# "THE UTILIZATION OF CHLOROQUINE CHEMOPROPHYLAXIS AMONG PREGNANT WOMEN ATTENDING MWANANYAMALA ANTENATAL CLINIC IN DAR ES SALAAM"

BY

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## DECLARATION

I declare that this dissertation has never been submitted for a diploma or a degree in any other University.

DATES 6th July, 1984 NAME ..........

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ABSTRACT

This study has been prompted by the recent appearance of severe malaria among children and pregnant women, which is a problem of public health concern in Tanzania. In this study the pattern of utilization of chloroquine chemoprophylaxis by pregnant women of Mwananyamala MCH Unit of the Hospital shows that out of 250 women interviewed, 49 (19.6%) of the women attending antenatal clinic have malaria parasitaemia and 13 (5.2%) only excreted chloroquine in urine samples taken, although 146 claimed regular weekly prophylaxis. Younger women with smaller families had highest occurence of parasitaemia. Those who were relatively older and had bigger families had relatively higher negative blood smears for malaria parasites. Personal protection mechanism had no significant role in breaking transmission. The itch after taking chloroquine was reported by 55 (22%) of these women suggesting its negative role among other sociological reasons for not using chloroquine.

This study points out the ineffectiveness of the present malaria chemoprophylaxis programme as seen in one MCH Clinic. Health education both to individuals and groups needs to be increased and improved, in order to convience the patients and their families of the importance and necessity of suppression of malaria in pregnancy.

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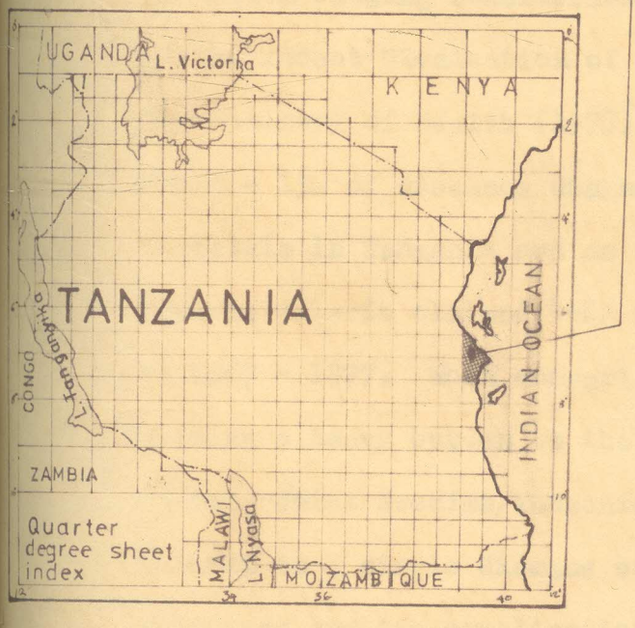
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## REFERENCE

- Main roads
- Other roads
- Motorable trucks
- Foot paths
- Former City boundary
- Tidal or seasonal swamps
- Rivers and lakes / seasonal lakes.
- Dar es salaam area on which the above magnified area is located
- △ MCH Clinic & Hospital

# CHAPTER I

## INTRODUCTION

Malaria has been the most prevalent infection of man since ancient times. Efforts by man against malaria have been taking place all the time, but the most intense and organised fight was intiated in the early 1950's when the World Health Organisation endorsed the concept of malaria eradiction. Introduction of residual insecticides and the use of chemotherapy with chloroquine as the mainstay strategy in malaria eradication brought about as dramatic disappearence of malaria in North America and Europe However, in the tropics especially Sub-Saharan Africa, the malaria situation is much the same and there are no prospects of overcoming this in the near future.

In Tanzania, malaria is probably the most widespread infection causing considerable morbidity and mortality. In the recent "Evaluation of the Health Sector" report of the Ministry of Health (1978), malaria was responsible for 9 - 13% of diseases diagnosed in out patient in Hospitals in Tanzania and as a cause of hospital deaths, malaria claimed 4-8% in the ten-year period of 1967 - 1977. When comparison of the top ten conditions causing a heavy burden to the health sector were made in the recent "Joint Swedish/Tanzania Health Sector Review (1982)" malaria as a single disease entity ranked second to pregnancy and its complications.

The distribution of malaria in all regions of Tanzania has been described with an intensity of hyperendemic to holoendemic in about 2/3 of the country Kihamia (1983). In a recent report, the epidemiology of malaria has been observed to by chnging, with high numbers of cases being observed for the first time in the high altitude areas of Iringa, Arusha, Tanga and Kilimanjaro where they have not been seen before, (Dahoma 1983)

The disease vectors commonly found in Tanzania are the Anopheles gambiae and Anopheles funestus, both of which are well known for their rapidity of reproduction especially after the rains when hot humid conditions are favourable, and their efficiency in malaria transmission as well as their longevity in life span.

All four human species of malaria parsites occur in Tanzania but prodiminantly P. falciparum (90%) while P. malariae is found in (10 - 20%) of infections, while P. vivax and ovale shae the 5%. Although transimission occurs in most areas of the country throughout the year, the highest intensity is seen following the rainy seasons and it is influenced by humidity and tempprature with the low lying costal areas having the heaviest occurence of the disease.

The brunt of the morbidity and mortality in endemic areas is born by the non-immunes particularly children after 1-6 months of life with waning maternal antibodies. During the first five years of life prevalence is very high, in the region of 70 to 80% and this continues to diminish in the age-group who survive, and by the age of 16 years, with constant building up of immunity, the prevalence is about 25%. It is estimated that 10 - 15% of all childhood mortality during the first five years in malaria endemic areas is due directly to malaria and the same situation obtains in Tanzania, (Clyde 1967).

During pregnancy, women are particularly exposed to the risk of acute malaria attacks. The prevalence and intensity as well as the frequency of their occurance are increased by 4 to 12 times that of their non-pregnant women counter part. This risk is high not only to the non-immune entering endemic areas but even the residents of endemic area. The malaria hazard during pregnancy is particularly serious during the second trimester (24 weeks). Bray & Anderson (1979), confirmed that in Gambia prevalence and ensity was greater in pregnant than in on pregnant women and that the primiparas pregnant women were proportionately more usceptible to malaria than multiparous women.

The increased risks of malaria in pregnancy has a multifactorial causation. The pregnancy state appears to reduce the immune status of the host therefore making her own malaria worse (McGregor, 1972), and (Playfair 1982). Malaria alters the immune reactivity with evidence of depression of antibody formation as well as suppression of cell-mediated immunity. (Weidang 1982). The presence of the placenta probably offers increased opportunity for infected erythrocytes to sequestrate in fairly dense numbers a process which allows the development of erythrocytic schizogonic stages which exposes the host to the risk of releasing large numbers of erythrocytic merozoites into the circulation and the attendant risk of acute malaria attacks within relatively short periods. When all this is taking place, a peripheral blood smear for malaria may give a misleading picture of the true state of parasitaemia in a pregnant woman.

The adverse effects caused by malaria to the pregnant woman and her foetus have been documented by many authors. Among the effects, malaria hyperpyrexia in the pregnant mother could be fatal in a relatively short period but commonly leads to abortions if appropriate treatment is not instituted. Sometimes, the use of quinine is called for in serious cases, (personal observation), but in addition, full supportive treatment is essential (Bruce-Chwatt 1983).

In the tropics severe iron deficiency anaemia is a frequent occurence. This is in part due to malaria infection although other parasitic and helminthic infestations also cause deficiency of iron and folic acid The anaemia in malaria is due to haemolysis. The rapidity with which haemolytic anaemia occurs depends on the density of infection and the rate of destruction of infected erythrocytes by the reticuloendothelial system. However it has been observed in recent studies that immune destruction of non-parasitized sensitized erythrocytes also takes place, (Weatherall and Abdallah 1982).

Recent studies of women admited in the antinetal ward of Muhimbili Medical Centre, Dar es Salaam show that 95% of these women are anaemic, (Ngvale, 1984 personal communication). Similarly studies on P. falciparum antibodies among women hospitalized in the same ward for various causes using the Indirect Haemaoglutination technique (Gill and Mtimavalye 1983) demonstrated significant antibody levels among the anaemic women and those with malaria parasitaemia. These findings confirm that haemolytic anaemia resulting from malaria infection is a common cause of morbidity as well as folate and iron defic y among mothers during pregnancy. Depressed erythropoiesis was reported by (Weatherall 1982) as another contributing cause of anaemia in pregnant women with P. falciparum infection.

Additional complications of malaria infection are cerebral malaria which causes profound central nervous system disturbance and may terminate in death, disturbed fluid and electrolyte balance, release of toxic substances into the circulation either due to the disease process or the use of drugs in the process of treatment and onset of acute glomerulonerhritis or cardiac failure.

The frequently reported feetal morbidity and mertality in malaria endemic areas occur through abortions in early gestation, prematurity or still births in late pregnancy or reduced survival opportunity for neonates who are low birth weight. Heavy placental infiltration with P. falciparum in endemic tropical areas has been shown by Mc Gregor et al (1983) in the Gambia, and that the consequences of this infiltration is disrupted transplacental transport of both antibodies and nutrients. This complex pathology probably explains well the high frequency of low birth weight babies (below 2500 gm, WHO 1965) so common in malaria endemic areas and reported by many prominent scientists among them Bruce-Chwatt (1952) Jellife (1983) and Kortmann (1972). They have thus advocated the use of chemossuppression through out pregnancy to reduce morbidity and mortality.. Gilles et al (1969) has shown that protecting pregnant women from malaria with regular chomssuppression has a tremendaous improvement of birth weight. Similarly in countries where malaria eradication programmes have succeeded these

birth weights also increased tremendously (McGregor & Avery 1974).

The launching of the malaria protection programme through MCH described by Tarime & Chagula (1974) is an important milestone in the history of the nation, in its efforts to reduce the morbidity and mortality of this vulnerable group.

Chloroquine in small doses of 5 mg/kg freely distributed to the vulnerable population utilising MCH facilities in malaria endemic areas in Tanzania has recently been questioned as to its effectiveness in the wake of developing resistance by P. falciparum in E. Africa and largely reported among non-immune visitors (Campbell et al 1973). This is no cause for hasty action to stop its use in our programme for in the words of an eminent malariologist, chloroquine and amodioquine seem to be the best and least harmful drugs for protecting pregnant women, even in areas with some resistance, (Bruce Chwatt 1983). The regular administration of frequent small dosses in a symptomatic residents of endemic areas offers the possibility of body defence mechanisms to eliminate light infection and prevent the possibility of parasitaemia to build up to cause clinical disease.

RATIONALE OF THE STUDY

Although possible resistance of the local strain of plasmodium has been reported, mapping up of the spread of this resistance in the mainland has not been possible to date. Recent findings of the resistant strain of P. falciparum to chloroquine and the possibility of this spreading to the mainland is a reality to be reconed with (Schwartz et al 1983). But the introduction of this resistant strain to the mainland from the neighbouring countries or elsewhere will only have a dilution effect to the local strain of plasmodium and will take some time to be established. This serves as a reminder to be more practical in our evaluation of the programme and identifying the areas where changes are necessary to be made according to the identified needs.

Given the situation where malaria is a major public health problem in Tanzania, particularly among the under fives and pregnant mothers, the approach by Ministry of Health to contain the situation by instituting regular malaria chemosuppression in this population group, ie. regular weekly chloroquine administration is justifiable and more practicable in the absence of other feasible and effective control measures.

The free weekly administration for chloroquine 300 mg base to all pregnant women attending ante-natal care in our health unite and appropriate doses for the under five children has in theory been acclaimed to be routinely given to them. However, no systematic evaluation of the extent to which this has been achieved in practice has been assessed in Tanzania, the results of which would enable the Ministry of Health and the programme planners to have a clear picture of how much the routine chloroquine chemoprophylaxis to underfives and even pregnant mothers has been helpful in reducing the morbidity and mortality of these two vulnerable groups.

## CHAPTER 2

## REVIEW OF LITERATURE

### THE EPIDEMIOLOGY OF MALARIA MORBIDITY & MORTALITY

The epidemiological variable governing malaria morbidity and mortality in any country include measures aimed at the control of the enviroment, men to vector and the parasite. But measures on the control of the enviroment, man and the vector have proven to be problematic, unrealistic and too expensive particulalry in the developing countries.

Hence the measures against parasite are the only remaining alternative, despite the very minimal role this contributes to the whole malaria control programme in any country.

For any antimalaria measures therefore, the reduction in mortality due to malaria remains an ultimate common target, and in this case, reliance will be placed on the antimalarial drugs that are effective under local conditions. For Africa the commonly used approach in malaria control is the administration of curative doses of an effective schizontocidal drug, mostly the 4 - amino quinolines. Even this approach may be too difficult to implement in which case reduction and prevention of mortality and morbidity by giving special attention to

reducing morbidity in high-risk groups has become essential. The aim here is not only to provide effective antimalarial drugs in different quantities for the early treatment of acute malaria cases, but also to pay special attention to certain vulnerable groups such as infants and children below the age of 5 years, nursing and pregnant mothers after the fifth month of pregnancy, the labour force working on high priority economic development projects, school age children or unit of the armed forces. The overall achievements of a successful programme will have resulted in the reduction in frequency of acute malaria attacks in improved growth curves in children, reduction in the frequency of abortions and stillbirths, reduction in school absenties and improved scholastic performance and improved work out by adults. Provided the tablets are taken regularly, morbidity and mortality should decrease greatly in the protected population but the effects on the prevalance and transmission of the desease is likely to be minimal.

## IMMUNOLOGY OF MALARIA

Malaria generally and particularly P. falciparum infection is extremely hazardous during pregnancy due to depressed immunity, a result of pregnancy status, Mc Gregor (1972). The immune reactivity of pregnant women has shown to be altered, (Playfair 1982), (Weidanz 1982), but the point of concealation in highly endemic malarious areas is that semi-immune adults usually have a substantial acquired resistance to local strains of the plasmodia. Despite the high degree of acquired immunity in local residents, malaria prevelance, severity and frequency of clinical attacks during pregnancy is quite substantial especially during the second timester with the greater burden being experienced by priminarous women, (Bruce, Chwatt 1983, McGregor 1972 and Playfair 1982).

Malaria infection during pregnancy, notably P. falciparum infection, causes heavy placental parasitemia leading to primaturity, (Archibald 1956). In south East Nigeria, it occurs at the rate of 2% of all Births, while in West Nigeria, (Spitz 1959) recorded 9% the later finding being similar to that shown by (McGregor et al) (1983) in the Gambia where the tendency t prematurity was higher among first born infants than subsequent deliveries. Malaria immunity is not destroyed by administration of chemosuppression whose aim is to reduce foetal and maternal morbidity and mortality.

Sera of persons exposed to frequent repeated malaria infections demonstrated antibodies of erythrocytic components. (Mayer and Weilberger 1946). Complement fixing antibodies to red cell stroma have been found in sera of cases of P. vivax malaria infection. (Ademiyi & Jones 1967) showed that macroglobulin agglutinins increased in the sera of Nigerians with age using tanned sheep red cells, suggesting that there was an astiological relationship with malaria.

(Bray & Anderson 1979) in a study of 1000 pregnant and 1000 non-pregnant women in the Gambia, established that pregnancy caused ana increase in prevalence and density of P. falciparum. The increase was at its height early in the second trimester with malaria prevalance and density decreasing over the second half of pregnancy.

(Anderson 1979), did find a slightly lower values of antimalaria IgG, by immunofluorescence during the second trimester compared to the third trimester. Bray and Anderson (1979) also found that malaria apparently inhibited the passage of maternal antimalaria IgG, across the placenta to the foetus thus providing less protection to infants during the first months of life.

The natural development of acquired immunity to human malaria infections is a very slow process. Generally, the only individuals to show a strong resistance to infection are those resident in regions highly endemic of malaria and have been infected regularly for many years, their immunity is maintained because the bites of infected mosquitoes provide further and frequent antigenic stimulation. In such an area, new born babies are passively protected but only during the initial 4 to 6 months of life. There after malaria is predominantly a disease of children particularly during the first five years.

Malaria therefore is implicated since malaria treatment leads to rapid resolution of the anaemia. (Hamilton et al 1966) showed that pregnant women with tropical splenomegaly syndrome which is also thought to have an immunological nature are particularly likely to undergo severe haemolytic episodes.

The mechanisms involved in the loss of immunity to P. falciparum malaria during pregnancy are not clearly understood. The remarkable features of P. falciparum intense placental accumulation with all the asexual stages of development taking place are that schizonts are found there as well as trophozoites.

These high placental parasite smears are not reflected in peripheral blood smeaks of the mothers. The well known fact that P. falciparum schizogony development stages take place in deep organ capillaries rather than in the peripheral blood but the degree of parasitization of the placenta is greatly in excess of that resulting from the normal released from the peripheral blood of schizogony.

Because of lessened immunity during pregnancy, protection of the immune and non-immune with chemosuppression drugs throughout pregnancy and six weeks postpartum is essential in endemic areas, (Barnes 1980). Gammaglobulin transport protect neonatal malaria in semi-immune mothers. Plasmodium Falciparum occasionally passes through damaged placenta to the neonate causing neonatal malaria particularly in non-immunes (Body 1949).

## MALARIA AND THE OUTCOME OF PREGNANCY

Most of the researchers agreed that malaria and infected placentas were most common in primigravidae and that the prevalence of malaria and infected placentas decreased with succeeding pregnancies, (Gilles et al 1969 & McGregor 1978). Although effective immunity to malaria is slowly acquired and prevalance and density of malaria continues to drop with increased age, the common malaria infections seem in primigravidae as reported in tropical Africa have been attributed to the tender age of first pregnancies, which is about 15 years.

Spits (1959) in Nigeria found that among 136 single deliveries from placenta - infected mothers, 41 o/o weighed less than 2500 gm while 440 deliveries of mothers who had no placental infection with malaria, showed 27 o/o of their babies weighed less than 2500 gm. The average weight on the first group was 2851 gm and in the second group it was 2010 gm. The differences was strongly apparent in later parities.

In a prospective study involving 60 mulliparous women (Gilles 1969) found out the frequency and density of P. falciparum malaria infection was higher during pregnancy and that 63 o/o of pregnant women becameaanaemic. The anaemia developed between 16 and 24 weeks of pregnancy and was haemolytic in nature. Anaemia on the other hand was absent in the group which had been receiving malaria protection. The author concludes that "the single most important antenatal medical procedure on a country where malaria is endemic is the administration of anti malaria drugs prophylactically throughout pregnancy.

The effects on pregnancy are hyperpyrexia, abortion and in advanced gestation, intrauterine foetal death or neonatal loss. Destruction of parasitized erythrocytes become antigemic stimulants of normal cells as auto antibodies develope causing severe anaemia of haemolytic type, of which P. falciparum is notorious, high turnover of red cells may lead to folate deficiency causing megaloblastic anaemia, semi-immune individuals develope recurent parasitaemia.

In P. falciparum infections accumulation of parasites in the placenta is a frequent accurence in which blocking of intervilleous spaces may occur with macrophages and parasites delaying or blocking maternal circulation. This delay in intervilleous spaces may lead to foetal retardation and ante and intrapartum anoxia with resultant perinatal loss.

Protenuria is a common accurence. Cerebral malaria may develop with convulssion and coma which may terminate in death. Cerebral malaria may also cause eclampsia and this is a common occurence among semi-immunes in malaria endemic areas.

Morbidity due to Plasmodium falciparum infection is particularly high during this period in life, being estimated to vary between 10-15 o/o of causes of death in under five years old children.

Acquisition of resistance in those children who survive gradually takes place, showing first as clinical immunity in which the frequency of symptoms subside and later the levels of parasite fall though rarely to zero.

In areas where transimission is less intense, an effective level of resistance is not obtained, equally chemotherapy or a relatively short period away from the endemic area, results in the loss of acquired immunity (Bruce-Chwatt 1980).

## MALARIA IN PREGNANT IN AFRICA

In a series of investigations carried out in the vicinity of Lagos, the men incidence of malaria parasitaemia (mainly P. falciparum) from a sample of 23 323 African parturient women, 33 o/o of these women had higher than the normal women population parasitaemia placental infection was 23.8 o/o and none of the 323 children born developed, congenital malaria. The mean birth weight of 237 babies of mothers with non-placental infected cases was 145 gm higher than that of 73 babies born of mothers whose placentas

were found to be infected. There was a statistically significant difference between the two groups despite the different group sizes. Neonatal mortality had no relationship with placental infection.

In a survey anaemia among pregnant Zambian women, Van Dongen (1983) found out that anaemia was a frequent feature among 424 women being given antenatal care, and that anaemia was more common in those with malaria than those without malaria during pregnancy. Anaemia was also found to be more frequent and more severe in primigravidae than multigravidae.

Gilles et al (1969) showed that the onset of haemolytic anaemia occured during the period of 16 - 24 weeks of pregnancy in Nigerian women and that this could be prevented by regular chemoprophylaxis using pyrimethamine weekly. The anaemia was not comensurate with recorded density of parasitaemia in patients. Sometimes demonstration of decrease in PCV occured before onset of parasitaemia and the haemolytic process continued for 2 weeks of parasite elimination.

Jellife (1968) in Kampala observed that among 570 parturient African women, 5.6% had a positive blood slide for malaria 16.1% had placental infection with P. falciparum and only 1% cases of congenital malaria was seen.

The average birth weight of 92 babies was 263 gm less than that of 478 babies of non-infected women which was significant at P. o.ool level. The younger mothers mostly primiparous women had 21.7% parasitaemia with a higher frequency of infected placental compared to 14.7% of the multiparous women. This suggest that routine chloroquine chemosuppression is essential among endemic malarious areas during pregnancy.

Herd & Jordan in Zimbabwe (1981) reporting on the adverse effects of heavy placental infection with P. falciparum noted that acute renal failure which mimics E.P.H. Gestosis cerebral malaria, severe anaemia are among conditions which pregnant women are exposed to the hazards of and this poor state of health renders these women incapable to face the realities of the stresses of pregnancy. The incidence of congenital malaria among the endemic areas is less than 0.1%.

## MALARIA AND EFFECTS ON PREGNANT MOTHERS IN TANZANIA

In a recent report in which anaemic hypertensive and healthy pregnant women were investigated for P. falciparum malaria antibodies using I.H.A. technique Gill & Mtimavalye (1983) in Dar es Salaam showed that the highest titres were found among pregnant anaemia women with a rate of 92.1% while hypertensive women had rate of 86.8% and health pregnant women recorded a rate of 81.2%

In this study it was concluded that pregnant anaemic women had a significantly high P. falciparum antibodies at (P 0.0 1) with titres of 1:2560 and above in comparison to healthy pregnant women who had significant low antibody levels with (P 0.001). Malaria therefore contributes to anemia in pregnancy in endemic areas although the extent of severity in causing anaemia and folate defficiency is unknown.

In a recent MCH evaluation programme (1982) 45% of the mothers interviewed stated that they had their last confinements/deliveries in a health institution. The reasons given by some mothers for not delivering at a health institution included among others, long distances to health institutions (25%), abrupt onset of labour (39%) and lack of transport (8%).

In analysing the causes of childhood mortality, MCH evaluation programme (1982) found that the top 5 childhood killers were, Measles (14.6%) of all deaths, Malaria (7.6%) convulsions (5.1%) malnutrition (2.2%) and anaemias (1.7%). Although convulsion has been reported separetely as a cause of childhood death most convulsions seen are due to fever and most fevers are probably due to malaria in the malaria endemic tropical areas. Similarly, the anaemia is probably

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brought about by malaria. Because of the complexicity with which malaria interact in the community and the silent way in which the mortality occurs, often picking on the innocent juniour members of the community, the true impact of the malaria problem is not seriously appreciated. From the analysis of the MCH evaluation report (1982) malaria mortality in under fives in Tanzania is probably in the region of 15 o/o.

The health facilities within Tanzania were analysed in the (1978) Ministry of Health evaluation report. The Regions found to be relatively poorly served were, Coast Singida, Tabora, Rukwa and Shinyanga, in which just over 50 o/o of the villages were beyond 5 km of a health unit. Kilimanjaro was reported better off with only 10 o/o of their villages beyond the 5 km. distance. The 1973/74 villagisation programme, reduced markedly the disparity of health facilities distribution within the country, by no means 100 o/o but this has offered opportunity for more sensitive and accessible planning of distribution of health units in future.

The MCH goals is to achieve a covarage of 90 o/o immunization against the 6 common diseases in the vulnerable population, 80 o/o ante natal attendance was

reported in the 1982/83 Health statistics. However, only 70% of the under-fives attended and among these only 35% get fully immunized.

When awareness of the standard activities offered in the MCH programme was analysed, personnel in the primary health care facilities gave malaria chemoprophylaxis a low profile with only 32% the District MCH co-ordinators being aware of malaria protection being a standard service while only 40% of the District Medical Officers answered correctly. The level of awareness has a reflection on the performance in actual day to day practice and calls for the need to improve the situation.

Barnes (1980) suggested that non-immune pregnant women entering malaria endemic areas should be protected with chloroquine 300 mg. weekly or pyrimethamine 25 mg per week. The use of quinine (though not suitable as a suppresant) was suggested in the absence of other drugs giving a dose of 600 mg daily, but this use should best be avoided during the first trimester. Similarly protection of semi immune pregnant women resident in malaria endemic areas, is essential since their immunity breaks down with the stress of pregnancy. Dormant exo-erythrocytic infection may relapse especially in primiparous women who have overt parasitaemia developing typical hyperpyrexia and rigors.

Kortmann (1972) in N.E. Tanzania reported an increased infection and density of pregnant women with P. falciparum malaria, that those who complied with regular chemosuppression chloroquine intake completely cleared of the parasites and those who did not, had both the parasites, and their neonates were significantly under weight in compasison to those mothers who were not infected.

MALARIA CHEMOSUPPRESSION

Nigerian pregnant women were reported effectively protected by pyrimethamine given every two weeks or regularly every four weeks in holoendemic areas Manson Bahr & Apted (1982). They suggested that those pregnant women under protection should be treated with chloroquine or other schizontocides in the event of developing a fever.

Commenting on the administration of Fansidar to pregnant women Manson Bhhr and Apted (1983) condier consider that this drugs has no ill effects in pregnancy or on the human foetus, except that it should not be given in late pregnancy. However, fansidar was considered inappropriate for prolonged prophylactic use because of side effects brought about by deposition in tissues. Maloprim and fansidar were considered suitable for children in the dosage of 25 o/o of the adult dose for those

under one year and 75% of the adult dose for those over 12 years old.

Woodruff (1974) reviewed malaria in pregnancy and showed that P. falciparum infection may cause abortion during any stage and lead to premature delivery. He noted that in holoendemic areas, pregnant women in a advanced stages of their pregnancy may loose their immunity and suffer from severe attacks of malaria, sometimes fatal if untreated. A similar observation, was development of severe anaemia among pregnant women in advanced stage, associated with folate and iron deficiency as well as haemolytic type. When those anaemic women go into labour, any considerable blood loss exacerbates the condition and death is a frequent occurence. In addition organomegally (Spleen and liver) associated with these complications, may obstruct uterine expansion and lead to abortion or difficult labour. Higher still births are seen frequently with P. falciparum infectio n.

## CHAPTER III

### BROAD OBJECTIVES

The studies on malaria situation in Tanzania have clearly shown that both the morbidity and mortality rates are on the increase. Owing to the fact that pregnant women and underfive children are routinely given chloroquine for malaria chemoprophylaxis, one would expect considerably less morbidity and mortality rates in these two groups. However, only a few such studies have been documented in Tanzania so far. It is the purpose of this study, therefore to attempt to find out the chloroquine chemoprophylaxis utilisation pattern, the malaria parasitaemia rate and other problems that are inherent with the implementation of this programme in a group of pregnant women attending one of the regular MCH clinics in the city of Dar es Salaam.

SPECIFIC OBJCTIVES

1. To determine the proportion of women who have chloroquine in their urine using Mayer-Tanret test.

2. To determine their socio-economic characteristics and their pregnancy history.

3. To determine their husband and family characteristics.

4. To determine the mosquito preventive measures used at home

5. To determine the frequency of side effects as they relate to chloroquine use.

## CHAPTER IV

### METHODOLOGY

Area of study: The study was carried out at Mwananyamala MCH clinic located about 6 km. to the North of Dar es Salaam City centre in Kinondoni District. This area is accessible by bus and cars via Mwanayamala road which originates from Morocco road connecting the two major roads of Morogoro and Bagamoyo.

The place is highly populated by residents of low income and middle income occupations in and arround Dar es Salaam. The housing consists of mainly traditional six-roomed concrete structures shared by several families with common service facilties in the back yard.

The topography consists of clay subsoil lying on unevenly distributed coral which accommodates numerous water collection sites during the rainy season, and the water table is high. This fits in with a description of a marshy area in which famous permanent water bodies exist i.e. Lake Tandale, Lake Mwananyamala and Lake Magomeni the drainage is poorly achieved through one ill-maintained furrow which leads water towards Msimbazi creek into the Indian Ocean.

The basic health infrastructures of the area is undeveloped to maintain adequate sanitation for the dense population. Slackening of vector control activities during the past decade of hadships has enable the Anopheleines to multiply from the numerous breeding sites as well as swelling up of the numbers of nuisance mosquitoes which breed in pit latrines. Transmission of malaria and filariasis must of necessity be taking place intensely. Appended is a map showing the main features and unfortunately showing the old city boundary which has now been extended to beyond 16 miles of the city centre.

Target population and sampling method:

The target population was all pregnant mothers attending ante-natal clinic at Mwanamyamala hospitals an area with a total population of 44,614 (23,262 males and 21352 females). Taking the crude birth rate to be 50 per thousand, the clinic would expect to have at least 22307 deliveries per year, (1978 population census). But since it has been shown that only 46% attend MCH service at least 8923 attendances per year, were expected to be seen every year. A total 250 women were seen

which is about 2.8% of the total ante-natal clinic attenders in Kwamanyamala.

After getting clearance from CCM and Government leaders including the City MOH and DMO Kinondoni District to conduct the survey in October 1983, the preliminary Survey was carried out. In November 1983, the actual survey was carried out by the author, public health nurse and a competent laboratory technician. The method of selection into the survey was based on first come first seen basis of the pregnant mothers attending ante-natal clinic at Kwamanyamala hospital on ten consecutive clinic consultation days.

SURVEY AND INTERVIEW

A questionnaire was specifically designed for the present study, a copy of which is presented in the Appendix. Each respondent was interviewed individually. After the interview every woman was asked to give a sample of her urine in a universal bottle which was provided to her. A thick blood smear for examination of malaria parasites was also taken from every woman.

Blood smears: The fourth finger was prepared according to the standard procedure before pricking it with sterilamet. To obtain a thick film the ensuing drop of blood was touched with a clean glass slide held above it and then after reversing the slide, spread the blood evenly with a corner of another slide to make a urinear patch of moderate thickness, which was then allowed to dry horizontally in air.

LABORATORY PROCEDURE

The Mayer-Tanret test and the staining of the blood slides for examination to determine the presense of malaria parasites was done in a well aquipped parasitology laberatory and the work was done by the author and the qualified technician who both examined every specimen of urine and blood slide for consistency and better agreement on positivity or negativity of a test.

At the end of each working session the slides were packed in the appropriate glass slide boxes and transfered to the University laboratory Giemsa staining. The stock solution of Giesma was prepared by using the following ingredients:-

Giemsa powder 3.8 g

Glycerol, pure 250 ml

Methyl alcohol - pure 250 ml

Alcohol and glycerol were mixed together before gradually adding small quantities of the powder in a mortar and grinding until dissolved. The prepared stock solution was then filtered and kept in a brown bottle with a close fitting ground glass stopper.

Staining of thick films using Giemsa stain:

The staining solution was prepared by diluting 7mls of the stock solution of Giemsa to 100 ml using distilled water. Dilute stain ws poured on the horizontally placed blood films suspended on a staining rack over a water sink and allowed to stain for 30 minutes, before being gently flushed with tap water.

These were then positioned upright to dry.

Examination of blood films:

The thick films were examined under high power microscope fields enumerating malaria parasites against 200 leucocytes, the result multiplied by 40 and expressed as parasites per $mm^3$. These slide were also examined by an experienced technician to ascertain correctness.

(III) 2. Urine testing for chloroquine

Preparation of the Mayer-Tamret reagent

Mercuric chloride ($HgCl_2$) 6.75g

Potassium iodide ((KI) 25.0g

Distilled water 500mg

The mercuric chloride was dissolved in 375 ml of water and the Potassium iodide in 100 ml. The first solution was then poured into the second solution while shaking and made up to 500 ml.

A few drops of this ragent were added to 5 ml of cold urine in a test tube. The urine specimens were actually stored in the labortory refrigerator after the morning session and examined in the afternoon of the same day.

The ppearence of a white turbidity that cleared or heating but reappered on cooling was the criterion of chloroquine positive specimen. A few specimens whose tubidity increased on heating, were boiled than filtered cooled in a refrigerator before adding the Mayer Tamret reagent.

NB: The test is positive within 12 hours after administering a single dose of 600 mg chloroquine base orally and remains so in most subjects for 5 - 6 days.

It measures urine content of 0.1 to 1.0 mg chloroquine. Other drugs that may give false positive reaction are quinine primquine, codeine, ephedrine and pethedine.

QUALITY CONTROL OF THE MAYER-TAMRET REAGENT

Urine from six volunteers was obtained to check the presence of chloroquine using the prepared Mayer-Tamret reagent.

The results of urine samples on day 0 were all negative These volunteers were then given the same Resochin Bayer used at the MCH Clinic, a dosage of 5mg/kg taken orally and from then on urine samples were collected daily for chloroquine excretion.

TABLE I

THE RATE OF CHLOROQUINE CLEARANCE IN URINE SAMPLES OF THE CONTROLS USING MAYER - TANRET TEST

| DAY | CHLOROQUINE 5 mg/Kg | CHLOROQUINE POSITIVITY IN URINE |
|---|---|---|
| 0 | Urine produced before giving Cq 5 mg/Kg | All 6 urine samples were negative for chloroquine |
| 1 | | 6 + ve |
| 2 | | 6 + ve |
| 3 | | 6 + ve |
| 4 | | 6 + ve |
| 5 | | 6 + ve |
| 6 | | 4 + ve |
| 7 | | 3 + ve |
| 8 | | 0 + ve |

Despite the small dose of chloroquine given the test produced results within the expected documented range

(2) The Mayer - Tanrest test procedure and blood-slide examination for malaria parasites were rather expensive tests. Hence the smallness of survey's sample, although a bigger one would have been more desireble.

(3) Because of funds constraints, time Limit and transportation problem, the need to conduct the survey in as short a time as possible was necessary and hence the employment of extra staff in the conduction of the survey.

## CHAPTER V

### RESULTS

Two hundred and fifty pregnant women interviewed. Blood slides for malaria parasite examination and urine samples for chloroquine excretion examination were obtained from all. Out of 250. only 49 women (19.6%) had positive blood slides for asexual parasitaemia.

2 (0.8%) had microfilaria bancrofti. The urine samples examined showed that out of 250, only 13 (5.2%) were positive using Mayer-Tanret reagent, and only two of the chloroquine excretors had positive blood slide for malaria.

Table 2 presents the age, education, family income and pregnancy history of women. It shows that there is a positive relationship between having malaria in pregnancy with age, a relatively better education, fewer number of pregnancies as well as fewer number of surviving children. Those who have malaria are younger, have higher education, fewer number of pregnancies and fewer number of surviving children.

Table 3(a) presents the relationship between husband and family characteristics and malaria parasitaemia. It shows that the burden of malaria parasitaemia was born by those with smaller families who had in turn a lower record of reported fevers. Table 3 (b) presents the relationship between reported chloroquine use, hospital visit and malaria parasitaemia. It shows that the malaria parasitaemia was higher in those with less than five weeks of chloroquine chemoprophylaxis and these had, a five fold mean

record of reported hospital visits.

Table 4 presents the relationship between mosquito preventive measures used at home and malaria status. It shows that the various mosquito preventive measures used at home had no impact on the malaria parasitaemia status of respondents.

Table 5 presents the perceived side effects of chloroquine use and malaria status. It shows that the malaria parasitaemia status had some relationship with the number of reported fevers and previous history of itchiness associated with chloroquine use. It was found that there were statistically significant differences between women with and without malaria with regard to fever, dizziness, and skin itchiness.

TABLE 2

THE RELATIONSHIP BETWEEN SELECTED SOCIO-ECONOMIC STANDARDS, PREGNANCY AND MALARIA

| | HAVE MALARIA Means | HAVE NO MALARIA Means | D/F | SEDiff | t | df | P |
|---|---|---|---|---|---|---|---|
| Number | 49 | 201 | | | | | |
| Age | 22.88 | 24.14 | 1.26 | 0.34 | 5.71 | 244 | .001 |
| Age at pregnancy | 22.57 | 22.34 | 0.23 | 0.33 | 0.69 | 248 | .245 NS |
| Family income | 1053.09 | 1210.31 | 168.16 | 168.16 | 0.99 | 193 | .161 NS |
| Education | 9.83 | 5.11 | 0.72 | 0.20 | 3.06 | 244 | .001 |
| No. of pregnancies | 2.61 | 3.51 | 0.09 | 0.14 | 6.42 | 248 | .001 |
| No. of surviving children | 1.55 | 2.07 | 0.52 | 0.13 | 4.00 | 231 | .001 |
| Duration of pregnancy | 28.86 | 30.72 | 1.86 | 0.39 | 4.76 | 248 | .001 |

TABBE 3 (a)

THE RELATIONSHIP BETWEEN HUSBAND AND FAMILY CHARACTERISTICS AND MALARIA PARASITAEMIA

| | HAVE MALARIA Means | HAVE NO MALARIA Means | D/F | SEDiff | t | df | P |
|---|---|---|---|---|---|---|---|
| Number | 49 | 201 | | | | | |
| Age of husband | 30.15 | 30.84 | 0.69 | 0.43 | 1.60 | 176 | 0.550 |
| Husband's education | 6.95 | 7.13 | 0.18 | 0.20 | 0.09 | 225 | .184 |
| Family size | 3.74 | 4.41 | 0.67 | 0.16 | 4.18 | 244 | .001 |
| No. of reported fevers | 0.96 | 8.79 | 0.26 | 0.18 | 2.06 | 244 | .004 |

TABLE 3 (b)

THE RELATIONSHIP BETWEEN REPORTED CHLOROQUINE USE, HOSPITAL VISIT AND MALARIA PARASITAEMIA

| | HAVE MALARIA Means | HAVE NO MALARIA Means | D/F | SEDiff | t | df | P |
|---|---|---|---|---|---|---|---|
| Number | 49 | 201 | | | | | |
| Weeks on prophylaxis | 4.27 | 5.36 | 1.08 | 0.26 | 4.19 | 247 | .001 |
| No. of pills used | 1.46 | 1.59 | 0.13 | 0.05 | 0.26 | 246 | .397 Ns |
| Hospital visits | 1.36 | 0.24 | 0.62 | 0.10 | 6.02 | 242 | .001 |
| Days since last use | 4.82 | 5.04 | 0.58 | 0.34 | 0.70 | 247 | .045 |

TABLE 4

THE RELATIONSHIP BETWEEN MOSQUITO PREVENTIVE MEASURES USED AT HOME AND MALARIA STATUS

| 1. | HAVE MALARIA | HAVE NO MALARIA | Chi sq | P |
|---|---|---|---|---|
| 1. With windowmesh | 6 | 22 | | |
| Without windowmesh | 43 | 179 | 0.067 | .79 Ns |
| 2. With bed-nets | 25 | 102 | | |
| Without bed-nets | 24 | 99 | 1.185 | .93 Ns |
| 3. Using space spray | 3 | 11 | | |
| Not using space spray | 46 | 190 | 0.032 | .84 Ns |
| 4. Using mosquito coils | 28 | 92 | | |
| Not using mosquito coils | 21 | 109 | 2.041 | .15 Ns |
| 5. Cleaning surroundings | 14 | 74 | | |
| Not cleaning surroundings | 35 | 127 | 1.174 | .27 Ns |

TABLE 5.

SHOWING PERCEIVED SIDE EFFECTS OF CHLOROQUINE AND MALARIA STATUS

| | WITH MALARIA | WITHOUT MALARIA | Chi sq | P |
|---|---|---|---|---|
| 1. Reported fevers | 24 | 63 | | |
| No fevers | 25 | 138 | 5.40 | 0.02 |
| 2. Dizziness | 8 | 8 | | |
| No dizziness | 41 | 193 | 10.04 | 0.002 |
| 3. Vomitting | 1 | 48 | | |
| No vomitting | 11 | 190 | 1.054 | 0.31 NS |
| 4. Insomnia | 0 | 49 | | |
| No insomnia | 5 | 196 | 1.244 | 0.26 NS |
| 5. Skin itch | 16 | 39 | | |
| No skin itch | 33 | 162 | 4.031 | 0.04 |

## CHAPTER VI

## DISCUSSION

The present study on the use of chloroquine chemosuppression by women attending antenatal clinic of MCH was carried out in an area hyperendemic to holoendemic malaria situation. Other studies have been conducted in similar areas with perhaps identical epidemiological ecolelogical situations and offer opportunity for comparison.

Of the 250 pregnant women who had thick blood smears examined for malaria, 20o/o were found with asexual P. falciparum parasitaemia while only 0.8o/o had gametocoytes. Two smears collected during the day had W. bandcrofti, suggestion a much higher infection rate. Earlier studies conducted by Kouznestov et al (1979) in N.E. Tanzania had a parasitaemia rate of 60.3o/o among 5 - 14 year olds, at the end of the main malaria transimission season. This disparity is explained by the fact that, the present study was carried out in November/ December when minimal conditions of transimission exist. When comparing with findings by Matola (1982) where pregnant women of similar age group were examined for malaria the prevalence rate was 60.4o/o. The parasite densities are in both instances very high, and all are

but outlines the importance of the high sense of motivation in maintaining disciplined regular use to achieve the protective value.

Brabin (1983) in his analysis of malaria in pregnancy in Africa established a more frequent and more severe malaria in infection in primigravidae both during pregnancy and at delivery. Pregnant women in holoendemic malaria area in Western Kenya had peak prevalance of infection in primigravidae (85.7%) and multigravidae (51.7%) occuring at 13 - 16 weeks gestation.

It was found that 49 (19.6%) respondents had malaria. They were relatively younger with a mean age 22.88 years in comparison to those who had no malaria with a mean age of 24.14 years. The education status of all respondents is generally low with most having attended primary school, but the mean education for those with malaria is significantly higher at 5.83 years. The occupation is a reflection of their educational status, many are ordinary house wives the rest doing semi-skilled jobs.

Respondents with malaria have fewer number of pregnancies and fewer number of surviving children. Their pregnancies are also younger with a mean age 28.86 weeks as opposed to 30.72 for those who have no malaria (Table 2).

The findings of the present studies have some similarity to those of West Africa by Belcher (1979) where it was shown that utilization of chloroquine chemoprophylaxis increased with age (30 years and above) compared to 26.2 years of those women in Dar es salaam.

Respondents were found to have been attending MCH clinic for the first time for their antenatal care during the second trimester (mean 22.5 weeks) whereas the period recommended as to initiate protection against malaria and be carried through to term (WHO 1981). This is also the period when the effect of malaria infection on the pregnant women showed highest prevalance and density (Bray & Anderson 1979).

Women of gravida three and above had parasitaemia but those of gravidallaand22 had the highest. These women are liable to the risk of acute malaria attacks within a short period of time and are likely to have profound morbid effects not only to themselves but also to their foetuses. This suggests that all effeorts to

organise effective protection should be undertaken and sustained within the frame work of Primary Health Care. Health education is an important component towards informing the community about malaria disease and the appropriate protective measures at individual and community level. This has to be sustained and supported by appropriate health care personnel at all levels.

The husband and other family characteristics of chloroquine users show that the women using chloroquine chemosuppression are older, mean 26.23 years, have more pregnancies and haver lager numbersoof surviving children, findings in similarity with those of Belcher, (1975). Their husbands are also relatively older, meanx age 32.42 years, and have better education with a mean of 9.25 years of schooling. The family sizes are bigger and the number of hospital visits for care more, and the women use their supplies of drugs within fewer number of days.

The extent to which the role of the husband influencos participation may be difficult to determine in view of the fact that they were not interviewed. But given the situation of edemic malaria with

frequent morbidity in a large size family, perhaps with a precarious income to sustain life in the city, a husband would be motivated to supervise hospital visit which are free, when the need arose and equally superise the taking of drugs supplied to achieve an early recovery. No head of a family would be able to attend to his daily routine of work and other activities well with a sick member of the household.

Determination of measures being applied to reduce man-mosquito contact show that there was no significant relationship between them.

However, the number involved in whichever measure applied are very small and may not have significant protective value. Under present economic circumstances no single measures is available within easy reach of affordability of ordinary individuals to motivate any of their use.

In a hyperrendemic to holoendemic area where vector control measures have recently been deteriorating (Kilama 1983) in addition to personal protection using available drugs to treat or suppress malaria, time honoured methods of protection from mosquito bites like bed nets, space sprays, and so on, should be used (Bruce-Chwatt 1983). These should be made available at the price the common man can afford if necessary with state subsidy, the cummulative return being regained through increased production by the workers who have been relieved of malaria morbidity.

The frequency of fevers and perceived side effects resulting from the use of chloroquine were related. Although the numbers are small there is an increased occurence of the frequency of fevers in the respondents. Dizziness has featured, but not to a significant level indicating perhaps an expected morbid condition due to the state of being pregnant. The extent to which skin itchness has been reported (22%) suggest that it could play a negative role towards programme compliance as

recently observed by Mac Cormack & Lwilula (1983).
The incidence of itching after taking 4 aminoquinolone has been reported frequently among Africans, Olatunde (1981) who reported an incidence of 11% of the Nigerian population. Some developed the itch while taking curative doses, others with suppressive doses and most following subsequent doses.

The exact role of the itch reaction in influencing participation in chemosuppression programme in our situation is not yet known and it may be useful to investigate it.

## CHAPTER VII

### CONCLUSION

The present study supports the already available knowledge of the inadequacy of the chemosuppression programme under the present circumstances. Chloroquine is made freely available to the vulnerable population. It has been observed that only on few occassions this is not made available to the women. In some instances there has been incorrect ticking of supply when in fact it was not, but this can be considered a possible oversight where large popultion groups are being handled. However, if the initial health education information that has been made available in groups and finally on an individual basis has been adequate, then those who have missed certain medication would CONSULT their primary health care personnel.

Where the drug has infact been given, there is a serious lack of conviction that it has protective value and that it should be used routinely weekly. Only 5.2% have evidence of using it and as a result of this 20% of eligible population has malaria.

There are a number of reasons that obviously contribute to non use of the drug. Among others, taking of bitter drugs when the subjects have no symptoms, and the itchiness that people experience has featured in this study as well as the Mara studies. There are other social cultural reasons not yet being communicated to medical personnel. The belief that is associated with quinine that it cause abortions has unfortunately been passed on to the chloroquine. Some people obviously see no reason why they should use bitter drugs in pregnancy at all.

The North East Tanzania studies have similar results of non-compliance as a factor of non-effectiveness of the protection programme. Matola (1982) found 60% malaria positive among the eligible group while Kortmann (1972) found out that even them supervised, compliance was a major setback. The problem of drug compliance has been documented in a number of diseases.

However, attempts to exhaust all available resources should be made to minimise the magnitude of this problem in a serious and endemic disease like malaria and especially to the valumurable population. The chloroquine chemosuppression programme in Tansnia needs to be

intensified to achieve optimal effectiveness. However, the following facts stand. There is still inadequate knowledge as to how much coverage has been achieved to date. Two the exact areas where chloroquine should be abandoned in view of ineffectiveness due to resistance is not known. Proper supervision of the programme should be ensured, for we have the manpower with the capability to do that. The DMO, DMCHC, are people given the correct push can actually achieve this in collaboration with the MA i/c if PHC and Dispensaries.

RECOMMENDATIONS:

1. Research into social factors that contribute into programme non-effectiveness and non-compliance
2. Susceptibility tests to map out areas of chloroquine sensitivity should be conducted country-wide to deliniate those which need to have alternative drugs to chloroquine.
3. While in agreement that possible drug pressure building up towards mass small dosage use of chloroquine its applicants in pregnancy and undefives is not considered a missuse and should be continued. However, continued search for alternative safe, cheep and widely available

drug for prophylaxis during pregnancy should be searched for. Meanwhile chloroquine should be used until further recommended by WHO malaria programme.

4. The problem of malaria is so serious that it should be taught in all schools beginning with Primary schools throughout to University. Mass Media should be made use of much more using properly designed health education material which should be regularly evaluated.

5. The present Health Education available has not created adequate impact. Proper socialogical studies should be made with a view to improve the current health education knowledge given on group scale. In addition individual health education should be made available to each subject when opportunities arise e.g. when examing patients.

6. Consideration for giving a loading dose of chloroquine 600 mg base for each first antenatal attender should be evaluated.

7. The current giving of chloroquine 300 mg base weekly is satisfactory when regular but this has been proven irregular and effectiveness is questionble.

The use of volunteers to supervise chloroquine swallowing in appropriate doses in addition to actual swallowing supervised at the clinic each visit should be seriously considered. The traditional birth attendant is a potential resource, but each area has to be considered according to its merit. Where appropriate village health workers, Tencell leaders, school teachers party and affiliated organ leaders living with the people are a potential resouce but must get the appropriate knowledge and facilities with which to implement this and should have appropriate supervisor organ.

The (respective) ministry of Industry should be recommended to produce sufficient and easily affordable personal protection material such as mosquito nets, wiremesh, mosquito coils and sprays so that the ordinary people have access to more healthfall living from the scorge of malaria.

Abandoned vector control mechanisms should be re-established and new ones implemented having put in the necessary research input as to the appropriateness of each measure to a respective area. In particular a measure of intersectoral planning and community participation should be involved for the multisectoral approach is the only means left at our air disposal for combating the great probelm of malaria. To be effective it must be sustained and have full government support. Finally the necessary training of appropriate manpower should be a top priority in collaboration with International bodies using as far as possible their previous experience in other Regions as well as Regional Cooperation. Above all our own initiative must be on the forefront otherwise we will falter.

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