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Fighting malaria in India

V. P. Sharma

A brief account of malaria problem in India has been described bringing out important landmarks in fight against malaria. Control of resurgent malaria has become a formidable task in view of the problem of vector resistance, parasite resistance, low social acceptability of spraying and inadequate knowledge of malaria in many ecotypes. National Malaria Eradication Programme's current strategy of malaria control has been discussed.

Everything about malaria is so moulded by local conditions that it becomes a thousand epidemiological puzzles. Like chess, it is played with a few pieces but is capable of an infinite variety of situations.

– L. W. Hackett (1937)[1]

HISTORICALLY, malaria is full of examples of the decisive role played by it in war and peace. Malaria destroyed the splendour of Greece, caused the fall of the Roman empire, diminished the Egyptian civilization, and extinguished the ancient culture of Ceylon. In ancient India, malaria was known as the 'King of Diseases'. Malaria and famine formed the vicious cycles of sickness, death and poverty, and thus malaria was largely responsible for the poverty of nations. India remained the hot bed of malaria until the time of independence, generating annually an estimated 75 million cases and 0.8 million deaths in normal years. In this connection it is noteworthy to mention that Ronald Ross' painstaking research on the etiology of malaria led to the discovery of oocysts on the stomach wall of 'dapple wing' mosquitoes (probably *Anopheles stephensi*). This was the first experimental evidence of extrinsic cycle of malaria parasite in the mosquitoes. This discovery was made in Secunderabad on 20 August 1897 and for this discovery Ronald Ross was given the Nobel Prize in 1902 and knighted by the king of England. Later in 1898 Grassi and his colleagues working in Italy demonstrated human malaria transmission through the bite of mosquitoes[2].

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Environmental management era

In 1902 Ronald Ross suggested the demonstration and practicability of drainage and minor engineering works in the control of malaria. Mian Mir a cantonment near Lahore (now in Pakistan) was selected for detailed studies. The work was started by S. P. James in 1902 (ref. 3) and supported by the Royal Society, London. Anopheles breeding in rain-filled pits, irrigation ponds, canals, and miscellaneous places was controlled by simple and inexpensive methods of drainage and minor engineering works. After two years of work it was concluded that Mian Mir experiment had failed and the primary reason for its failure was the lack of knowledge of the biology of malaria carrying mosquitoes, thus emphasizing the need for more field research[4]. However, principles of drainage were successfuliy applied by W. C. Gorgas[5] in 1910 to reduce malaria rates in Havana during the construction of Panama canal and by Malcom Watson in the control of malaria in federated Malay States[6]. In India, Assam Medical Research Society in 1940 supported studies on *An. minimus* and successfully controlled malaria in some selected tea gardens by sluicing and flushing under the guidance of Ross Institute[7]. The anti-malaria campaign in 1942 during the second world war in Assam theatre was successful by clearing jungles and organizing drainage to prevent the breeding of *An. minimus* and thus establish malaria-free zones in Assam, Chittagong and Cox's Bazar[8]. In those days malaria was rampant in development projects and therefore the Government of India in 1946 prepared documents on the subject of antimalaria measures to be adopted by railway board; borrowpits in land acquired temporarily for road construction; Delhi improvement trust on construction

of road embankments without creation of borrowpits; and control of malaria in parties engaged in road and rail construction[9]. Similar recommendations were made to control malaria at the sea ports.

Heuristically, drainage was considered an essential component of irrigation. This is borne out by the fact that the first irrigation scheme on Sarda canal was prepared in 1870 to irrigate famine hit Oudh province to abolish the recurring famines. The scheme was not sanctioned till 1919. The delay was *inter alia* due to lack of sufficient drainage cuts to prevent water logging. In this scheme upsurge of malaria (similar to the opening of Ganga canal in 1854) was guarded by providing drainage cuts and prohibiting irrigation in water logged areas and also where sub-soil water level was high. Spread of malaria was arrested by drainage, filling, oiling, application of Paris green, screening of houses, etc.[10]. Irwin canal (now Visveswaraya canal) came into operation in January 1932 in Mandya district (now in Karnataka state), and within one year widespread epidemic of malaria was in progress. Institution of preventive measures by the creation of dry belt, depletion of all tanks, canalization of valleys, lining of channels and shifting of hamlets and small villages to healthy sites were adopted in 200 villages with excellent results[11]. Cauvery–Mettur irrigation project in Pattukkottai taluk of Thanjavur district (Tamil Nadu state) became malarious following the introduction of large-scale irrigation project. Reduction of malaria was brought about by the use of environmental management methods in six villages in a population of 3,400 (ref. 12). Thus it was concluded that untidy irrigation and not the irrigation *per se* was the cause of malaria.

Early in the century in India following the demonstration of the role of mosquitoes in malaria, transmission health impact assessment to prevent malariogenic conditions for new projects was made mandatory. When the capital of India was moved from Calcutta to Delhi in 1912 the site selected was adjacent to Jamuna river near the coronation pillar in north Delhi. This site was rejected by E. C. Hodgson, a malariologist in the armed forces as the area was considered unhealthy and malarious due to low-lying terrain prone to water logging. Hodgson surveyed Delhi and recommended the present location of Raisina ridge area which has an excellent natural gradient for drainage[13]. With the introduction of DDT in malaria control health impact assessment concept was given up and what we see today are the mushrooming of settlements in the unhealthy areas all over the country. Bombay (now Mumbai) was endemic for malaria and the vector was *An. stephensi*. Covell in 1928 studied the problem of malaria in Bombay and made recommendations for its control including the penal provisions under the Bombay Municipal Act[14]. Malaria was practically eliminated from old Bombay city and this status was maintained till recently. The return of malaria in Mumbai is the result of relaxed field operations permitting the rise in *An. stephensi* populations.

Delhi was notorious for malaria prevalence. Stringent application of legislative measures, drainage, land filling and intersectoral cooperation brought reduction in spleen rates in school children from 55 to 94 per cent[13,15]. Bangalore city had spleen rates of 23.2% and parasite rates of 6.5 to 21.2%. Control of mosquito breeding in wells and introduction of Gambusia fish in a few years brought down spleen rates to < 1% and parasite rate to < 5%[16]. In Pune city institution of antilarval measures was practical and economical and within 2 years dispensary figures fell by 75%, and spleen and parasite rates were reduced from 1/3 to 1/5 (ref. 17). From 1939 to 1941 spray killing of mosquitoes by Pyrethrum was practised to control *An. culicifacies*-transmitted malaria[18]. In India in the first half of the century, environmental management methods were implemented only in the military establishments; port areas; tea, coffee and rubber plantations, etc. However, the malaria situation in the country remained unchanged until the discovery of the insecticidal properties of DDT, and its eventual use in public health.

DDT-era

The dreadful malaria situation took a dramatic turn with the introduction of DDT in malaria control. The residual insecticidal action of DDT provided protection from infective mosquito bites for 8 to 10 weeks or more, and therefore spraying of 2 rounds of DDT annually, was all that was required to control malaria. Initially DDT was sprayed to protect troops at the Burma (now Myanmar) front in 1944 (ref. 8). The first operational rural malaria control project by spraying DDT received a telegram of blessings from Mahatma Gandhi. The project was launched in north Kanara and Dharwar districts of Karnataka to protect one million population living in highly malarious villages[19]. Between 1945 and 1952 DDT spraying in several states involving 30 million population produced spectacular success in reducing malaria-related morbidity. In 1952, Planning Commission in consultation with the Indian Council of Medical Research (ICMR) advised the Ministry of Health to launch nation-wide malaria control. This decision led to the launching of the National Malaria Control Programme (NMCP) in 1953. Under the NMCP, 165.57 million population was protected from malaria by 1957. In DDT-sprayed areas epidemiological indices fell by 63–79% raising hopes of victory over malaria. The VIII World Health Assembly which met in Mexico city in 1955 passed a resolution to eradicate malaria, and this urgency was necessitated by the possible interference of DDT resistance in vectors resulting in control failure.

Following this resolution the Government of India (GOI) launched the National Malaria Eradication Programme (NMEP) in 1958. NMEP was therefore mandated with malaria eradication as the final goal to be achieved within 7–9 years in a phased manner. Progress in malaria eradication was so spectacular that by 1965 DDT spraying wiped out malaria in 373 million population, and only 93 million population remained in the attack phase. In subsequent years more areas were transferred to maintenance phase. By 1968–69 malaria was eradicated from 90% population, i.e. 296 million population in maintenance phase plus 157 million in consolidation phase, and only 50 million population remained in the attack phase. Furthermore deaths due to malaria were completely eliminated[20]. Success in malaria control was so overwhelming that India's malaria eradication programme became a show piece in the world, and NMEP was heading towards freedom from malaria. These were the days of highest achievements under the NMEP.

Reverses

Although euphoria of success prevailed in the country reverses had started early in the 1960s. In 1963 and 1964 focal outbreaks occurred in two million population. In subsequent years, the malaria situation deteriorated further, and malaria that had retracted in the early 1960s took upward swing and cases multiplied in the entire country wherever malaria receptivity prevailed. Analysis of Annual Parasite Incidence (API) in the maintenance phase showed unprecedented increase in API over the previous year, i.e. 237% in 1965, 255% in 1966, 234% in 1967, and the situation rapidly deteriorated in the subsequent years[20,21]. Initially DDT was supplied free under the United States Assistance for International Development (USAID), but from 1965 onwards DDT had to be purchased against the hard currency which was not readily available[22]. As a result, NMEP suffered setbacks due to DDT shortages which varied from 15 to 30%, and these shortages persisted throughout[23,24]. Simultaneously DDT resistance started building up in *A. culicifacies*, a major vector of malaria in rural India. In areas lacking epidemiological impact of DDT, HCH was introduced, but *An. culicifacies* became resistant to HCH as well. Chinese aggression in 1962 and war with Pakistan in 1965 added fuel to the residual and resurgent foci of malaria by diversion of resources for war efforts. Floods, labour problems in the factories producing DDT and insurgency, etc. all contributed to the rise in malaria. By 1968–69, out of 71.385 operational units reverted to attack phase from the consolidation and maintenance phases, 41.6 units never moved out of attack phase, and these units were distributed in 20 states and union territories (a unit comprised 1 million population). By 1970 DDT and HCH resistance was widespread in the country, and to contain epidemic situations in Gujarat and Maharashtra malathion was introduced to control *An. culicifacies*, and resistance developed against this insecticide in just three years[25]. In the 1970s malaria had returned to become a serious public health concern, and its control required renewed attack which dwindled at the most crucial juncture. Thus the in-depth evaluation of NMEP in 1970 reported that while eradication was feasible in 91% of the population living in previously malarious areas, there remains 9% of the population (48 million) living in hard core areas where attack operations continued for up to 12 years. These were predominantly *Plasmodium falciparum* areas, and later designated as the hard core areas where the technology of residual insecticidal spraying had failed.

Urban malaria

Malaria in India was primarily a rural disease as most urban areas lacked piped water supply, and therefore breeding habitats for *An. stephensi* were few and limited, and this situation rapidly changed with piped water supply installed in most urban areas. As a result, during the eradication phase, malaria cases were seen rising in urban areas, and diffusing to rural areas which had been enjoying malaria-free status. To arrest this rising trend, Urban Malaria Scheme (UMS) was launched in 1971–72 in 131 urban areas in 18 states and union territories. Urban areas with >40,000 population and >2 Annual Parasite Incidence at 10% Annual Blood Examination Rate (ABER) were included in the UMS[26]. Beginning from 23 towns UMS covered 131 towns (74 million population) in phases over a period of 2 decades. In towns with <40,000 population, spraying was to be followed, but spraying has always been impractical in the urban areas, except in peri-urban settlements. There has been no further addition in the list of towns under the UMS, although malaria is a common ailment spreading unchecked and most of the country's urban conglomerations remain unprotected. According to the 1991 census, class I towns (>100,000 population) were 300 and class II towns (>50,000 and <100,000) were 345; and the total number of urban conglomerations plus the towns were 3,768. From 1981 to 1991 population of class I cities in Andhra Pradesh, Madhya Pradesh, Gujarat, Punjab, UP and Pondicherry had increased by 50% and this increase was highest in Kerala (100.85%). In the last 5 decades urbanization has already swallowed 1 million hectare of agricultural land. Greater Calcutta had 10 million population, of which 3.5 million population had malaria control activity under the Calcutta Municipal Corporation but in the remaining 6.5 million population with 35 municipalities there was no activity related to mosquito control. Malaria in Mumbai was under effective control but in the 1990s it has surfaced

as a major public health issue. New Mumbai has remained hyperendemic as the various nodes undergoing intense construction activities supported *An. stephensi* breeding. During this critical phase of urbanization New Mumbai was under the control of Panchayat and malaria control was based on residual spraying, thus ignoring the control of *An. stephensi*. In Tamil Nadu, Chennai contributes up to 60% or more malaria cases to the total cases in the state, but the strategy of chemical larval control under the UMS has not produced desired results, and this is true for most towns in Tamil Nadu and elsewhere. In urban areas malaria vector control is based on anti-larval methods often supplemented by thermal malathion fogging. Fogging is expensive and unproductive as a routine method of malaria control[27], but often it is in great demand because of its visibility and social acceptability. It may be noted that field operations under the UMS are directed to control mosquitoes rather than emphasizing species sanitation, i.e. the control of the vector *An. stephensi*.

Constraints

In the 1970s and 1980s NMEP encountered further setbacks due to technical, financial and administrative problems. The programme was stuck with insecticide shortages, refusals for domestic spraying, insecticide resistance in *An. culicifacies* and or refractory behaviour of vector(s), inadequate surveillance under the general health services, deteriorating malaria situation in the urban areas, and dismantling of research on malaria[23]. NMEP's administration gradually collapsed by rank and file. Experienced personnel opted for incentive-based health programmes such as small pox eradication, family planning, guinea worm eradication, etc., thus depleting malaria expertise. Frequent transfers interfered with the proper implementation of the programme. Key positions remained vacant and those in position were demoralized. India became signatory to the Alma Ata declaration 'Health for All by 2000 AD'. As per the Health For All (HFA) directive, NMEP's vertical operations became horizontal under the primary health care system. Thus malaria control was handled by the inexperienced and unwilling technical cadres. Surveillance instituted for early case detection and prompt treatment suffered for the want of staff and laboratory support. Backlog of 6–8 weeks in slide examination during the peak transmission season was common. There were 30–40% vacancies in the multi-purpose worker (MPW) category and these vacancies have continued till date; thus surveillance which was the sheet anchor became casualty. Malaria was a centrally sponsored scheme and a decision to change over to 50 : 50 cost sharing with the states at the beginning of the 7th Five-Year plan resulted in unfilled targets of field operations due to financial constraints[20]. Entomologists essential for the successful implementation of the programme were scarce and worked at low rung, remained unrecognized, and demoralized. They also lacked professional opportunities and promotions, and appreciation of their role in malaria control[28].

Control of urban malaria faces many constraints *inter alia* staff strength has remained static disregarding expansion of cities and increasing colonization. Shortage of trained staff and those in service require re-training. Unprecedented urban population increase far exceeding the limited capacity of municipal services is a worrisome problem in all towns. The problem of peri-urban settlements in low-lying and unhealthy areas often lack civic facilities, and constant inward movement of population further increase such settlements. Pressure in the piped water supply lines in many towns in south, e.g. Tamil Nadu is so weak that water is routinely delivered below ground level and carried in buckets or pumped. Water is subsequently stored in containers. In many towns acute water shortages and its erratic supply forces people to store water. Stored water provides breeding habitats for the *An. stephensi* and *Aedes aegypti*. The construction of faulty water storage tanks and their installation in the inaccessible areas makes supervision and larviciding nearly impossible. Building construction activities leads to tropical aggregation of labour resulting in focal outbreaks. Municipal and building bye laws to prevent mosquitogenic conditions are non-existent in most towns. The problem is further complicated by the multiple agencies engaged in malaria control and their lack of expertise and coordinated effort. Surveillance based on malaria clinics in hospitals is inadequate and misleading and thus the true picture of malaria remains unknown. Reliance on clinical diagnosis by the private sector which handles the bulk of malaria cases and increasing reliance on chemotherapy rather than vector control is a major issue.

Resurgence

In the 1970s malaria cases continued to rise unabated in the rural and urban areas, and in 1976 NMEP reported 6.47 million parasite positive cases, highest since resurgence. Deaths due to malaria that had been completely eliminated in the 1960s had returned. Earlier a task force was constituted under the Ministry of Health, (GOI) to suggest remedial measures, as it became clear that eradication strategy had failed. To arrest the rising trend of malaria, NMEP implemented the Modified Plan of Operation (MPO) in 1977. The World Health Assembly in 1978 approved the decentralization of responsibility for malaria control to the Primary Health Care Services. Malaria control was decentralized and handed over to the general health services. MPO was aimed to reduce morbidity and mortality due to malaria, retain the achievements gained under the NMEP and protect the green

revolution and industrial areas. MPO envisaged spraying all transmission areas with > 2 API at 10% ABER and free availability of antimalarial drugs throughout the country[29]. Simultaneously in India MPO was strengthened by the *Plasmodium falciparum* Containment Programme (PfCP) funded by the Swedish International Development Agency (SIDA). PfCP was initially launched in north-eastern states mandated to contain the spread of falciparum malaria. PfCP expanded in phases to protect 110 million population later reduced to 98 million population living in predominantly *P. falciparum* tracts in the country[30]. These were largely the same areas earlier identified as the hard core areas. Malaria responded to the MPO and cases declined and leveled at about 2 million during the 1980s. Epidemiological analysis showed that improvement in malaria situation was due to selective reduction in *P. vivax* but not in *P. falciparum*. After 12 years and spending US$ 20 million PfCP had lost its mandate and the programme had to be terminated.

Figure 1 shows malaria cases in India. During 1970s and 1980s malaria continued to raise its ugly head step by step, engulfing the entire country. In the 1990s there has been further rise of malaria, from 2 million cases in the 1980s to 3 million parasite-positive cases. Deaths due to malaria have increased to 1,000 annually; and epidemics covering the entire eco-epidemiological zones have returned, e.g. in western Rajasthan, eastern Rajasthan, Indo-Bhutan border, Manipur, Mewat (Haryana), north Gujarat and many towns. This is due to unresponsive nature of malaria, making inroads in new altered haven in the development areas.

Malaria also takes advantage of NMEP's problems in achieving spray targets. Cost escalation is adding fuel to the fire. In 1985–86 cost of spraying one million population with DDT, HCH and malathion was Rs 33, 36 and 192 lakhs respectively. In a decade this cost had escalated to Rs 99 lakhs for DDT, Rs 90 lakhs for HCH and Rs 361 lakhs for malathion, and this trend is continuing. In 1996 targeted population for spraying was 120.95 million for DDT, 33.59 million for HCH and 6.97 million for malathion respectively, and the population covered was 58.42 million (48.3%) with DDT, 6.65 million (19.8%) with HCH and 3.06 million (43.9%) with malathion. Total projected population for residual insecticide for 1997–98 is 164.75 million, out of which 123.37 million for DDT and 41.38 million for malathion as against the total population projected by the NMEP under high risk category in various states is 218.78 million, i.e. 24.57% living in 1,135,834 (23.13%) villages in 353 (69.9%) districts[31]. Lack of transmission control leads to a shift towards the antimalarial drugs to reduce morbidity and mortality disregarding primary emphasis on vector control. Chloroquine consumption increased substantially, e.g. in 1986–87 it was 206.5 metric tonnes and in 1994–95, 466.68 metric tonnes; and this increased drug consumption further intensified drug resistance, and the introduction of new antimalarials. Simultaneously *P. falciparum* was rising and in the 1990s accounted for 35–40% cases. Monitoring by the NMEP of drug resistance showed that about 30–35% of *P. falciparum* had developed some level of resistance to chloroquine[32]. Replacement drugs are few, more costly, produce adverse reactions, and often resistance builds up rather quickly. In the last 25 years the problem of drug resistance has surfaced as a big challenge in diagnosis and the treatment of malaria, largely in areas earlier identified as the hard core areas.

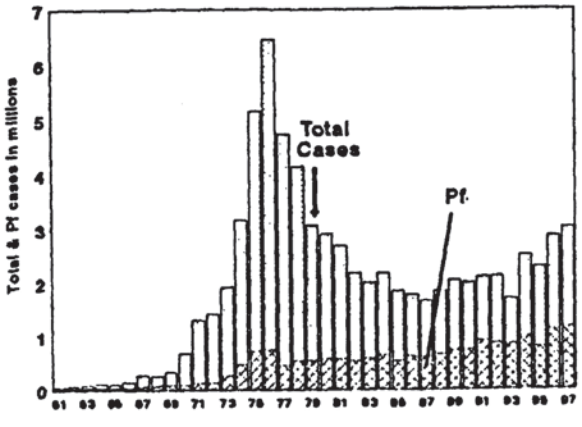

Figure 1. Total parasite positive and *P. falciparum* cases in India. (Source: NMEP).

The vectors

There are > 3,000 species of mosquitoes in the world. Genus Anopheles has 422 species, of which 60 are vectors of malaria. Figure 2 shows the distribution of malaria vectors in India. Of the 58 Anopheles species prevalent, 6 species are major vectors of malaria in India[33]. Mosquitoes belonging to Anopheles genus are characterized by the presence of 2 or more sibling species and these species vary in their biology, response to insecticide, vectorial capacity and distribution. Table 1 gives the relative importance of vectors in the transmission of malaria. *An. culicifacies* is the vector of rural and peri-urban malaria, and its natural distribution is in the peninsular India. This mosquito alone transmits 60–65% cases of malaria annually, and therefore control of malaria in India is largely the control of *An. culicifacies*. It breeds in river margins, irrigation systems, seepages, borrowpits, hoof marks, wells, ponds, and low-lying grounds all over the country in rural surroundings. *An. culicifacies* has become resistant to DDT, HCH and malathion, and as a result in areas with multiple resistance synthetic pyrethroids are being used.

GENERAL ARTICLES

An. culicifacies is a complex of 5 species designated as A, B, C, D and E. Species A, C, D and E are efficient vectors of malaria whereas species B is a very poor vector and has no role in the transmission of malaria. In nature sympatric populations of 2 or more sibling species are common[34]. *An. stephensi* comprises of two races namely type form and variety *mysorensis*[16]. Type form is the vector of urban malaria. It breeds in water stored for domestic use and in small water collections following rainfall. Wells are another preferred place for its breeding. The vector has developed multiple resistance but its control is based on anti-larval methods,

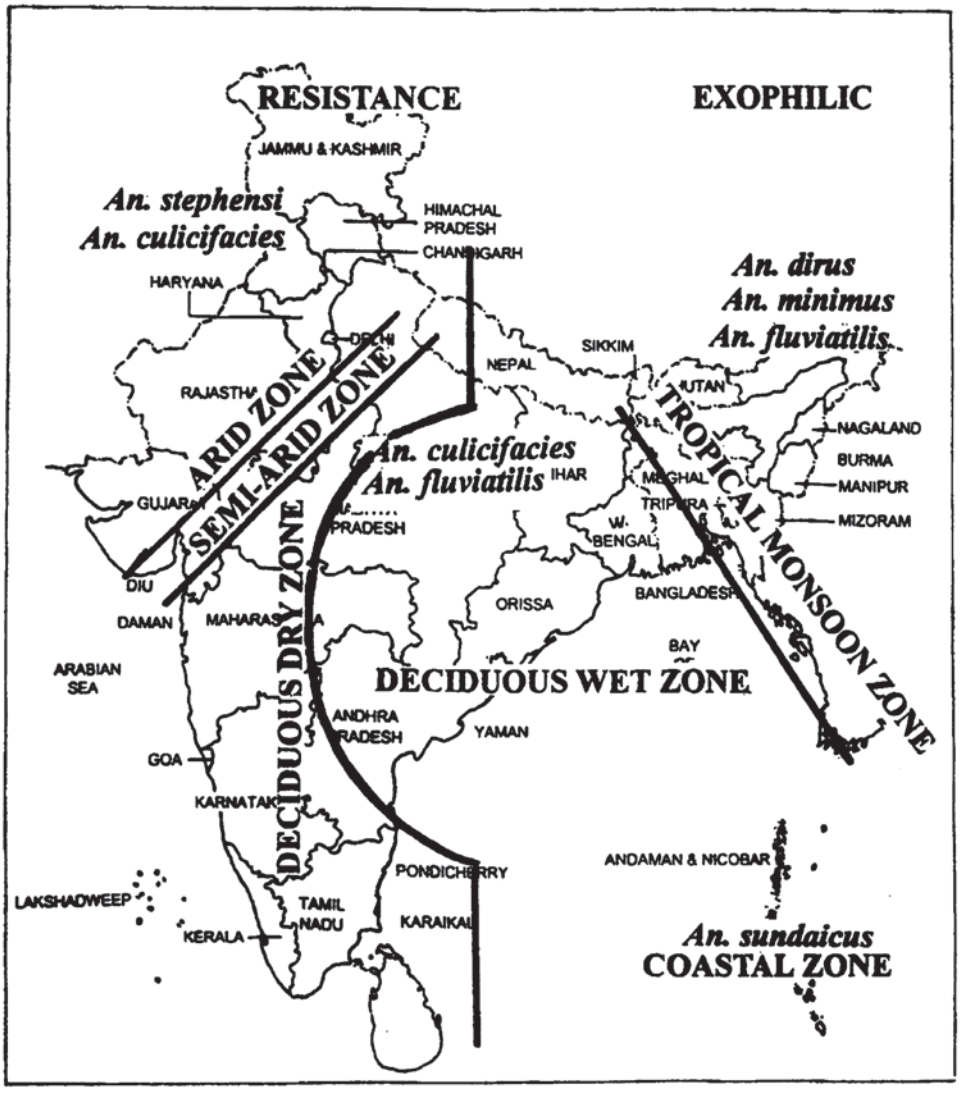

Figure 2. Distribution of malaria vectors in India. In arid and semi-arid zone vectors are resistant to insecticides. Exophilic and or exophagic vector behaviour becomes pronounced in the east.

Table 1. Role of *Anopheles* mosquitoes in malaria transmission

Malaria vectors	Anthropophilic index	Species-wise contribution (%)	
		Malaria cases	Pf cases
Major malaria vectors of India			
An. culicifacies	+	65	55
An. stephensi	++	12	5
Major malaria vectors of regional importance in India			
An. fluviatilis	++	15	30
An. minimus	+++	5	5
An. dirus	+++	3	5
Major malaria vector of the coastal areas			
An. sundaicus	++	0.039	0.001

Broad categorization. +, predominantly zoophilic; ++, zoophilic and anthropophilic; +++, anthropophilic.

and therefore resistance is not an obstacle in its control. The main problem is to search mosquito breeding sites and apply control methods at weekly intervals. This is rather difficult and therefore urban malaria has emerged as one of the major challenges. *An. stephensi* var. *mysorensis* is a species widely distributed in the arid zones in rural areas. Since the sporogony in this species takes >2 weeks, this mosquito is not important as the carrier of malaria. *An. fluviatilis* is an efficient vector of malaria and it breeds in slow running streams in the foothills along the Himalayan range and seepages in irrigation channels. Most populations of *An. fluviatilis* are susceptible to DDT and other insecticides, and therefore residual spraying with a suitable insecticide can interrupt transmission. It is a complex of three sibling species designated as S, T and U, of which S is the vector and the other two species lack vectorial potential[35]. *An. minimus* breeds in slow running streams and its present distribution is in the northeastern states in the degraded forests. *An. minimus* is fully susceptible to DDT but because of its exophilic behaviour, large vector populations successfully avoid contact with sprayed surfaces and maintain extra-domiciliary transmission. Although this is a species complex, populations in Assam (India) were exclusively of species A. In the deep jungles in the northeastern states *An. dirus* is the vector. It breeds in puddles in the sunshade. This is a very efficient vector of malaria and has exophilic and exophagic behaviour and maintains extra-domiciliary transmission. *An. sundaicus* was an important vector of malaria in the east coast. It breeds in brackish water. It has now retracted to the Andaman and Nicobar group of islands. It is susceptible to DDT and maintains extra-domiciliary transmission. There are other malaria vectors of minor importance such as the *An. annularis*, *An. varuna* and *An. nivipes*, and these vectors participate in malaria transmission in some localized areas[36].

The parasite

Mainly *P. vivax* and *P. falciparum* parasites are prevalent in India. The former accounts for 60–65% cases and the latter 35–40% cases. *P. malariae* is also found but in small numbers in certain foothill areas. The percentage of *P. malariae* may be up to 3% in areas of its prevalence such as in Sundergarh district, Orissa[37]. *P. vivax* almost exclusively occurs, except few cases in Himachal Pradesh, Jammu and Kashmir, Punjab, Tamil Nadu, Chandigarh, Daman and Diu and Pondicherry, whereas *P. falciparum* occurs predominantly in Orissa, Madhya Pradesh, northeastern states, Andhra Pradesh and Gujarat[31]. During spring, malaria transmission potential is very limited due to unfavourable environmental conditions and relapses of *P. vivax* are common leading to active transmission of malaria with the onset of rains. Initially during the rainy season almost all cases are *P. vivax* with small number of asymptomatic carriers of *P. falciparum* but after 6–8 weeks of rainy season, parasite formula begins to change in favour of *P. falciparum* and from late August onwards almost all cases are due to *P. falciparum*. Malaria transmission stops with the onset of winters, although relapses and chronic malaria cases continue to persist during unfavourable weather conditions. On an average about 30% *P. vivax* infections relapse and relapses may continue for at least 2 years in some cases[38]. *P. vivax* malaria may cause abortion and anaemia but deaths are rather rare. Five-day treatment schedule with 15 mg primaquine

is inadequate in achieving radical cure of vivax malaria. Some cases do not respond even to the 14-day treatment with 15 mg daily dose. There are also *P. vivax* strains with short and long incubation period so that primary attack and even relapse may take several months. *P. vivax* is therefore a mixture of various strains in response to their incubation period, relapsing pattern and response to primaquine[38].

As early as in 1973, resistance to chloroquine was reported in *P. falciparum* from Karbi-Anglong district in Assam[39]. Resistant *P. falciparum* strains multiplied and spread westwards and in the south, far and wide. Drug-resistant strains were more pronounced in high transmission areas and in the projects with aggregation of tropical labour. Migrant population from endemic areas transported new parasite strains seeding new areas. Imported strains intermingled with the indigenous parasite populations spreading and exploding in an epidemic form among the non-immune population to the new parasite strains[40]. In areas with RII and RIII level of resistance to chloroquine, which were largely in north-eastern states and Orissa, sulphalene/sulphadoxine pyrimethamine combination drugs were introduced as the first line of drug. Within 5–6 years, resistance to these drugs was also reported requiring the use of replacement drugs. In 1995 NMEP reviewed the anti-malaria drug policy to introduce new drugs to treat drug-resistant and serious and complicated malaria cases, but there are reports of resistance against mefloquine and even to quinine although limited to a few pockets in the country[32]. In the 1990s malaria situation deteriorated further as evidenced by the explosive epidemics. To this has been added the problem of chloroquine resistance in *P. vivax*[41,42]. Control of drug-resistant vivax is more complex, expensive and unattainable due to its survival through the relapses. The second line of drug, sulphadoxine or sulphalene pyrimethamine combination is not useful in the treatment of vivax malaria. Drug-resistant vivax malaria would require treatment with life-saving drugs like mefloquine and quinine which are more expensive and may produce adverse drug reaction. Large-scale use of these drugs may eventually result in resistance to these drugs as well. At present there is no monitoring of drug resistance in *P. vivax* but this is a resurgent problem and may lead to serious consequences from economic and public health point of view. Resistant *P. vivax* parasite may therefore keep on relapsing and since in *P. vivax* gametocytes are produced concurrently with the merozoites, there will be a rapid spread of resistant vivax malaria.

Microscopic diagnosis of malaria parasite is the standard method practised all over the country. However in the last few years Dip Stick and Immunochromatographic tests (ICT) have become available. These are simple non-microscopic tests which are highly sensitive (> 95) and specific (> 90) for the detection of *P. falciparum*[43,44], and a similar test for the detection of *P. vivax* is currently undergoing trials. *P. falciparum* is the killer parasite and early diagnosis and prompt treatment is the key to success. Diagnosis of resistant malaria is difficult and therefore in areas with > 25% cases of chloroquine resistance second line of drugs, i.e. sulphalene or sulphadoxine pyrimethamine drug combinations are recommended.

The rational approach to malaria control is the vector control, chemotherapy should be supportive and reduce morbidity and mortality due to malaria. Spraying residual insecticides is unsustainable due to high cost of repeated field operations, compounded by the problem of insecticide resistance environmental contamination and interference with the human immune system. Non-insecticidal methods of vector control are still in infancy and the general health services are not tailored to adapt these methods. Malaria is finding new grounds and getting deeply entrenched in receptive areas which are ever increasing, and any further delay of compromise with vector control could become disastrous.

The man

Population increase had the most profound effect on ecology promoting vector production. India's population stood at 361.1 million (1950) and life expectancy at birth 32.1 years (1950–51). Improved economy, food production and better health delivery gradually increased population to 915.9 million (1994–95) and life expectancy at birth to 60.8 years (1992–93). National developments are unable to cope with the population growth and therefore in terms of absolute numbers more people are poor today than at any other time in the history of India. Poor segment of our society is badly hit by malaria as they live under unhygienic conditions and suffer from malnutrition, infectious diseases, and unable to pay for medical treatment. Immune system is already under stress in this population and it may be further compromised as a result of food chain contamination by persistent organic pollutants, e.g. DDT leading to health problems[45].

Man is the definitive host of malaria. There is no animal reservoir of the human malaria parasites. Malaria is therefore contracted through the bite of mosquitoes from sick to the healthy man. All age groups of both sexes are susceptible to infection. New born babies up to the age of six months are generally protected from malaria due to the presence of maternal antibodies. Infants and children below 5 years are worse sufferers. There is progressive increase of malarial attacks up to 25 years of age followed by a downward trend.

In India stable malaria is prevalent in the northeastern states where *An. dirus*, *An. minimus* and *An. fluviatilis*

are the vectors. Transmission is high producing mortality in the infants, pregnant women and non-immune migrants. Immunity to malaria in this population is high and therefore people living in these areas are invariably asymptomatic carriers. Population movement to unstable areas disseminates new parasite strains resulting in malaria outbreaks. Malaria is unstable in the rest of India where vectors are less efficient and transmission is low. Epidemics erupt during favourable vector breeding years and deaths may occur in all age groups. Malaria comes in waves of 7 to 9 years or more depending on the environmental conditions and immune status of the population.

Malaria infection is also regulated by certain types of haemoglobinopathies and thus reduce the risk of dying from malaria. Negroes are resistant to *P. vivax* malaria as they lack Duffy group antigen in the red blood cells. Sickle cell trait provides protection from serious episodes of malaria, as also some other haemoglobinopathies[46]. Antimalarial drugs may also produce adverse reactions such as the primaquine treatment in patients with G6PD deficiency, and some drugs are contraindicated, e.g. chloroquine in psoriasis. Adverse drug reactions of antimalarial drugs are well known, e.g. quinine causes cinchonism, long acting sulpha drugs as suppressive therapy may cause fatal skin reactions and mefloquine neurological problems, etc.

The environment

Return of malaria in the 1970s found high receptivity in the new environments created under the successive 5-year plans to sustain the growing population and improve living standards. Five-year plans transformed the country into self-reliant economy. In 1996 population covered with drinking water supply in the rural and urban areas was 82 and 85% respectively. Piped water supply promotes the breeding and spread of *An. stephensi*, the vector of urban malaria and *Ae. aegypti*, the vector of dengue and dengue haemorrhagic fever[47,48]. Developments in agriculture had the most profound effect on the ecology. Food production in 1950–51 was 50.8 million tonnes and in 1995–96 it increased to 185.1 million tonnes. Area under irrigated rice paddy in 1951 was 30.6 million hectares and in 1995 this area increased to 42.2 million hectares with production capacity of 90 million tonnes per year. Although rice cultivation in India has an inverse relationship with malaria[49] in rice growing areas, which are increasing as a result of command area development, Japanese encephalitis becomes endemic, the vector being *Culex vishnui* group of mosquitoes which prefer to breed in the rice fields. However several studies have recorded breeding of *An. culicifacies* and *An. fluviatilis* in the rice agro-ecosystem but the epidemiological impact of breeding of malaria vectors is not visible. In command areas where *An. culicifacies* was not present before the irrigation, *An. culicifacies* has entered and replaced the earlier vectors[50]. Use of pesticides and other agro-chemicals in cash crops has resulted in the development of resistance in disease vectors, e.g. resistance in *An. culicifacies* to malathion in Andhra Pradesh[51] and Maharashtra[52]. Environment is also getting constantly degraded by creation of borrowpits in vast areas under mining, road construction, laying of railway tracks and digging pits in rural areas. Tropical aggregation of labour required in agriculture, forestry, industries, etc. is one of the major causes of malaria outbreaks.

Temperature has the most profound effect on the development of malaria parasite in the mosquito. At average temperature of 16°C, malaria parasite takes 55 days to reach sporozoite stage; 19 days at 20°C; 10 days at 25°C and 7 days at 28°C. Similarly high humidity enhances vector longevity and favours malaria transmission[53]. In the last 2 decades average minimum temperature in north India has increased by 2°C (Source: Dept. of Agricultural Meteorology, Punjab). Furthermore global warming is universal and its impact would be seen in the enhanced transmission of malaria in more regions of the world by extending transmission season and transmission zones. Already there are reports of malaria in the mountains of central Africa and the highlands of Papua New Guinea. Changes in humidity gradient resulting from expanding irrigation projects have their implications on the geographic spread of malaria.

New ecotypes

In the last four decades malaria has undergone paradigm shift from rural to man-made ecosystems[54]. Man-made malaria in India accounts for > 60% cases. Malaria control in the new ecosystems has become the most formidable challenge. Tribal population in India largely lives in hard core areas where malaria control has failed so far. Tribal population also has high proportion of haemoglobinopathies and thus these genetic traits modify the host–parasite interaction, and generally provide protection from serious episodes of malaria[55]. Malaria control in this population is difficult because of low literacy rates, settlements in remote areas, primary health care is inadequate and often non-existent, cultural taboos, and invariably local healers/quacks treat malaria. Deforestation leads to ecological succession of vectors, e.g. in Nainital district *An. minimus* was the vector in the 1930s, and deforestation resulted in the succession of *An. fluviatilis*, and further colonization of Terai and irrigation introduced *An. culicifacies* which is now the vector of malaria[56]. Malaria in forests with tribal settlements now comprises two ecotypes: these are the malaria in the deep forests and forest fringes (50 million

population); and malaria in the proximity of forest-fringe areas with disturbed ecology (20 million population).

Irrigation has increased from 22.6 million hectares in 1950 to >90 million hectares in 1995–96. Irrigation brings malaria due to dam construction, seepages, water logging and consequent ecological changes resulting in the introduction of new vectors. Increase in irrigation, storage practices, urban and rural water supply, villages in the vicinity of dams, reservoirs and canals, poor drainage, rain water accumulation, etc. all enhance vector breeding and longevity, and thus promote the transmission of malaria. Malaria in the rural India now comprises irrigated areas of arid and semi-arid plains (200 million population); and areas without irrigation (100 million population). The first census after independence in 1951 reported 62.44 million urban population and in 1991 this population increased to 217.18 million. Doubling of urban population was observed in 2 decades, i.e. from 1961 to 1981 and 1971 to 1991. This unprecedented increase in population is resulting in shortages in almost all areas of basic infrastructure. Some of these have direct influence on the breeding of vectors, e.g. settlements in unhealthy and low-lying areas and poor housing enhancing mosquito bites, piped water supply in the rural and urban areas promoting vector breeding inside houses and in the peri-domestic surroundings, water shortages leading to storage practices which become breeding grounds, and enormous breeding potential being created as a result of increasing colonization and poor sanitary standards. Urban malaria has emerged as a major ecotype comprising malaria in the towns (75 million population); and in peri-urban areas (75 million population).

India has emerged as a major industrial force in the world and industrial production index (1980–81 = 100) has increased from 18.3 (1950) to 283.3 (1995–96). Malaria in the industrial areas involves an estimated 10 million population. There are several examples of high malaria transmission in industrial complexes from throughout the country, e.g. during the construction phase of Mirzapur thermal power project there was sudden increase in malaria cases from 2,421 in 1979 to 11,145 cases in 1980. At the Visakhapatnam steel plant, Vizag >50% malaria cases in the district were reported from the steel plant complex. Epidemic situations often prevail at other industrial complexes, e.g. Mathura Oil Refinery, Bhilai Steel Plant, Bharat Heavy Electricals Ltd., Surat Industrial Complex, and a large number of other industrial belts of the country.

India has very long international borders involving 1600 km along Pakistan with *An. culicifacies* and *An. stephensi* vectors; 900 km along Nepal with *An. annularis* and *An. culicifacies* vectors; 375 km along Bhutan with *An. dirus*, *An. minimus* and *An. fluviatilis* vectors; 1200 km along Myanmar with *An. dirus* and *An. minimus* vectors; and 1700 km along Bangladesh with *An. dirus* and *An. minimus* vectors. Malaria along the international borders thrives uninterruptedly because of 16 km wide no man's land on either side of the borders, and there are no vector control activities all along the borders. Antimalarial drugs are used excessively, and often sub-standard drugs are smuggled across the porous borders, thus creating problems on both sides of the international borders. Malaria control is a problem even along the interstate borders, although to a lesser extent. An estimated 5 million population is involved in border malaria problem.

Migration of population for agriculture, industrial, forest and civil works influences malaria transmission almost throughout the country. Migration of population from endemic regions cuts across all types of malaria and transports various parasite strains to new areas where local population lacks immunity. It was estimated that at least 1/6th of the country's population migrates annually from one place to another for agriculture and construction-related works. Most migration is during the rainy season for sowing and harvesting of crops, e.g. from east UP and north Bihar to west UP, Punjab and Haryana. This is the period of active malaria transmission and the disease strikes during the productive period in agriculture. Malaria transmission is invariably intense and an outbreak of malaria involving drug-resistant strains is often a serious problem. An estimated 0.75 million population is employed daily in road and canal construction, and 50% of this labour is imported largely from endemic areas. Migration malaria in resettlement projects is a serious problem, e.g. in Koraput (Orissa) and Bastar (MP) districts malaria API increased from 40 to 160 in 10 years (1977–1988) and *P. falciparum* percentage increased from 32 to 82 (ref. 20).

Socio-economic factors

Malaria thrives in poverty and >39% of our population lives below poverty line. People belonging to this strata contract malaria easily due to life style and local environment that favours high receptivity and vulnerability. One glaring example is the tribal malaria in India. Tribal population is 7.8% and largely belongs to endemic regions of the country. In the country tribal population contributes >30% malaria, >60% falciparum malaria and >50% deaths due to malaria. Malaria control in this population has always been difficult and unattainable, and these are basically the hard core areas refractory to malaria control. In many backward and inaccessible areas alternate day fever is common and communities depend on local remedies which may resolve fever but not malaria. This population continue to suffer from malaria, disseminate the disease and eventually acquire immunity. The price they pay is high, i.e. high mortality among the non-immunes, extended morbidity; heavy loss

to the household economy, and to the region in agriculture and other labour-intensive developmental activities.

Malaria diagnosis and treatment is free under the primary health care system. Backlog of slide examination in the endemic areas during the transmission season may take up to 6 weeks or more, but not less than 15 days which is the normal beat of the multi-purpose worker. A large population of the country utilizes medical services of the private sector where malaria diagnosis is invariably based on clinical experience. Studies have shown that large number of cases are misdiagnosed leading to serious consequences in some cases. Pathological laboratories may charge from Rs 50 onwards. Diagnosis of drug-resistant malaria is difficult, time-consuming, and also not done except for monitoring purposes. In terms of economic loss a 7 day wage loss to the individuals is common. Average cost of malaria treatment comes to Rs 200 to 300, and in complicated cases the treatment cost may go up to Rs 20,000 to 30,000 or more[57]. The cost of malaria treatment is beyond the affordable limits of the poor people who suffer most from malaria.

Cultural habits adversely affect the impact of interventions, e.g. success of insecticide mosquito bednets may depend on the sleeping habits. Use of repellents, creams, oils, protective clothing, etc. help in providing protection from mosquito bites and contracting malaria. Traditionally people in India prefer the indigenous system of medicine and there are no proven remedies for malaria in the Ayurvedic or Unani systems of medicine. An Ayurvedic herbal anti-malarial drug Ayush-64 currently used in the treatment of malaria provided relief to only 50% vivax cases and there were serious problems in compliance, and it was unsuitable to treat falciparum malaria cases (Neena Valecha, unpublished results).

Malaria control is important for the prosperity of the nations. The technique to control malaria in the rural areas is to spray insecticides with residual action. There are serious operational problems in the spraying of houses and the room coverage seldom exceeds 25–30% (ref. 58). Spray rounds are often missed due to shortages or delayed supplies and the movement of staff. The spiraling cost of insecticides and over-used equipments make field operations difficult and financially unsustainable.

The Government of India has been spending 30–35% health budget (ca. Rs 120–140 crore annually) on malaria control alone and an equal amount is shared by the state governments, except by the northeastern states where it is 100% centrally sponsored scheme. Some states are unable to provide 50% matching grant and therefore field operations are seriously jeopardized. There are about 50% shortages in the demand and supply of insecticides and therefore a compromise in spraying targets results in the rise of malaria and eventually epidemics. In vast rural areas, e.g. in Orissa and MP the cultural habits of mud-plastering houses at weekly or fortnightly intervals and during the festivals results in the loss of insecticide. There has been no satisfactory solution to this problem, and these are the areas with intense malaria transmission, particularly *P. falciparum*. In some areas insecticides are diverted to agriculture resulting in poor malaria control and food chain contamination. Misuse of insecticides can produce harmful effects, e.g. may induce various types of diseases including cancers[59]. *An. culicifacies* the vector of rural malaria in India prefers to breed in the freshly dug out pits; and in almost all rural areas earth is used for house construction and mud-plastering, etc. Furthermore communities consider that malaria control is the sole responsibility of the government but the fact is that malaria is a local disease and government alone cannot control malaria on long-term basis without the active support of the communities. This concept has to percolate in our villages through health education and people should be persuaded to supplement government's efforts. A well planned community based programme can reduce malaria transmission to low levels at reasonable cost and malaria control can become sustainable[60]. Sustainability could be further enhanced by linking malaria control with income-generating schemes, e.g. carp production in village ponds[61]. To further reduce cost, intersectoral coordination can be elicited and all projects must be subjected to health impact assessment to ensure preventive and corrective measures through the intersectoral coordination committees at the central, state, district and lower levels set up for this purpose. Malaria is a serious disease and *P. falciparum* may kill a non-immune patient just in about 40 h, thus besides tragedy it may completely upset household economy. People should be made aware of the serious consequences of contracting malaria and high cost of treatment. All fever cases must be diagnosed for malaria promptly. A study of the economic burden of malaria in India showed that malaria in 1991 was responsible for economic loss of US$ 0.5 to 1 billion annually, and since the malaria receptivity is constantly increasing this cost is likely to increase further[57]. Another study by World Bank on the morbidity and mortality due to malaria estimated 0.9 million disability adjusted life years (DALY) in 1990 (ref. 62). This figure when converted in monetary terms also comes to economic loss between US$ 507 and 631 at the static malaria situation of 2 million cases. In sub-Sahara Africa the annual economic burden of malaria was estimated US$ 0.8 million and it was expected to rise to 1.7 billion by 1995 (ref. 63). Economic studies on losses due to malaria can attract funding which is becoming a serious problem with most malaria control programmes.

Research support

Since the discovery of malaria transmission by mosquitoes in Secunderabad in 1897, India has remained in the forefront of malaria research. At the time of launching of NMCP/NMEP India had some of the world's best malariologists. Therefore when DDT was introduced in malaria control, it wiped out malaria from the sprayed areas, and DDT spraying became the standard method of malaria control. Success in malaria control by the early 1960s was so overwhelming that malaria eradication seemed imminent, and as a result research on malaria was considered unnecessary and therefore de-emphasized. Publication of the *Indian Journal of Malariology* was terminated in December 1963 as there were neither the readers nor papers for publication. Furthermore, in 1964 Malaria Institute of India supposed to provide research and training support to the NMEP was re-named as the National Institute of Communicable Diseases (NICD) with a revised mandate. Such was the impact of DDT, and eventually it turned out that DDT failed to control malaria and successfully wiped out malariologists. As a result, during the resurgent phase of malaria there was no research support to the NMEP. Therefore in 1977 research on malaria was re-organized under the auspices of the Indian Council of Medical Research (ICMR) and operational research became an important component of the Modified Plan of Operation (MPO) of the NMEP. Sustained research on malaria in subsequent decades provided many new technologies in malaria control. Some notable technologies introduced in malaria control in the country are: bioenvironmental malaria control, insecticide-treated mosquito nets, selective spraying, *Bacillus thuringiensis* H-14, non-microscopic test for *P. falciparum* detection, i.e. Dip stick and ICT, alpha beta arteether, mosquito repellents, mass production and application of larvivorous fishes, etc.

Current strategy

World Health Assembly in 1989 declared malaria control a global priority. In response to this concern WHO convened a ministerial conference on malaria in October 1992. Member countries from the endemic and non-endemic countries signed a World Declaration on the control of malaria[64]. In 1993 World Health Assembly endorsed the World Declaration on malaria and emphasized the need to develop sustainable malaria control programmes adapted to local needs. The same year WHO study group met in Geneva to provide guidance for the implementation of the Global Malaria Control Strategy[65]. In 1995 WHO study group on vector control for malaria and other vector-borne diseases met in Geneva and prepared guidelines for the implementation of the vector control component of the global malaria control strategy[66]. Broadly speaking, the member countries of the WHO have adapted the same guidelines.

As we approach the next millennium, the malaria parasite *P. falciparum* is showing signs of multiple resistance and resistance is fast spreading in *P. vivax* to chloroquine, malaria vectors have become refractory either due to resistance or exophilic behaviour, the environment is becoming more hospitable for the vector proliferation, chemical vector control is losing grounds due to harmful effects on the ecosystem and human health. Urbanization, industrialization, opening up of hinterland and related developments continue to create more and more mosquito production grounds. Malaria thrives in poverty and erupts in epidemic form under favourable environmental conditions. Malaria control therefore has become a formidable task requiring new technologies. Government has a strong commitment towards malaria control as is evident with the increasing allocation of funds in the successive five-year plans. Already ca 35% health budget of the Government of India (GOI) is earmarked for malaria control and an additional equal amount is contributed by the state governments. Since 1995 malaria control in the north-eastern states has become 100% centrally sponsored scheme, thus removing the financial bottlenecks from stable malarious areas. Malaria control has been further strengthened by World Bank financing of Rs 891.04 crores (US$ 215 million) for a five-year period from 1997 to 2002. A revised malaria control strategy known as the Enhanced Malaria Control Project (EMCP) has been launched in the country. More than 200 million population (specially 62.2 million people living in rural areas with severe malaria) living in 1400 PHCs, in 100 districts in Andhra Pradesh, Bihar, Gujarat, Madhya Pradesh, Maharashtra, Orissa and Rajasthan states would be the beneficiary of the EMCP. Largely population under the EMCP is the same as had been previously identified, i.e. the hard core areas. Impact of EMCP on malaria would be variable. Success in malaria control would depend *inter alia* on research support in unfolding the epidemiological determinants of malaria transmission, and on the careful planning and monitoring, decision-making capability at the local level, and frequent reviews to apply integrated innovative interventions.

Epilogue

Malaria is an ecological disease and therefore fighting malaria would require ecological approaches based on the sound knowledge of vector biology and transmission dynamics of malaria generated locally for a particular ecotype. In this connection the bioenvironmental malaria control strategy developed by the Malaria Research Centre is an example of need-based research directed

to control malaria by simple, low cost and indigenous technologies. This was possible by organizing basic and applied research leading to the feasibility cum demonstration projects on malaria control with the final goal of mounting a decisive assault on malaria. In the last decade or so we have successfully demonstrated that malaria control is feasible and sustainable in large parts of the country without the use of insecticides. The strategy has many positive outputs such as the field operations are cost effective, sustainable, and improve the environment. The interventions work in harmony with nature, demystify the disease, inculcates scientific temper, provide scope to incorporate income-generating schemes and malaria control can be linked with other developmental activities leading to the holistic development of rural areas. Successful demonstrations have been made in the control of urban, rural, industrial and coastal malaria[50,60]. Currently the strategy is being implemented in Hassan district, Karnataka (S. K. Ghosh and co-workers, MRC unpublished results) and the state of Maharashtra through the existing primary health care system (P. P. Doke, Maharashtra Government Health Department, personal communication). For the first time bioenvironmental interventions are being applied in the control of rural malaria in vast endemic areas, and this movement is spreading. As we move into the next millennium, malaria control is moving away from chemical control in favour of age old methods of drainage, species sanitation, biological control and environmental interventions. After the Nobel Prize winning discovery of mosquitoes as carriers of malaria Ronald Ross himself applied these methods in malaria control, and this is one of his intellectual legacies. Today we are better equipped with modern technologies and a century of experience accumulated to attain freedom from malaria.

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