Like any other disease, natural transmission of malaria depends on the presence of, and relationship between the three basic epidemiological factors: the agent, the host and the environment. While the malaria parasite is the true agent of infection, the female anopheles mosquito is the agent of transmission. The environment is considered from three aspects; physical, biological and socio-economic.

There are four species of human malaria parasites *Plasmodium vivax*, *falciparum*, *malariae* and *ovale*. In India 60 to 65% of the infections are due to *P. vivax* and 35 to 40% due to *P. falciparum*. Only few cases of *P. malariae* have been reported from Orissa and Karnataka. The life cycle of the malaria parasite comprises of an endogenous asexual phase (schizogony) with multiplication in the human host and an exogenous sexual phase (sporogony) with multiplication in certain anopheline mosquitoes. The minimum time from infection by mosquito bite until the first appearance of the parasite in RBC is termed as the pre-patent period. The incubation period which is characteristic of each species is the time interval from infection to appearance of clinical symptoms which is when parasitaemia reaches a sufficient density and is usually two days longer than the pre-patent period. Incubation period ranges from 8 to 21 days depending on species, host immunity and climatic conditions. The asexual life cycle of parasite is completed in human host, and for all species of malaria parasite is essentially the same, except that life cycle of *P. falciparum* and *P. malariae* do not have the persistent tissue phase (Hypnozoite stage). Schizogony is repeated until the increasing immunity or chemotherapy inhibits parasitaemia. Schizogony periodicity is characteristic for each species. Usually at least two cycles of schizogony in the blood must elapse before sexual forms appear in human malaria parasites other than in the *P. falciparum* in which gametocytes appear in peripheral circulation after the tenth day of patency. Recrudescence is renewed manifestation of infection due to the survival of erythrocytic forms as seen in *P. falciparum* (Pf.) and *P. malariae*. Relapse is renewed manifestation of infection arising from the survival of hypnozoites either at relatively short intervals or after long periods. In human malaria relapses are confined to *P. vivax* (Pv.) and *P. ovale*. Sexual Cycle (Exogenous sexual phase) of the parasite is completed in female anopheles. The cycle is completed between 7 to 15 days depending upon the species. Antigenic diversity is present among different malaria parasite species and within a species either between or within a
geographical area. Among *P. falciparum* blood stage antigens, there is a great diversity both between geographic areas and within the same area. In the course of a single infection antigenic variations have been demonstrated in *P. falciparum*. Virulence is expressed by the severity of acute disease in the non-immune. Virulence differs greatly between species. There are reports of differences in virulence within species. *Pf* can cause severe and complicated malaria and mortality. Response to antimalarials varies greatly between and within the species both spontaneously and under drug pressure.

There are about 400 species of anopheles mosquitoes throughout the world, but only 60 species are vectors of malaria. In India 9 species out of 45 anopheles species have been incriminated as malaria vectors. The capacity of the vector to transmit malaria results from the interaction between the environment, both natural and man-made and genetically determined characteristics.

The relative immunity of infants to malaria has been attributed to maternal immunity, low attack rate by vectors which could be due to low attractiveness and/or lower exposure, the persistence of foetal haemoglobin which is unfavourable for the development of *P. falciparum*. A milk diet may have protective effect due to para-amino-benzoic acid (PABA) deficiency. Marked depression of erythropoiesis characteristic of the first 2 to 3 months after birth leads to relative scarcity of young erythrocytes. Though both the sexes are equally prone to malaria some observations suggest that females mobilise stronger antibody response and stronger cell mediated immunity than males. Pregnant women especially primigravida show increased susceptibility to malaria especially *P. falciparum*. This expresses itself in increased prevalence and density of parasites, especially second trimester. Anaemia may lead to intra-uterine growth retardation (IUGR), low birth weight and increased risk of abortion and still births.

Each infection tends to raise the immune level and thus accelerates the clearance rate of parasitaemia. Heavy inoculation may overwhelm the incipient immune response. There are interactions between different species of *Plasmodium* in the human host where more than one species are endemic in an area, their co-existence in the same human host is very common. However *Pt* tends to suppress patent parasitaemia of other species present in the same host.

Genetic factors affect the distribution of malaria in several ways. Sickle cell trait is associated with relative protection against *P. falciparum* especially cerebral malaria. The Duffy negative RBC is specifically resistant to penetration by *P. vivax* and this is the reason why *Pv* is absent in West Africa. The Hb variants like Hb E seem to afford protection against cerebral malaria. Normal homozygous thalassemia patients have relative risk of morbidity 2.1 times that of trait carriers. G6PD deficiency is associated with low prevalence and density of *P. falciparum*. Hereditary elliptocytosis provides resistance to penetration by all species as well as due to reduced membrane deformity. Anomalies for the receptors of *P. falciparum* in erythrocytes of several blood groups, which lack certain glycoporphins in the cell membrane, are partially resistant to invasion by *P. falciparum*.

The interaction between malaria parasites and the immune response to them is one of the main determinants of the distribution of malaria parasites in human population. Active immunity develops with increasing age, with resultant decrease in the density of asexual parasites and even more of gametocytes and a reduction in the number of patent parasitaemic episodes. Loss of immunity results from removal from exposure and chemo-suppression. Immunity to malaria is species specific and also strain specific. Immunity in *P. vivax* is acquired faster while there is greater antigenic diversity in *P. falciparum*. Infants enjoy protection due to maternal antibodies till the age of six months. Malaria associated immuno-pathology may play a role in the distribution of some of the pathological consequences of malaria infection namely anaemia, tropical splenomegaly syndromes and nephrotic syndromes.

Environmental factors like rainfall directly or indirectly affect the abundance of breeding sites and also the physiology of the vectors. Malaria parasites cease to develop in the mosquito when the temperature is below 16°C. 20 to 30°C represents an optimal range for most malaria vectors. Humidity over 60% is optimal and within limits the longevity of adult vectors increases with the relative humidity of the air.

Increasing socio-economic development is accompanied by decreasing malaria. Man-made malaria is the result of economic development divorced from social development. The reduction of malaria by socio-economic development is a slow process in comparison with the impact of specific
malaria control programmes but the results have greater intrinsic stability.

Urbanisation leads to lack of proper drainage of surface water and use of unprotected water reservoirs favour vector breeding. The occupations like bamboo cutting, mining and soldering are a few high-risk occupations with regard to malaria. Breakdown of social order has an impact on malaria itself with increased vector breeding through disruption of agriculture and water management, increase in man-vector contact through destruction of housing and cattle and increased inter-mixing of both non-immunes and reservoirs of infection.

Treating physician should consider all these factors while eliciting history from a suspected malaria case.

Malaria Status and its Control – India

Malaria has been known in India from times immemorial. J.A. Sinton, the first Director of the Malaria Institute of India, estimated in 1935 that at least 100 million people suffered from malaria in India and about one million deaths occurred annually in endemic areas. In 1947, after independence, it was estimated that 75 million people suffered from the disease every year. The mortality, as direct result of disease, was placed at 0.8 million per annum.

A countrywide programme to control malaria was recommended in 1946 by Health Survey and Development Committee (Bhore Committee). The recommendation was endorsed by the Planning Commission in 1951. In April 1953, Govt. of India, launched the National Malaria Control Programme (NMCP) with the primary objective to bring down malaria transmission to a level at which it would cease to be a major public health problem. The strategy was vector control by DDT spraying. The 8th World Health Assembly in 1955, urged governments to intensify plans of nationwide malaria control so that malaria eradication may be achieved. National Malaria Eradication Programme (NMEP) was launched in 1958 in India. By 1965 the annual malaria incidence fell from 75 million cases to an all time low of 0.1 million cases. No deaths were recorded. From 1968 onwards there were setbacks, 1976 recorded the highest ever post-eradication incidence of 6.47 million cases. In 1977 attempts at malaria eradication were given up and under the revised policy, a Modified Plan of Operation (MPO) was launched with the objectives of:

i) preventing deaths due to malaria,
ii) reducing morbidity,
iii) and maintenance of industrial and green revolution due to freedom from malaria and retention of achievements gained so far.

Strategies under MPO

i) Fortnightly blood smear collection by domiciliary visits, from fever cases, their examination and treatment with antimalarial drugs.
ii) Decentralisation of laboratory services to the PHC level.
iii) Establishment of Drug Distribution Centres (DDCs)/Fever Treatment Depots (FTDs).
iv) Insecticidal spray with appropriate insecticide during the transmission period in rural areas recording Annual Parasite Incidence (API) 2 or above. In urban areas, through recurrent antilarval operations.
v) Health Education and Community Participation.

Since the implementation of MPO, the malaria situation in the country has shown a definite improvement, as there has been a gradual downward trend in incidence. The malaria situation after 1984 has remained more or less static. Due to focal outbreaks in some parts of the country from 1994 onwards, the incidence of malaria and deaths due to it increased during the recent past. The proportion of *P. falciparum* to the total malaria cases also increased and reached up to 40%, which is a major programme concern. Malaria deaths were below 500 annually till 1993 for a decade, but their number has crossed the 500 mark since 1994, due to local outbreaks of malaria in various parts of the country.
The detailed epidemiological situation during 1976 and since 1984 is shown below:

<table>
<thead>
<tr>
<th>Year</th>
<th>Malaria (Million)</th>
<th>Pf. (Million)</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>6.47</td>
<td>0.75</td>
<td>59</td>
</tr>
<tr>
<td>1984</td>
<td>2.18</td>
<td>0.65</td>
<td>247</td>
</tr>
<tr>
<td>1985</td>
<td>1.86</td>
<td>0.54</td>
<td>213</td>
</tr>
<tr>
<td>1986</td>
<td>1.79</td>
<td>0.64</td>
<td>323</td>
</tr>
<tr>
<td>1987</td>
<td>1.66</td>
<td>0.62</td>
<td>188</td>
</tr>
<tr>
<td>1988</td>
<td>1.85</td>
<td>0.68</td>
<td>209</td>
</tr>
<tr>
<td>1989</td>
<td>2.05</td>
<td>0.75</td>
<td>268</td>
</tr>
<tr>
<td>1990</td>
<td>2.02</td>
<td>0.75</td>
<td>353</td>
</tr>
<tr>
<td>1991</td>
<td>2.12</td>
<td>0.92</td>
<td>421</td>
</tr>
<tr>
<td>1992</td>
<td>2.13</td>
<td>0.88</td>
<td>422</td>
</tr>
<tr>
<td>1993</td>
<td>2.21</td>
<td>0.85</td>
<td>354</td>
</tr>
<tr>
<td>1994</td>
<td>2.51</td>
<td>0.99</td>
<td>1122</td>
</tr>
<tr>
<td>1995</td>
<td>2.93</td>
<td>1.14</td>
<td>1151</td>
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<tr>
<td>1996</td>
<td>3.04</td>
<td>1.18</td>
<td>1010</td>
</tr>
<tr>
<td>1997</td>
<td>2.66</td>
<td>1.01</td>
<td>879</td>
</tr>
<tr>
<td>1998 (P)</td>
<td>2.15</td>
<td>0.93</td>
<td>658</td>
</tr>
</tbody>
</table>

Malaria is prevalent in all the parts of the country except in areas more than 5000 feet above sea level. Some of the states are highly endemic for malaria and contribute about 90% of the total malaria in the country. These states are Orissa, U.P., Gujarat, West Bengal, Maharashtra, Madhya Pradesh, Rajasthan, Karnataka, Andhra Pradesh, N-E States. Percentage contribution by these states during 1998 is shown in Fig. 1.

New approaches for Malaria Control

In view of recent upsurge of malaria, the following new approaches are being adopted under the programme.

i) Prediction, early detection, prompt response to epidemics of malaria for prevention/effective containment.

ii) In view of high endemicity of malaria and resource constraints, 100% central assistance since December 1994 to all the north-eastern states.

iii) Intensification of Information, Education and Communication (IEC) components by observing anti-malaria month throughout the country for increasing the awareness of malaria and its control among the community to ensure their participation.

iv) Implementation of accelerated urban malaria control programmes.

Outbreaks of Malaria

After a more or less static situation of malaria for a decade up to 1993, there have been focal outbreaks since 1994. During 1994, the states of Rajasthan, Manipur and Nagaland reported outbreaks. During 1995, the states of Assam, Maharashtra and West Bengal reported outbreaks. During 1996, the states of Rajasthan and Haryana had malaria outbreaks and during 1997, Gujarat and Goa reported malaria outbreaks. During 1998 there were focal outbreaks in Bhandara district in Maharashtra, and Calcutta in West Bengal. Goa has been recording increasing malaria incidence continuously for a few years. However, during 1998 there was a decline in malaria deaths in Goa compared to previous year. The main reasons for these outbreaks were natural calamities like heavy rains and floods coupled with operational deficiencies.
scheme in the problematic towns as urban malaria is on the increase due to developmental activities and population movements.

v) In view of rising incidence of *P. falciparum* malaria in the various parts of the country NMEP drug policy has been revised. Under the revised drug policy there is provision for administering radical treatment along with presumptive treatment for fever cases in high risk areas to prevent mortality due to malaria.

vi) An Enhanced Malaria Control Project with World Bank assistance has been launched with effect from September 1997 primarily to provide additional inputs for the control of malaria in the 100 identified hard-core tribal predominant districts of seven peninsular states, namely, Andhra Pradesh, Bihar, Gujarat, Madhya Pradesh, Maharashtra, Orissa and Rajasthan. 19 problematic towns have also been included under this project. Under this Project, newer technologies like insecticidal spray with synthetic pyrethroids, bio-environmental methods for vector control including use of larvivorous fish and biolarvicides, and rapid diagnostic methods for prompt detection of *P. falciparum* cases, introduction of injectable forms of artemisinine for the treatment of severe and complicated malaria are envisaged. The components like Information, Education and Communication, Capacity Building, and Management Information System under this project are being extended to the entire country.

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**Flavedon 20**

**3 TABLETS DAILY**

*A major antianginal for all patients*

- As first line treatment
- Uncontrolled on conventional drugs
- To replace a poorly tolerated antianginal
- At risk (elderly, diabetic CAD patients)

*When it comes to the heart do not compromise on quality*