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MATERIALS FOR AND APPROACHES TO MALARIA STRATIFICATION IN RELATION TO THE RATIONAL USE OF ANTIMALARIAL DRUGS IN SOUTH ASIA[1]

by

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CONTENTS

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1. INTRODUCTION

During the last 10 to 15 years the development of resistance to insecticides among malaria vectors and a considerable increase in the cost of insecticides have been instrumental in diminishing the role which insecticides used to play under the Malaria Eradication Programme (MEP).

To counterbalance this situation, the attention of the national authorities was drawn towards a wider use of antimalarial drugs in their respective country programmes which were converted into Malaria Control Programmes (MCP) in the early 1970s. A wave of post-eradication malaria epidemics (WHO, 1979), which occurred throughout the countries of South Asia at about the same time, further promoted this interest in control programmes. Moreover, a dangerous upward trend in the incidence of Plasmodium falciparum malaria with a high fatality rate was observed.

The interrelationship between two principal antimalaria measures, i.e. the detection and treatment of malaria cases and control of the malaria vector(s), was discussed at length at the Twenty-second World Health Assembly which passed a resolution (WHA22.39) strongly advocating the rational use of all possible as well as of all readily available methods and means of malaria control in antimalaria programmes (WHO, 1973). In this context detection and treatment of malaria cases may often be the main and, in certain circumstances, the only method of malaria control which a country can afford.

At present, the role and place of antimalarials in the countries of South Asia are determined by the general objective of preventing malaria mortality and reducing morbidity. The extent to which antimalarials are used in each country programme may vary widely depending upon local epidemiological conditions, as well as on the operational capabilities of the programme and the financial resources of the country. The selection of particular antimalarial drugs or of the drug regimen to be applied will also depend upon the prevailing epidemiological conditions in each country.

The study, the grouping and the analysis of these epidemiological conditions and, on the basis of the data obtained, the subsequent designing of appropriate variants of the use of antimalarials, are the objectives of operational malaria stratification.

First of all, the mosaic character of the spatial distribution of different malaria species (e.g. in some areas P. vivax is prevalent, while in other areas it is P. falciparum) should be given due consideration. Another related character is that, even in territories with a predominance of any one malaria species, there are areas where the parasite populations differ in their intrinsic features, as for example, drug-resistant populations of P. falciparum. Although areas with P. falciparum populations sensitive to antimalarials still constitute the majority in South Asia, there is, nevertheless, a danger of the establishment of local transmission of resistant strains as a result of the intensive importation of such resistant strains particularly into areas with development projects.

The first stage of operational stratification for the rational use of antimalarials should therefore be the time when the objectives of drug use are formulated and its priorities identified.

Of particular importance in this respect, are certain special situations which may be encountered in South Asian countries:

(a) Areas with an overwhelming prevalence of P. vivax malaria:

(i) Areas where the local population is free of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency;

(ii) Areas where the local population is affected by different levels of G-6-PD deficiency.

(b) Areas with an overwhelming prevalence of P. falciparum malaria:

(i) Areas with a prevalence of P. falciparum populations sensitive to antimalarials;

(ii) Areas with a prevalence of P. falciparum populations resistant to antimalarials at RI and RII levels;

(iii) Areas with a prevalence of P. falciparum populations resistant to antimalarials at the RIII level;

(iv) Areas where the human population is affected by various haemoglobinopathies.

(c) Areas with a prevalence of P. malariae malaria.

(d) Areas with a more or less equal distribution of different malaria species.

(e) Areas with a large migrant population (e.g. development projects; agricultural schemes employing seasonal labourers; places of worship, religious centres, etc.; resorts, tourism centres, etc.).

In order to identify the optimal drug regimen or dosage to be used as well as other related questions, more detailed information on the various areas outlined above is provided in the following sections. The types of antimalarial treatment in the countries of South Asia continue to be the same as under MEP (i.e. presumptive treatment, radical treatment, mass drug administration).

2. AREAS WITH AN OVERWHELMING PREVALENCE OF P. VIVAX MALARIA

2.1 Seasonal incidence of P. vivax malaria

Perennial transmission of malaria is possible in the countries of South Asia; nevertheless, the incidence of the disease follows a seasonal pattern, the one exception being when the malaria incidence is so high that it becomes practically impossible to identify the seasonal pattern.

In the countries of the Indian subcontinent, the P. vivax incidence peak falls primarily in the months of July through September. In some instances a spring wave of P. vivax incidence may also occur, consisting in either manifestations of long incubation P. vivax or relapses. Recently, however, there had been a few publications on the possibility of spring transmission of P. vivax in northern and western India (Vaid et al., 1974; Pattanayak et al., 1977).

2.2 Relapse rate and its seasonal pattern

This is an extremely important issue in relation to both the use of 8-aminoquinolines and the planning as well as timing of antirelapse treatment.

The local P. vivax populations in the countries of South Asia are apparently less prone to produce relapses even without the administration of primaquine as compared with other geographical areas. The reason for this is still obscure and it may be due to various factors, such as nutritional preferences and habits of different ethnic groups, the status of immunity, genetic peculiarities, etc. Viswanathan (1945) estimated the natural relapse rate among P. vivax infections in India at about 52%-63%.

Moreover the relapse rate of P. vivax cases after single dose treatment with primaquine (45 mg) differs from that after five-day treatment (75 mg). In India, several investigators (Yaswant Singh et al., 1953; Basavaraj, 1960; Sharma et al., 1973; Roy et al., 1977) reported that after administration of five-day treatment with primaquine the relapse rate varied from 1.28% in southern India to 8.4% in central and northern India.

Studies on the efficacy of five-day treatment with primaquine among Nepalese who had acquired P. vivax infections in Uttar Pradesh and Bihar in India have shown that the relapse rate was about 8% (Kondrashin & Shakya, 1981). On the other hand, studies undertaken on the same subject among Nepalese infected in the north-eastern states of India (e.g., Assam, Meghalaya, Nagaland) have revealed a relapse rate of 16%-18% after single dose treatment (Parajuli et al., 1982).

The P. vivax relapse rate among indigenous populations in Nepal after the administration of five-day treatment with primaquine was also observed to vary from one geographical belt to another. In the central region of Nepal, the relapse rate was about 54% (Kondrashin & Shakya, 1981) while in the eastern region, it went up to 7.5% after single-dose treatment with primaquine (Parajuli et al., 1982).

The P. vivax relapse rate among indigenous populations in Nepal showed fluctuations depending upon the altitude and the season at which infection was contracted. For example, the relapse rate was higher in the inner terai areas than in the plains and hills, and the frequency of relapse was much greater among those infected during the late autumn months than during any other season of transmission (Kondrashin & Shakya, 1982).

Studies similar to those described above are currently being conducted in Sri Lanka. Preliminary results have shown that the relapse rate among local P. vivax infections after single-dose treatment and five-day treatment with primaquine was relatively low and operationally acceptable for the programme (Ruberu - personal communication, 1981). In Sri Lanka also, P. vivax infections treated during summer months are known to relapse much less than those treated during autumn or winter months (Gill, 1936).

2.3 Distribution of P. vivax populations with short and long incubation periods

For some time it has been almost unanimously considered that P. vivax populations with a long incubation period are confined exclusively to areas with a temperate climate. However, already in the 1920s there were indirect indications and in the 1930s direct indications of the existence of P. vivax strains in northern and north-western India with a long incubation period (Sinton, 1931; Covell & Bailey, 1932, 1935, 1936). Recent publications support these views (Lysenko et al., 1977; Warwick et al., 1980; Kondrashin & Orlov, 1987).

The existence of P. vivax with a long incubation period in the subtropics and tropics is an important factor in the epidemiology of malaria today. Certain investigators even believe that it was instrumental in some instances in failures to eradicate malaria (Lysenko et al., 1977).

2.4 Prevalence of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency

Certain genetic characters of the human erythrocytes are known to decrease their susceptibility to invasion by the malaria parasites, but none, so far, has been found to increase it. The study of human genetic markers and their relationship to malaria is assuming importance in the countries of South Asia due to the resurgence of the disease.

As primaquine is known to produce haemolysis in G-6-PD deficient individuals, it is important to know the genetic background of populations/ethnic groups before recommending a dosage schedule.

G-6-PD deficiency of the B type is prevalent in most parts of India (Viswanathan, 1945; Kondrashin & Shakya, 1981). A high incidence of the deficiency of this enzyme is found in the Parsi (16%) and Cutchi Bhanushali (13%) of western India, the Koya Dora tribe (13%) of Andhra Pradesh, the Santal tribe (14%) of west Bengal, the Mikir, Rabha and Rajbonshi (12-16%) of Assam and the Angemi Naga (27%) of Nagaland.

In general, the G-6-PD deficiency gene is more frequent in those belonging to the tribes of Maharashtra and Andhra Pradesh than in those who do not. This gene has a frequency varying from 3% to 5% among Assamese, Bengalese and Punjabese. In southern India the gene is present with a frequency of 5% to 9% in the Trula and Kurumba tribes but it is absent in the Toda and Kadar tribes.

Tomar et al. (1983) reported a prevalence of G-6-PD deficiency of 25% to 28% in populations of the Bastar district which is highly endemic for malaria. In another recent study, a high frequency of G-6-PD deficient allele was found among tribal populations as compared to non-tribal populations, living in malarious areas of the Hyderabad region (Sharma, 1985).

The problem of G-6-PD deficiency is quite acute in Sri Lanka. Clinical manifestations and epidemiological consequences of this phenomenon were particularly prominent during the last two malaria epidemics in the country in 1968-1969 and 1974-1975. These epidemics were mainly associated with P. vivax; therefore the 14-day treatment course with primaquine was replaced by the five-day treatment course and in many instances the drug was given to the patients for self-administration. This resulted almost immediately in a considerable increase of cases of intravascular haemolysis; and eventually, in some places, the administration of primaquine was suspended. The epidemiological consequences of such an act were obvious. Studies undertaken by local investigators showed that the prevalence of G-6-PD deficiency was relatively high in the north-eastern part of the island. Representatives of the Sinhalese, Tamil and Moslem communities were screened and it was found that in the Anuradhapura district the general prevalence of G-6-PD deficiency was 5.3%; however, the prevalence in purana (ancient settlements) reached 21%, with Sinhalese and Moslems being the most affected (Abeyratne & Halpe, 1968; Abeyratne, 1976). Similar investigations were carried out in Kegalle district of Central Province where a prevalence of 1.3% was found among Sinhalese (Nagarathane, 1969). In Western Province, the prevalence was 2.0% (Abeyratne, 1976) and in South Province it was as high as 6.0% (Abeyratne, 1981 - personal communication). Finally, investigations by Kondrashin (1981) revealed that the prevalences of G-6-PD deficiency in the Anuradhapura and Badulla districts (south-eastern part of the island) were 2.9% and 18.7% respectively.

Extensive investigations on the prevalence of G-6-PD deficiency are being conducted in Nepal and in Bangladesh.

3. AREAS WITH AN OVERWHELMING PREVALENCE OF P. FALCIPARUM MALARIA

3.1 Seasonal incidence of P. falciparum malaria

The distinguishing feature of P. falciparum incidence as compared to P. vivax incidence is its confinement to the late autumn and winter months of the transmission season in most countries of South Asia. This phenomenon is not without practical consequences. Operational staff of the malaria eradication/control programe, as if mesmerized by the first peak of malaria incidence, often pay far more attention to the initial period of malaria transmission primarily associated with P. vivax, than to the second period associated with P. falciparum. Moreover, in South Asia the most celebrated religious festivals fall in the late autumn months, resulting in a slackening of any type of antimalaria activity during this period.

3.2 Endemicity: current and past status

Information on endemicity may be useful for estimating the immune status of a population (semi-immune, non-immune, etc.) so as to differentiate drug schedules (Clyde & Shute, 1959).

The different response to chloroquine of infants and children in areas with intensive malaria transmission is well known. Therefore, the impact of established chloroquine resistance is likely to be most manifest at first in persons with no (or little) immunity, such as the very young and those coming from non-malarious areas.

Experience in India showed that malaria had never been eradicated in the hyperendemic belt of the country, inhabited mainly by tribal populations. P. falciparum was the prevalent species in those areas throughout the period of the malaria control/eradication campaign in India. There are reasons to believe that the foci of resistant malaria were initially confined to those areas of the country (Kondrashin & Orlov, 1983; Kondrashin & Orlov, 1984; Orlov et al., 1983).

3.3 Spatial distribution of P. falciparum

Data on the spatial distribution of P. falciparum may be instrumental in isolating the so-called "nuclei" of prevalence of this species. For example, the studies undertaken by Kondrashin & Orlov (1984) have shown that for the last 50 years P. falciparum has been consistently confined to the north-eastern and eastern states of India and to those areas from which malaria had never been eradicated. The present spatial pattern of P. falciparum in India is as follows:

(a) highly intensive foci of P. falciparum - north-eastern states and the State of Orissa;

(b) foci of P. falciparum with moderate intensity - central group of states;

(c) foci of P. falciparum with low intensity - Northern and North-Western States, South India.

3.4 History of the use of antimalarials

This aspect is of great importance when identifying resistant foci of P. falciparum and when designing appropriate drug regimens or choosing antimalarials.

3.5 Geographical distribution of foci of P. falciparum resistant to antimalarials

Chloroquine and other 4-aminoquinolines continue to be the mainstay in the treatment of malaria in South Asia. However, the efficacy of chemotherapy shows all the signs of diminishing.

In India, the first report of P. falciparum resistance to chloroquine came from Diphu and Nowgong in Assam in 1973. This was followed by several reports of chloroquine resistance from other parts of the north-eastern states, and the states of Orissa, Maharashtra, Uttar Pradesh, Haryana and Delhi. The geographical distribution in India of known foci of resistant P. falciparum is shown in Fig. 1.

In Sri Lanka and Nepal the establishment of local transmission of resistant strains of P. falciparum took place in October-November 1984.

The problem of P. falciparum resistance to the 4-aminoquinolines in the countries of South Asia is considered to be of high priority. To cope with it, the South-East Asia Regional Office of WHO had introduced in 1976 a programme for the monitoring of drug resistance in the Region. The objectives of the programme were to determine the prevalence, frequency and level of P. falciparum resistance in the countries concerned in order to define measures for containing the spread of resistant strains. By 1981, as a result of the creation of 25 specialized teams trained to detect the resistance of P. falciparum, baseline data had been obtained from different countries and data on the geographical distribution of resistant foci had also become available (Orlov, 1981).

Furthermore, it was observed that the dissemination of P. falciparum-resistant strains had taken place in many countries, particularly in India (V. P. Sharma, 1983). Fortunately, this resistance of P. falciparum is still mainly at the RI level. However, in Bangladesh, it is not so rare to encounter foci of P. falciparum resistant at the RII and even the RIII level.

3.6 Abnormal haemoglobins and P. falciparum infection

Research on the relationship between abnormal haemoglobins and P. falciparum infection is being conducted in a few countries of South Asia, but, at present, the findings are still preliminary (Gosh, 1983).

3.6.1 Sickle cell haemoglobin (HbS)

HbS provides protection from P. falciparum infection. It has been mostly reported from the tribal populations of India and its frequency varies from 0-30% (A. Sharma, 1983). A high frequency of HbS has been reported from Bastar district in Madhya Pradesh State. Further studies have revealed that the incidence of the sickle cell trait was high among tribal populations in comparison to non-tribal populations living in the same malaria endemic belt in Andhra Pradesh (Sharma, 1985). It is planned to study the correlation between HbS and the intensity of malaria infection (i.e. degree of parasitaemia) in different population groups of the country.

3.6.2 Thalassaemia

Direct evidence of the genetic trait thalassaemia being associated with resistance to malaria has not been convincingly demonstrated, but there is indication of a geographical correlation between the frequency of the gene and the regional history of malaria

(Ray et al., 1964; Roy & Choudhury, 1983). In India, a lower frequency of the trait among malarious groups as compared to non-malarious groups was reported from tribes in Dadar and Nagar Haveli by Vasantha et al. (1982).

3.7 ABO blood groups and P. falciparum infection

Among human red cell antigens ABO blood groups exhibit a world-wide polymorphism. Although a good amount of work has been done on the relationship between ABO blood groups and malaria, the results so far have been inconclusive. In Delhi, malaria was frequent in the A group (Gupta & Rai Chowdhuri, 1980) and a recent study showed that the B blood group was more frequent among malaria patients (Malaria Research Centre, New Delhi, 1983-1984 annual report, unpublished). However, Vasantha et al. (1982) did not find any association of ABO blood groups with malaria in a survey of Dadar and Nagar Haveli.

4. AREAS WITH A PREVALENCE OF P. MALARIAE MALARIA

Throughout the history of malaria in South Asia, P. malariae prevalence was of a rather limited importance. In general, the incidence was relatively low except in a few places like those in Karnataka State, India (Viswanathan, 1950; Jaswant Singh et al., 1952). During the implementation of the National Malaria Eradication Programme (NMEP) in India P. malariae almost disappeared despite a few outbreaks such as those in Karnataka State in the Tumkar district in 1969 (Dhir et al., 1969) and Hassan district in 1970 (P.R. Desai & H.M.L. Srivastava, 1971, pers.comm.).

In Maharashtra State, 67 cases of P. malariae were reported from 1961 to 1982, mainly from the remote inaccessible hilly areas, populated by the tribes (Vittal, 1983).

One of the most peculiar features of the epidemiology of P. malariae is that during an epidemic it is scanty whereas between epidemics it is usually more prevalent (Viswanathan, 1950).

P. malariae in South Asia is generally associated with forest areas. Susceptibility to infection with this parasite according to age, sex and ethnic or non-ethnic groups needs further investigation. It is also important to note that naturally acquired infections are apt to persist at submicroscopic densities for many years (Boyd, 1949) and are not easily detectable.

According to recent observations made in certain areas of India under the Plasmodium falciparum Containment Programme, P. malariae was not so rarely found (Ray - personal communication, 1985). The proportion of P. malariae in the total malaria incidence may represent up to 1%-2% (Beljaev - personal communication, 1985). It is therefore possible that in other areas P. malariae is not detected or has been wrongly identified.

5. AREAS WITH A MORE OR LESS EQUAL DISTRIBUTION OF DIFFERENT MALARIA SPECIES

This type of situation may often be encountered in areas where the process of species exchange is taking place.

In India and Nepal, it is mainly confined to forested areas with resettlement projects. Usually the people from the plains bring with them into the resettlement sites P. vivax, while among the local population the prevalent species is P. falciparum. It was found (Kondrashin & Orlov, 1985) that in time they exchange the species with the result that both species become prevalent in more or less equal proportions.

To deal with the situation described above, priorities need to be identified. Once this has been done, studies should be undertaken on the seasonal prevalence of each malaria species as well as on the epidemiological features of each species following the principles discussed in the above sections 2, 3 and 4.

6. AREAS WITH EXTENSIVE POPULATION MOVEMENTS

Population movement has been considered as an important factor in the epidemiology of malaria during all phases of malaria control throughout the world.

Various types of population movement may be defined by their spatial and temporal characteristics (Gould & Prothero, 1975). These characteristics are of major importance in the transmission and control of the disease. Spatial distinction can be made between the rural environment where most people are still located and the urban environment where the population is increasing. Moreover, large numbers move between the two, and, with the growing urban populations, movement between and within urban places is increasing. Movements can, therefore, be designated as rural/rural; rural/urban; urban/rural; or urban/urban (intra-urban and inter-urban) (Prothero, 1983).

The epidemiological implications of population movements became particularly evident during the final phases of MEP. WHO strongly advocated the absolute necessity to interrupt malaria transmission among migrants at the same time as among the stationary populations. WHO (1957a, b) also stressed the fact that the size of the population movement, its routes and its seasonal pattern may vary from one country to another. Some of these variations, however, have common features, on the basis of which Pampana (1969) suggested the following classification of different types of migration:

(1) Permanent migration primarily associated with the demographic consequences.

(2) Seasonal migration related to finding job opportunities.

(3) Pilgrimage (including tourism).

In addition to these general types of population movement a fourth type may be added: movements of troops and civilians during wartime. The epidemiological significance of this was shown in detail by Beklemishev (1946).

Migration as it occurs today in the countries of South Asia corresponds on the whole to the types described above. However, the size of the migrant population in those countries is very large, reaching sometimes 15-20% of the total population a year. In India, for example, permanent migration is of two kinds: movement to urban areas and settlement on a newly reclaimed area. The seasonal migration of agricultural labour and non-skilled industrial workers prevails over any other type of population movement in India. The size of the movement associated with pilgrimages and tourism is also on the increase.

From an operational point of view and for the practical planning of the rational use of antimalarials, the present types of population movement in South Asia may be grouped according to territorial delimitations as follows:

(1) Migration inside the territory of a State (inside administrative districts, neighbouring districts, etc.).

(2) Interstate migration (between neighbouring states, between remote states).

(3) Migration between neighbouring foreign countries (between frontier territories, between remote districts).

(4) Migration between remote countries (migration into countries free of malaria, migration into countries with a malaria problem).

Additional information for each type of the above indicated population movement patterns is needed, like:

- estimation of total migrants;

- seasonal pattern of migration;

- identification and mapping of migrants' routes;

- age and sex of migrants; identification of priority groups (infants, pregnant women, etc.);

- data on the epidemiological situation over the entire length of the route;

- duration (in days) and extent of each route and number of overnight stops;

- duration of the stay of migrants at the ultimate destination of each route;

- logistics and related problems encountered.

7. DISCUSSION AND CONCLUSIONS

Apart from collecting and analysing the specific data needed to delimit the different types of areas described in sections 2-6, it is also important to accumulate general information applicable to all these types of areas as follows:

(a) Identification of the most vulnerable population groups to be protected by antimalarials on a priority basis

At present malaria appears to be affecting more the older age groups as compared to what used to be the case two to three decades ago in the countries of South Asia (Pattanayak et al., 1978; Orlov et al., 1984). Adults and older children have been observed to be the most affected irrespective of the malaria species or the prevalence. The reasons for this are not clear; however, a few factors may contribute to this situation. In the first place, the quality and efficacy of the radical treatment prescribed for the different age groups may differ. Secondly, possible discrepancies in the annual blood examination rates among different age groups could also contribute to this phenomenon. However, there are strong indications that the current higher malaria incidence among the older age groups is closely associated with socioeconomic factors, such as extensive and uncontrolled population movement. Malaria incidence as related to sex also supports this view. Females, who on the whole are a less mobile group, are affected by malaria far less than males.

(b) Methods of malaria case detection

This is an important factor particularly in relation to the selection of an appropriate drug to be used for presumptive treatment by different agencies in either active or passive case detection activities.

(c) Inventory of institutions dealing with the distribution of antimalarials

Information is received on both government-sponsored institutions and community/public institutions which either deal or may deal with the distribution of antimalarials.

The different kinds of information required for the proper timing of drug application, as well as for the proper selection of the drug, drug regimen, and drug combination to be used, are indicated in Table 1.

From Table 2 it may be seen that, though the types of antimalarial treatment adopted under the present malaria control programmes in South Asia are the same as those previously used under malaria eradication programmes (presumptive treatment, radical treatment, etc.), dosages and drug regimens are worked out in accordance with the actual epidemiological situation prevailing in each stratum. The spectrum of antimalarials in use in current control programmes is apparently much broader compared to that in malaria eradication programmes. In many instances, the use of chloroquine for presumptive treatment has been replaced by that of amodiaquine, to which the development of resistance is somewhat slower. In areas with reported foci of resistant malaria, different drug combinations are widely used and not for radical treatment only. Distinctions are also made for the distribution of antimalarials through the network of different institutions.

Almost all countries in South Asia have switched over to the five-day primaquine course given along with 1200-1500 mg of chloroquine for the radical treatment of P. vivax malaria. The operational efficacy of this regimen appears to be still satisfactory, at least in India and Nepal. However, in some areas of these countries (terai belt in Nepal and

Rameshwaram island in India) the relapse rate after administration of the five-day treatment course has shown an upward trend reaching 20% in 1983-1984. However, more detailed studies are needed.

The role of primaquine in the countries of South Asia has apparently become much more important than it used to be. This drug, because of its gametocidal potency, became a necessary component not only of radical treatment of vivax malaria but also of treatment of falciparum malaria, especially in areas where P. falciparum has developed resistance to antimalarials and local malaria vectors to insecticides.

Mass drug administration at present is applied predominantly in development project areas, like road construction camps, irrigation schemes, dam construction sites, etc., and in areas where there are large groups of itinerant labourers coming from different parts of the country, or even from neighbouring countries.

Single-dose treatment is a most popular regimen, consisting of 600 mg of chloroquine (or amodiaquine) plus 30-45 mg of primaquine. Satisfactory epidemiological results were obtained with the mass administration of single-dose treatment in combination with insecticidal coverage in problem areas where residual insecticide spraying alone could not reduce malaria transmission to an appreciable level (Kondrashin et al., 1981). The use of a single-dose treatment with a sulfadoxine/pyrimethamine combination (Fansidar) and primaquine has been successfully applied in some check posts in Nepal established on the frontiers. The commendable work achieved by check posts was to some extent responsible for the prevention of local transmission of resistant P. falciparum strains in Nepal for many years. As can be seen from Table 2 pyrimethamine is never used alone in order to prevent rapid development of resistance to this drug.

Since the replacement of malaria eradication by malaria control programmes, the large-scale administration and the rational use of antimalarials, based upon epidemiological stratification of the malarious areas of South Asia, have played an important role in the containment of malaria epidemics and especially in the prevention of deaths due to malaria.

RESUME

PALUDISME : MOYENS ET APPROCHES POUR UNE STRATIFICATION
VISANT A L'UTILISATION RATIONNELLE DES ANTIPALUDIQUES
EN ASIE DU SUD

Toute stratification opérationnelle visant à l'utilisation rationnelle des antipaludiques devrait en premier lieu consister à fixer les objectifs de la pharmacothérapie et en identifier les priorités. Il convient tout particulièrement de noter à cet égard qu'il peut exister dans les pays de l'Asie du Sud des situations différentes :

a) Zones avec prévalence massive du paludisme à Plasmodium vivax :

i) Zones où la population locale est exempte de carence en glucose-6-phosphate déshydrogénase (G-6-PD);

ii) Zones où la population locale souffre, à des degrés divers, d'une carence en G-6-PD.

b) Zones avec prévalence massive du paludisme à P. falciparum :

i) Zones avec prévalence de populations de P. falciparum sensibles aux antipaludiques;

ii) Zones avec prévalence de populations de P. falciparum résistantes aux antipaludiques (degrés de résistance RI et RII);

iii) Zones avec prévalence de populations de P. falciparum résistantes aux antipaludiques (degré de résistance RIII);

iv) Zones où la population humaine est affectée par diverses hémoglobinopathies.

c) Zones avec prévalence du paludisme à P. malariae.

d) Zones avec répartition plus ou moins égale de différentes espèces de paludisme.

e) Zones à large population migrante.

Outre la réunion et l'analyse de données particulières qui doivent permettre de délimiter les différents types de zones dont il est fait mention plus haut et qui sont décrites dans le présent document, il convient également de recueillir des informations de caractère général applicables à l'ensemble de ces zones :

a) Identification des groupes de population les plus vulnérables qu'il s'agit de protéger en priorité par l'administration d'antipaludiques.

b) Méthodes de dépistage des cas de paludisme.

c) Inventaire des établissements chargés de distribuer les antipaludiques.

Avec le remplacement des programmes d'éradication du paludisme par des programmes de lutte antipaludique, l'administration massive et l'utilisation rationnelle des antipaludiques, sur la base d'une stratification épidémiologique des zones impaludées d'Asie du Sud, ont fortement contribué à endiguer les épidémies de paludisme et surtout à prévenir les décès provoqués par cette maladie.

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TABLE 1. INFORMATION NEEDED FOR PROPER TIMING OF DRUG APPLICATION AND APPROPRIATE USE OF ANTIMALARIALS

Information on:	Timing of application of antimalarial	Selection of:		
		Drugs to be used	Drug regimen	Combination of drugs
1. Most vulnerable population groups	+	+	+	+
2. Population movement	+	+	+	+
3. Relapse rate	+	+	+	+
4. Relapse seasonal pattern	+	+	+	+
5. Malaria seasonal incidence	+	+	-	+
6. Prevalence of G-6-PD deficiency	-	+	+	+
7. Resistance to antimalarials	-	+	+	+
8. History of antimalarials used	-	+	+	+
9. Population immune status	-	+	+	-
10. Methods of case detection	-	+	-	+
11. Institutions for distribution of antimalarials	-	+	-	+
12. Distribution of P. vivax with short and long incubation periods	+	-	-	-
13. Spatial distribution of malaria	+	-	-	-
14. Abnormal haemoglobins	-	-	+	-

TABLE 2. THE USE OF ANTIMALARIALS IN DIFFERENT TYPES OF AREAS IN SOUTH ASIA (1985)

Treatment	Type of area							
	1		2			3	4	5
	A	B	A	B	C			
Presumptive by ACD PCD DDC FTD	600 mg chloroquine	600 mg chloroquine	600 mg chloroquine	600 mg amodiaquine		As in 1	As in 1 and 2	1000 mg sulfadoxine/pyrimethamine + 45 mg primaquine; 600 mg amodiaquine or chloroquine
Radical	1200-1500 mg chloroquine + 75 mg primaquine (5 days)	1500 mg chloroquine + 30 mg primaquine (once x 8 weeks)	1500 mg chloroquine + 45 mg primaquine	1000-1500 mg sulfadoxine/pyrimethamine + 45 mg primaquine or 1500 mg sulfalene/pyrimethamine + 45 mg primaquine		As in 1	As in 1 and 2	1500 mg chloroquine + 75 mg primaquine (five days) or sulfadoxine/pyrimethamine or sulfalene/pyrimethamine + 45 mg primaquine
Suppressive	-	-	-	-	-	-	-	300 mg amodiaquine once a week
Mass drug administration	600 mg chloroquine + 45 mg primaquine	600 mg chloroquine	600 mg amodiaquine + 45 mg primaquine					600 mg chloroquine + 45 mg primaquine

Type of area

1 = Area with an overwhelming prevalence of *P. vivax* malaria:

A = Local population is free of G-6-PD deficiency
B = Local population is affected by different levels of G-6-PD deficiency

2 = Area with an overwhelming prevalence of *P. falciparum* malaria:

A = *P. falciparum* sensitive to antimalarials
B = *P. falciparum* resistant at RI and RII levels
C = *P. falciparum* resistant at RIII level

3 = Area with a prevalence of *P. malariae* malaria

4 = Area with a more or less equal distribution of different malaria species

5 = Area with a large migrant population

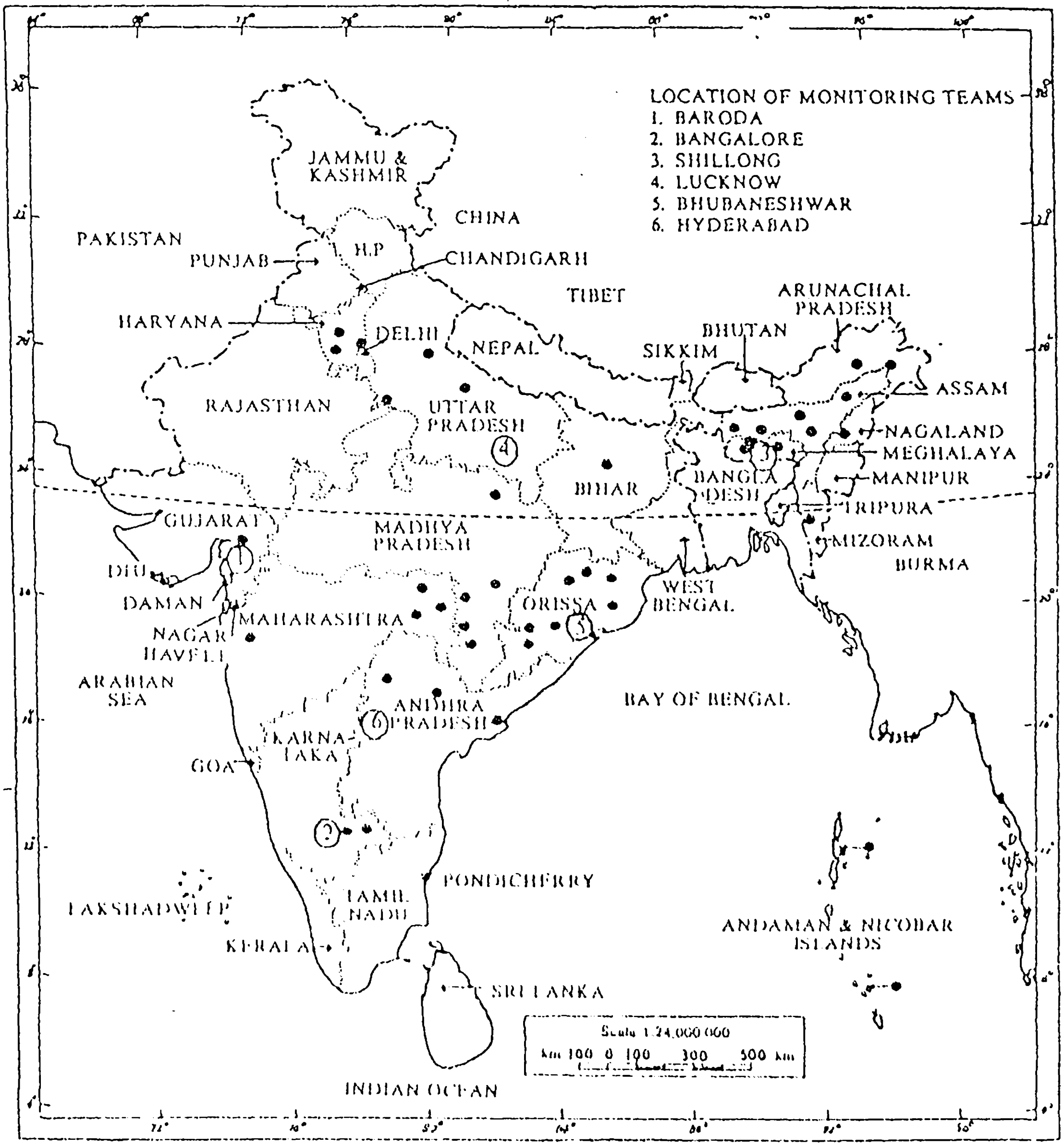
ACD = Active case detection

PCD = Passive case detection

DDC = Drug distribution centres

FTD = Fever treatment depots

FIG. 1. AREAS SHOWING P. FALCIPARUM RESISTANCE TO CHLOROQUINE IN INDIA



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