SUMMARY
Vector borne tropical diseases are major causes of morbidity and mortality in developing countries. Lymphatic filariasis caused by *Wuchereria bancrofti* is one of the major health problems and second most important leading cause of permanent disability in India. About 28 million people carry microfilariae in their blood and 21 million suffer from various forms of clinical manifestations. The *W. bancrofti* in India is transmitted by *C. quinquefasciatus*. The microfilariae released by the fertilized female reach peripheral circulation during night time and enter mosquito body through blood meal. Further development of mf in the vector host involves exsheathment of ingested mf, two successive moultings in thoracic musculature, which lead to the passage of larvae to L3 through L1 and L2. Infact, only a small portion of ingested mf reach L3 stage larvae and this is represented by ‘parasite yield’ which is the result of a complex interactions between vector host and the parasite. This interaction in turn is influenced by a number of variables like, parasite reservoir in human host, physiology, local climatic conditions etc. The L3 larvae when deposited on the skin of humans through mosquito bite find their own way into the circulation through the puncture site. The infective larvae that survive the onslaught of human immune system may reach lymphatics where the larvae undergo further development to adults. Several thousands of infective mosquito bites are therefore needed for successful inoculation of human host.

An integrated approach involving chemotherapeutic and vector control measures is the only solution for effective control of filariasis. Diethylcarbamazine remains the drug of choice in selective as well as mass chemotherapeutic programs against lymphatic filariasis.

A complete knowledge of the transmission dynamics of filariasis in a given endemic region is needed for devising and implementing appropriate control strategies. The vectorial capacity of *C. quinquefasciatus*, which to a larger extent determines the course of transmission dynamics, is under the influence of a number of environmental, epidemiological and physiological factors. Since these variables are under constant influence of local climatic factors, the findings of one region can not be extrapolated to another. The present study was focussed on factors affecting the vector efficiency of *C. quinquefasciatus* in an urban zone of Raipur

**Chapter I**

Study of bionomics of filaria vector that include the seasonal variation in indoor resting populations of *C. quinquefasciatus*, host preference of vector.
impact of climate on prevalence and distribution of vector infection and infectivity rates form components of Chapter 1.

The bionomics of *C. quinquefasciatus* assumes importance as it influences significantly the prevalence of human filarial infection in a given endemic region. Since the bionomics of vector mosquito is under profound influence of local climate, the findings of one geographic region can not be extrapolated to another. A systematic study on bionomics of *Culex* mosquito that included seasonal variation in indoor resting densities and host preference of *C. quinquefasciatus* was carried out at regular monthly intervals for over a period of two years between October 1995 and September 97 at six localities viz., Budhapara (locality 1), Fafadhi (locality 2), Gudhyari (locality 3), Kankalipara (locality 4), Rajatalab (locality 5) and Tikrapara (locality 6) of Raipur. *C. quinquefasciatus* constituted 70% of the eleven mosquito species recorded at Raipur during the study period and is prevalent almost throughout the year spanning all seasons at varying densities. The highest indoor resting density of 162.67 ± 59 per man hour was recorded in December and the lowest of 6.83 ± 1.47 per man hour was in the month of June. Winter season recorded maximum density followed by rainy and summer seasons. The density of *C. quinquefasciatus* was found to have an inverse relationship with the temperature. The vector densities catch up with decline in temperature during colder months. The lowest vector density in May, 1996 and June, 1997 could be attributed to high temperature (40°C) and heavy rain fall prevailing in those months. Thus, rain fall besides temperature and humidity appears to play a major regulatory role on the growth of mosquito species. The distribution of *Culex* followed almost identical pattern in all the six localities with locality 1 at the top of the list. Thus, the optimum climatic conditions for breeding of *C. quinquefasciatus* at Raipur exist during October, November, December and January months.

The study of bionomics of *C. quinquefasciatus* requires accurate information of their feeding habits and preferences as well. The host preference of vector mosquitoes in a given area influences the dynamics of infection. Analysis of 105 blood meal samples of *C. quinquefasciatus* from three different habitats viz., human, cattle and mixed dwellings reveal that the vector is preferentially anthropophilic with an anthropophilic index (AI) of 89.65% and 63% from human and mixed dwellings respectively.

The intensity of transmission of filariasis in a given area is evaluated mainly by examining the vector population for infection and infectivity rates. All species
of mosquitoes collected indoors were dissected individually for infection and distribution of filarial larvae. *C. quinquefasciatus* was the only species that harboured filarial larvae indicating that mosquitoes other than this species do not support the growth of filarial larvae at Raipur. Of the 3213 *C. quinquefasciatus* dissected, 130 were positive for one or other stage of filarial larvae. The distribution of developing and L3 larvae in randomly collected indoor resting *C. quinquefasciatus* were recorded at regular monthly intervals and the infection and infectivity rates were worked out separately for all six localities over a period of 12 months. A mean vector infection rate of 4.05% with the highest figure of 22.41% was recorded in the month of August when the mean maximum temperature was 30 ± 1°C, humidity, 93 ± 2% and rain fall of 58 ± 49 mm. February month recorded the lowest infection rate (2.8%) when the rain fall was 2 ± 4 mm. The December month, which recorded the highest vector density, did not record vector infection. Locality 2 recorded the highest infection rate followed by locality 1.

A mean vector infectivity rate of 0.25% was recorded from randomly collected indoor resting mosquitoes. The infectivity rate was higher in rainy season followed by summer and winter. The highest (1.15%) and the lowest (0.41%) figures were in the months of June and March respectively. Locality 6 recorded the highest vector infectivity rate. There was a negative correlation between the density of *C. quinquefasciatus* and vector infection or infectivity rates.

Study of frequency distribution of *W. bancrofti* larvae in infected vector population reveals a negative binomial pattern with an average density of 5.27 larvae per mosquito. The density of various stages of larvae varied widely, microfilariae being the dominant stage. The mean host efficiency index recorded was 0.44 with the highest figure in the month of February and the lowest in March. An annual transmission index of 32.72 was recorded at Raipur during the study period with higher values for January and February months. There was a significant rise in vector infection rates in all of the six localities when examined after a gap of 1.5 and 2.5 year.

**Chapter 2**

The infective potential of endemic population is determined by the rate of prevalence and density of microfilaraemia. A total of 5720 human subjects were examined for the prevalence of microfilaraemia by night blood smear test. A mean human infection rate of 4.37% with an average mf density of 3.5 per 20 cmm
capillary blood was observed. The incidence of microfilaraemia was more in males than females though the difference is not significant and the incidence increased with age up to 25 years in both the sexes. The highest mean mf count of 10 was recorded from females in the age group of 51-55. The distribution of microfilariae among the infected subjects followed negative binomial pattern.

Simultaneous examination of human and vector populations in six localities revealed mean infection rates of 4.41% and 4.05% respectively. Higher incidence (9.28%) was at locality 1. No relationship was observed between mean mf density in capillary blood of mf carriers and mean mf density recovered from infected vector population.

An attempt was made in the present study to find out the existence of relationship, if any, between blood group antigens and filariasis. A total of 542 subjects including normal and filarial subjects were examined for major blood group antigens viz. A, B and O. About 42% of normal healthy subjects expressed ‘O’ group followed by ‘B’ group (33%). Very few subjects expressed ‘AB’ group. The prevalence of blood group antigens amongst microfilaraemic subjects is in the order of AB>B>A>O. About 40% of filarial subjects with elephantiasis expressed ‘B’ group antigens and this is followed by A (24%) and AB (6.5%) groups. These observations tempt us to speculate that those mf carriers with ‘B’ antigens are at high risk of developing manifestations in due course of time.

Chapter 3

The vectorial capacity of *C. quinquefasciatus* depends on the efficiency of transmission of filarial parasites under various host and environmental conditions. An attempt was made to understand the development pattern of filarial larvae in wild caught *C. quinquefasciatus* in relation to initial mf density in the blood meal. The study was confined to eleven infected house holds that contained one microfilariae carrier each. The mean mf count of carriers from 11 infected house holds was $2.93 \pm 0.52$ 20 cmm throughout 12 month study period. The mean number of mf per fresh blood meal was found to be 471. Thus, the concentration power of *C. quinquefasciatus* at Raipur is 14.2 which is several times higher than the value reported from other geographic regions for the same vector. A very high infection rate throughout the year was recorded in vector population examined from every infected house. A mean infection rate of 18.21% and an infectivity rate of 3.26% was recorded from the infected households. These figures, as anticipated, are significantly higher than those observed from random vector.
surveys done in the six localities. Higher vector infection rates were in the months of November (28.5%) followed by December (21.38%), October (21.14%) and January months (21.13%) when the mean temperature was 22°C. November month also recorded the highest infectivity rate of 7.77%. A positive correlation (P<0.01) between vector infection or infectivity rates in vector population from infected house holds was observed. The distribution of developing filarial larvae in vector population was recorded at 4 day intervals for up to 16 days. Out of 773 larvae recovered from vector dissections on the day of collection, 94.57% were of mf while 3.36% were of L1; 1.81% were of L2 and 0.26% were of L3. Thus a very high proportion of C. quinquefasciatus from the infected households are freshly infected. The survival rate of mosquitoes in relation to the days required for completion of development of filarial larvae to L3 is a crucial factor for determining the efficiency of transmission. The rate of survival of mosquitoes was found high in rainy season while winter season recorded the highest mortality. Maximum mortality was observed during November, December and January months.

An attempt was made to workout the nature of vector-parasite relationship that exists in wild caught C. quinquefasciatus at Raipur. The number of microfilariae in the fresh blood meals of individual vectors was plotted against parasite yield (L3/mf) for every month and season. The parasite yield was high in winter as compared to summer and rainy seasons when the number of mf in the blood meal was 1-3, however, no seasonal variation in parasite yield was observed when the number of mf in the blood meal exceeded >7. A significant proportion of the mf ingested is lost during development in the vector host and this loss is influenced to a significant degree by the local climatic conditions. The percentage loss of mf is very high in rainy season followed by summer and winter seasons. The proportion of mf becoming L3 decreased with increase in mf number in the blood meal indicating that the vector-parasite relationship is ‘limitation’. It implies that existence of even ultra-low density mf carriers can sustain transmission and this aspect should be taken into consideration while initiating the filarial control programs at Raipur. The existence of vector infection throughout the year in infected houses indicate that entomological survey can be used as a tool for locating infected house holds in the endemic community for target oriented therapeutic measures.

The concentration of Wuchereria bancrofti microfilariae in the peripheral blood of humans follows a 24-hours periodic cycle which appears to synchronize with the biting habits of the mosquito vectors in the area. This study highlights importance on multifrequency rhythms in mf appearance and may have a bearing.
on strategies aimed at prevention, cure and management of filariasis. The time
series data were analyzed for documenting a circadian and circannual rhythms with
the help of Cosinor rhythmometry. Result of the present study revealed statistically
validated circadian and infradian rhythms in mf density in capillary blood of
microfilaraemic subjects. The population mean circadian rhythm in mf density with
the peak observed at 00:13 with a 95% confidence intervals from 22:54 to 01:19
can be best termed as a nocturnal periodicity. In addition, the periodicity index
was 132.79. The result of microfilariae of *W. bancrofti* is nocturnal at Raipur city.
The present study clearly documents statistically significant high amplitude circadian
rhythm in mf in human subjects, regardless of gender.

Of the circannual rhythm, the acrophase timing for microfilariae density was
recorded in July. Interestingly the peak appeared in July regardless of both age and
sex. However, unlike circadian rhythm, circannual rhythm in mf density was less well
defined. Individually only 4 out of 39 subjects exhibited a statistically significant
circannual rhythm. However, the group mean circannual rhythm in mf density was
highly statistically significant with a peak located in July. The spread of the peak was
quite wide from May 17 to September 17. The results of the present study suggest
that a seasonal periodicity in mf density has a profound bearing on the epidemiological
and clinical management of filariasis. The result of the present study depicted neither
a 7-day nor a 15-day rhythm in mf density. Since the examination of a possible 7-
day or 15-day rhythm was conducted in a single subject, it would be too early to
rule out the possibility of occurrence of such infradian rhythms.

The biting activity of *C. quinquefasciatus* was maximal between 00:39 and
00:22 with a peak at 02:37. The periodicity index was found to be 92.54. The
acrophase timing for biting periodicity has a spread of 3 hour. Thus there is an apparent
correlation between the periodicities of both microfilariae and biting activity of the
vector. This study, therefore, confirms the adaptation of *W. bancrofti* in Raipur to
the activity of the local vector for optimum transmission of the parasites.

It is important to mention here that the temporal dynamics of parasite transmission
observed in this study is sequential. The study demonstrate clearly that the peak of
mf in human blood, peak in the biting activity of the mosquitoes and the peak of mf in
mosquitoes are temporally linear occurring one after the other with a specified time
lag between them. Internal acrophase computed with respect to the biting cycle of
the mosquitoes, sunrise and sunset timings favour sunrise as well as sunset as possible
entrainers of mf density rhythm. Could it be that the host body temperature rhythm
which is entrained by the photoperiod eventually entrains the mf density rhythm?
That is to say the mf density rhythm is indirectly cued by the photoperiod. However, all these are subjects of speculation specially since no attempts have been made in the present study to resolve this assumption.

In a nutshell, the rhythms (bioperiodicities) assume an undoubted significance for the vector species in the transmission of filariasis. The transmission will be derailed if rhythms in the vector and the host would desynchronize from each other. Therefore, the application of chronobiologic principles in the control of filariasis may have future prospects by way of modulation of rhythm genes of the vector through latest techniques in molecular biology.

Chapter 4

This Chapter describes the studies on chemotherapy and socio-economic aspects of filariasis at Raipur region. Diethylcarbamazine being cost effective, less toxic and also due to its easy availability remains the drug of choice for filariasis. Comparative efficacy of two different DEC regimens viz., standard regimen i.e., 72 mg/kg body weight and single dose (6 mg/kg body weight) of DEC on microfilaraemia were studied on small groups of microfilariae carriers. In both the groups, house to house visits were made throughout the course of treatment and the drug was administered under personal supervision. The efficacy of DEC on microfilaraemia in both the regimens was assessed by estimating the rate of successful treatment, the percentage cure rate and percentage decrease in mf counts once immediately after treatment and at 3, 6, 12, 24 and 48 month intervals following treatment. The standard dose regimen proved superior with 100% cure rate and 100% percent decrease in mf count. In case of single dose regimen, the successful treatment was 100% with a cure rate of 36% when estimated at 24 h after drug administration. Both the indices showed a gradual decline by 24 and 48 months of treatment. The cure rate was 'zero' from 3rd month onwards. The percent decrease in mf which was 59% at 24 h therapy was reduced gradually reaching zero by 24 and 48 months. No side effects were recorded in any of the regimens. The single DEC regimen when assessed for its impact on vector infection rate showed marginal effect the reduction being 1% in vector populations from treated house holds soon after therapy. There was a significant rise, however, in vector infection and infectivity rates in the infected house holds when the vector survey was repeated 48 months after drug therapy.

Transmission of filariasis is not determined simply by vector and environmental factors but can also be influenced to a significant extent by socioeconomic factors.
Successful control of filariasis is therefore largely dependent on public awareness about the disease. The perception of filariasis may vary not only from place to place but also from person to person in the same community. A study was undertaken to record the knowledge, attitude and perception of residents of Raipur region. The objective was to gather evidence if the behaviour of affected community influences the probability of developing disease. A questionnaire was made in local (Hindi) language with input from a sociologist and the responses of about 1020 individuals, which included filarial and normal subjects of all categories of the society viz., literates, illiterates, high & low income groups, males, females of all age groups (>18). Gender based analysis reveal that female subjects irrespective of their socioeconomic and educational status have better perception of etiology of filariasis than their male counterparts. A low percentage of respondents are aware of mosquito as the cause of filariasis. The social stigma is an issue mainly with the upper socioeconomic groups of the community and is not a major issue among lower groups of the society. About 22% of elephantiasis subjects said that they face social ignorance. Majority of mf carriers does not have proper knowledge of filariasis or the treatment available. A sizable fraction of the respondents believe that the disease is caste based and infectious. The study emphasizes the need for community health education that will build more awareness about the causes, transmission of infection and preventive measures for successful control of filariasis. Rapid assessment of filaria endemic zones is needed for undertaking mass control programs. An attempt was made to identify other filaria endemic pockets through informants. About 10% of the subjects listed out endemic pockets other than Raipur and 70% of those pockets are located in Madhya Pradesh State alone. Thus, informants approach could be used for mapping filaria endemic pockets for mass therapeutic programs.