2 *Literature Review*

2.1 LF: Epidemiology and Disease Burden

LF is widely prevalent in tropical and subtropical countries. According to recent estimates, about 120 million people living in 73 countries in Africa, Asia and the Pacific are infected with LF, primarily by *W. bancrofti* and to a lesser extent, by *Brugia malayi* and *Brugia timori* (Ottesen and Ramachandran, 1995; Michael *et al.* 1996). Globally, about 1.1 billion people (constituting approximately 20% of the world population) live in areas endemic for this disease, and more than 90% of them are exposed to the risk of infection with *W. bancrofti*.

LF is one of the major public health problems in India. The magnitude and the extent of the filariasis problem in India was initially assessed by Jaswant Singh and Raghavan (1953), Indian Council of Medical Research (ICMR) (1961, 1961-70). Later Sharma *et al.* (1977) updated the information. Subsequently, Sharma *et al.* (1983) estimated that there were about 22 million microfilaria carriers and 16 million diseased people in India. WHO (1984) observed that India, China and Indonesia account for two third of the affected people in the world. According to recent estimates, India alone contributes about 47% of the global prevalence of chronic filariasis. Eighteen states/union territories in India are endemic for LF; 454 million people are at risk of infection and 48.11 million are infected, thus posing an important public health problem (Sharma *et al.* 1995., Biswas *et al.* 1996; Michael *et al.* 1996; WHO 1997; Ramaiah *et al.* 2000). Estimates of health burden suggest that LF is responsible for loss of 4,918,000 disability adjusted life years (DALYs), the highest of all tropical diseases after malaria, and that 44% of DALYs lost, worldwide, due to LF, occur in India (Murray and Lopez 1996). *W. bancrofti* causing bancroftian filariasis is the most prevalent species accounting for about 99.4% of the microfilaraemics and is distributed widely in this country. Brugian filariasis caused by *B. malayi* has restricted distribution and is reported to occur in Kerala but scattered foci of low prevalence were reported in Orissa, Assam, Madhya Pradesh, Andhra Pradesh and Tamil Nadu with over 90 million people at the risk (Das 1976). In Andaman and Nicobar islands, LF occurs in two different forms, the nocturnally periodic *W. bancrofti* which is reported from Port Blair and other areas of south

Andaman, north Andaman, and Little Andaman (Shriram *et al.* 1996) and diurnally subperiodic filariasis is prevalent only in Nicobar group of islands, here it is reported to be a major public health problem in remotely located Nancowry group of islands (Basu 1958; Kalra 1974; Russel *et al.* 1975; Das *et al.* 1975; Tewari *et al.* 1995). At present a population of about 25,000 constituted mainly by the Nicobarese tribe, is at the risk of acquiring this infection.

Microfilariae of diurnally subperiodic *W. bancrofti* were detected in the peripheral blood throughout the 24 h period with a peak at 18:00. Overall, studies undertaken so far in these islands report high microfilaraemia rates and a very low disease rate. The incidence of microfilaraemia was low in children less than 10 years of age but increased with increasing age; with the highest rate in the 41-50-age class (Russel *et al.* 1975), characteristic of areas with low force of infection (Sasa 1976) and is frequently associated with diurnally sub periodic *W. bancrofti* in French Polynesia (Cartel *et al.* 1992), Samoa (Murray 1948) and other South Pacific island groups (Kessel 1960). This is in contrast to the age distribution of periodic *W. bancrofti* on the mainland India, which increased until about 20 years of age, followed by a decline to about 40 years, after which the microfilaraemia levels stabilize (Rajagopalan *et al.* 1989) *Cx. quinquefasciatus* was present in very low densities. *Ochlerotatus* (*Finlaya*) *niveus* and *Aedes* (*Stegomyia*) *malayensis* were the species commonly biting the aborigine tribes. The former species has been found naturally infected with *W. bancrofti*. Kalra (1974) and Russel *et al.* (1995) showed experimentally that *Cx. quinquefasciatus* was an inefficient vector of subperiodic *W. bancrofti*, but still could play a role as secondary vector as it does in the South Pacific region where *Aedes polynesiensis* is the main vector.

Although microfilariae were first described from hydrocele fluid by Demarquay (1863) in Paris and from blood in India by Lewis (1872) the identity of non-periodic filariasis was not known, until Manson (1894) requested blood films from elephantiasis cases in the South Pacific Islands from filariasis survey carried out by Thorpe (1896) when he had actually discovered the absence of periodicity of microfilariae in this region. It was a discovery purely by conjecture, actually when he made some control observations during the daytime he found to his astonishment the microfilariae swarming in high numbers as observed during the night. He obtained microfilaraemia rates of 20% (Vavau island), 28.8% (Nomuka island), 57.5% (Lifuka island) and 29.2% in Tongatabu Island respectively. In the same year Manson observed 56 Samoans who were chronic elephantiasis patients, of whom 27 were found to harbor microfilariae, and his findings were comparable with the earlier observations of Thorpe. It was concluded that subperiodic filariasis was endemic in Samoa as in Fiji and Friendship islands.

Manson (1896) examined the blood films collected in 1884 by Davis in Samoa, who had also reported microfilariae from the blood of persons in Polynesia. Because Manson was acquainted with the periodic type of filariasis, he assumed the microfilariae from Samoa to be nocturnal in type but in reality it was Thorpe who observed that the microfilariae from South Pacific were present in the daytime as well as at night, thus first establishing the non-periodic form of filariasis, which is known to be prevalent in the other islands of the region viz., Fiji, New Caledonia, the Loyalty Islands and Polynesia.

O'Connor (1923) showed that this form of filariasis was endemic in the islands of Western Pacific. The age specific analysis showed that microfilaraemia and disease rate in persons aged above sixteen years were comparatively more than those under sixteen years. The clinico-epidemiological profile of this form of filariasis in this region showed that episodes of filarial fevers associated with lymphangitis and lymphadenitis were the commonest reported signs. Elephantiasis associated with hydrocele was known to manifest later in life (Weller *et al.* 1982).

New Caledonia, a French administered Territory in the South West Pacific, east of Queensland, Australia, comprises of mainly the Caledonian, the Loyalty Islands, Ile Des Pins and several other islands. Diurnally subperiodic bancroftian filariasis is endemic in these islands. The principal vector in this region is *Aedes (Ochlerotatus) vigilax,* a day biting mosquito that breeds in brackish waters. The prevalence of this infection was identified as early as 1878. Hydrocele and elephantiasis were the commonest clinical manifestation in this region (Sasa 1976). .However, Lang and Noc (1903) reported filariasis in humans and animals in the Caledonian region. Survey carried out after a long gap showed that microfilaraemia levels were comparatively less than in the past. Some foci had disappeared, while the other ones spread along the coasts towards north and east (Le Godinec and Fauran 1984) with high prevalence of *Ae. vigilax*. In Thailand, a nocturnally subperiodic *W. bancrofti* was endemic (Gould *et al.* 1982 and Khamboonruang *et al.* 1989).

Jachowski and Otto (1955), while studying the various aspects of the natural history of this disease, put forth an entirely new understanding on the epidemiology of the non-periodic filariasis in American Samoa. A concept of diffuse sylvan foci of transmission for non – periodic *W. bancrofti* as contrasted with peri-domestic transmission for the periodic variety of this human filarial parasite.

Ramalingam (1968) while dissecting wild caught and experimentally infected mosquitoes showed that the night biting *Aedes (Finlaya) samoanus*, and the day biting *Aedes (Stegomyia) upolensis* and *Aedes (Stegomyia) tabu* as the vectors in this region. Transmission was moderately high in the open villages than in the plantations. However, the pattern of transmission was slightly different from what was observed in American Samoa, as *Ae. samoanus* was found to be breeding prolifically in the leaf axils of *Pandanus* and *Freycinetia,* whereas in Western Samoa it was found to breed only in *Freycinetia.* Subsequent studies undertaken in this region throw light on the spatial distribution of vectors (Samarawickrema *et al.* 1987), importance of residual microfilaraemia (Kimura *et al.* 1985), microfilaraemia levels in relation to village ecotypes (Samarawickrema *et al.* 1987) and change in microfilaraemia levels (Reid and Kimura 1993).

2.2 Physiological Races of *W. bancrofti*

Three types of periodicity occur among the Filarioidea, the diurnally periodic, found in human loiasis, the nocturnally periodic of Bancroftian filariasis found in most areas of the world, and the non-periodic Bancroftian filariasis found in the south-east regions of the Pacific.

Several opinions have been put forth regarding the origin of non-periodic Bancroftian filariasis, which occurs in the South Pacific islands. Most anthropologists agreed that the major migrations of Polynesians originated in south – east Asia and followed an east ward trend, touching on many islands of the central Pacific as they progressed to the eastern triangle of the Pacific, with apexes at the Hawaiian Islands on the north, Easter Island on the east and New Zealand on the south, known as Polynesia. However, radio carbon dating (Carbon 14) indicated that many islands of Polynesia were inhabited by the first century A.D itself (Draper 1960).

One theory, which was an off shoot of an earlier work of Bahr (1912) in Fiji and studies by Buxton (1928) supposes that the Polynesians had harbored periodic strain of *W. bancrofti* and had migrated eastward along the northern borders of Melanesia. Upon arrival in the eastern parts of Melanesia and Western borders of Polynesia, suitable night – biting mosquitoes were rare or absent. In their place, day-biting sylvatic mosquitoes, which were most active in the morning and late afternoon and belonging to the *scutellaris*, group e.g. *Aedes pseudoscutellaris* and *Ae. polynesiensis* were prevalent. By natural selection of the microfilariae present in the peripheral blood during the day, a strain developed which is non-periodic in type. Canet (1952) reported the occurrence of nonperiodic filariasis among Mois, a Polynesian like tribe in the south east Asia, which could have been due to transportation of the strain by Polynesian migrations, and the availability of suitable vectors *en route*.

Subsequent studies carried out by Burnett (1959) and Symes (1960), emphasized the importance in the transmission of filariasis, in the above mentioned areas of Polynesia where nonperiodic form of filariasis were known to occur, *Aedes fijiensis* and other *Aedes spp* mosquitoes which could have bitten either by day or night, supported the theory for the development of the non-periodic strain. Extensive discussions on the role of dispersal of mosquitoes in the Pacific suggests, "that nonperiodic filariasis is not derived from the periodic type, but rather that it is a primitive generalized type which is relict in the South Pacific Area" (Belkin 1960, 1960a). He supposes that one or more stocks of filaria may have been introduced by Melanesians prior to the migration of Polynesians and that the latter upon arrival in the eastern South Pacific region merely acquired and spread the filaria already present.

Iyengar (1954) attempting to study the periodicity of microfilaria of *W. bancrofti* in New Caledonia, concluded that the microfilariae in this region lack periodicity. However, after nearly two decades Sasa and Tanaka (1972) subjected Iyengar's data to statistical analysis, and showed that the *W. bancrofti* in this region was diurnally subperiodic form, with a periodicity index of 22.8 and peak hour of appearance of mf was at 15.00 hours.

Khamboonruang *et al.* (1987) identified the presence of a subperiodic variant of *W. bancrofti* in Tak Province, Northwest Thailand. The microfilarial periodicity as determined from four carriers was found to be nocturnally (early evening) subperiodic type showing a distinct peak at 18:00 hours.

In 1992, a study on microfilaraemia periodicity confirmed the existence of a diurnally subperiodic filariasis in the French Polynesia by adopting membrane filtration technique and finger prick method. There was no significant nycthemeral variation between the microfilaraemia levels at 16:00, 20:00. 24:00, 04:00, 08:00 and 12:00 hours respectively. On the other hand, the finger prick method showed a significant difference between the microfilaria densities, the microfilaraemia was higher during the day (12:00-20:00 hours) than during the night (24:00-08:00 hours) (Moulia Pelat *et al.* 1993).

In India, Kalra (1974) for the first time undertook study on the periodicity in the appearance of mf in the peripheral blood, in three islands of Nancowry group. Microfilariae were observed throughout the 24-hour period without any distinct peak. The density of mf was relatively lower than that of periodic form.

Another such observation with 15 male volunteers from Chowra Island (Tewari *et al.* 1995) also showed that the circulating mf were present in the peripheral blood throughout the 24 hour period. The mf count was found to vary widely during different periods with a peak at about 18.00 hour and a trough between 03.00 and 06.00 hour in an individual.

Another study carried out by Das *et al.* (1975) on the periodicity of mf of this species showed the existence of nocturnally periodic form at Port Blair (Andamans) and diurnally subperiodic form in Nicobar group of islands. The existence of both forms in the same host was found in a settler in Nancowry Island.

According to the anthropologists, the Nicobarese - the natives of the Nicobar group islands have a marked similarity with the Indo-Chinese stock as distinguished from the Tibeto-Burman and Malayan tribes. The most definite link with the Indo-Chinese is the philology of the Nicobarese language which are the variants of Mon Annom groups. Establishment of a focus of a non-periodic filariasis in the Nicobar Islands of Andaman and Nicobar group of islands appears to be due to ancient migrations of some stock from Indo-China (Dudley Stamp 1962) and these islands may probably be the Western limit of the non-periodic filariasis in south east Asia.

2.3 Prevalence and Distribution of Subperiodic Filariasis

Subperiodic filariasis due to *W. bancrofti* is widely prevalent in the Pacific region, and poses a public health problem. It is highly prevalent in some of the islands in the South Pacific, in particular Tahiti, Samoa (Samarawickrema *et al.* 1985) Tonga and Fiji . Although these islands are free from malaria because of the absence of anopheline mosquitoes, filariasis poses a serious health problem to the inhabitants of these islands. The Pacific region includes Australia, New Guinea and adjacent islands of Melanesia, Micronesia, and Polynesia (Ottesen *et al.* 1997).

Among the early European explorers and settlers who reported elephantiasis from Polynesia and other related islands of the Pacific are Lloyd (1949) from Tonga, Wilson (1799) from Tahiti, Vinson (1858) from New Caledonia, Messer (1876) from Fiji, and Koniger (1878) from Samoa. Ellis (1833) is of the opinion that elephantiasis occurred among the Polynesians form their "earliest antiquity" and Montgomery (1831) estimated that four percent of the population of the Society Islands suffered from elephantiasis. Rosen (1954) however, made an interesting observation concerning elephantiasis in the Marquesas Islands, Tahiti. Rosen found 5 per cent of the population to have elephantiasis but pointed out that early European explorers did not observe cases of elephantiasis in these islands even in the latter part of the last century.

Filariasis throughout the world is noted for its marked spotty distribution. The island areas in the South Pacific are no exception to this, as evidenced by early reports from Fiji (Symes 1960a), which showed a low prevalence of 6.4% among the population inhabiting the Labasa, while a high prevalence rate (25.2%) was observed in Taveuni. Likewise Beye *et al.* (1953) in French Polynesia reported percentage ranging from 19% in Tubuai to 44% in Hitiaa. The prevalence rates in different populations appeared to be associated with the habits of the people and high densities of the vector population, in close proximity to the human population, had provided greater opportunity for transmission of infection.

It has long been recognized that LF is prevalent in many Polynesian archipelagos, which includes Society Islands in French Oceania. Earlier studies carried out in several representative island groups of Polynesia showed that the total microfilaraemia rates ranged between 14.2 % in Fiji and 40% percent in Tahiti, and disease rates from 0.8% in Fiji to 7% in Tahiti. (Iyengar 1954; Iyengar 1957a; Nelson and Cruikshank 1956; Jachowski and Otto 1955; McCarthy and Fitzgerald 1956). The importance of clinical manifestations in these areas was elucidated by the experience of the Armed Forces of the United States during World War II (Wartman 1947).

In India, diurnally subperiodic *W. bancrofti* is prevalent only in the Nancowry group of islands, of the Nicobar district. Nancowry group of islands is a small pocket comprising of seven remotely located islands, viz., Bompoka, Chowra, Kamorta, Katchal, Nancowry, Teressa and Trinket (Basu 1958; Kalra 1974; Russel *et al.* 1975; Das *et al.* 1975; Tewari *et al.* 1995).

The prevalence of lymphatic filarial infection in the Andaman and Nicobar islands was first identified by Wilcock as early as 1944. He found that 5.8% of the population surveyed in Nicobar group of islands was positive for *W. bancrofti*, while the Andaman group of islands was free from filariasis. Subsequently, a sample survey carried out in 1958 by Basu showed the prevalence of *W. bancrofti* in Port Blair (Andamans) and Nancowry (Nicobars). In Nicobar islands, 7 and 9% infection rates were detected in human population surveyed by day and night respectively.

The first report of diurnally subperiodic *W. bancrofti* among the Nicobarese tribe was from studies undertaken by Kalra (1974). Only two villages in Kamorta Island and one in Nancowry Island were covered during this survey, which showed mf rates of 12.3 and 1.7% respectively. Russel *et al.* (1975) carried out a day and night survey among 6250 and 491 individuals respectively in four islands from two study areas i.e., Nicobar and Andaman district (Port Blair town). The survey showed two distinct forms of *W. bancrofti* infection viz., a nocturnally periodic form in Port Blair and a subperiodic form in Nancowry and Chowra islands. A low mf rate (0.3%) in Car Nicobar, medium (4.9% and 3.9%) in Port Blair and Nancowry respectively and high rates of 15.8% in Teressa and 13.4% in Chowra were recorded. Clinical manifestations were recorded among 90 of the total 6741 individuals with both men and women being affected. Elephantiasis in association with hydrocele was the commonest disease manifestation encountered during the survey.

After a gap of another 15 years, another survey was carried out by Tewari *et al.* (1995) during the monsoon season, which confirmed the existence of subperiodic filariasis in Nancowry group of islands. This survey showed that the mf rate was the lowest in Trinket (1.2%) and highest in Kamorta (8.7%). The overall disease rate was only 1.9%, the highest recorded from Chowra. Elephantiasis of the legs was the predominant disease manifestation. However, no information on the prevalence of hydrocele was available.

In the same year another survey was carried out in the six of the seven islands of Nancowry group. A total of 1991 subjects were examined for presence of clinical manifestations of filariasis and for the presence of microfilaraemia. The microfilaria ranged between 0.29% (Katchal) and 12.5% (Teressa), while the disease rate ranged from 0.27% (Nancowry) to 5.88% (Teressa) (Anonymous, 1995-96). Age and gender specific pattern of disease observed in the studies undertaken so far show that microfilaraemia and disease prevalence was higher in males when compared to females. The microfilaraemia rate was low in children below 10 years in both the sexes and increased with increasing age. Thus field studies undertaken during several points of time in the past four decades by several workers have shown varying microfilaraemia levels in the remotely located Nancowry group of islands, indicating that this form of filariasis is an important public health problem.

2.4 Life History of The Parasite

W. bancrofti are thread like nematodes having five morphologically and biochemically distinct stages in their life cycle (Nanduri and Kazura, 1989). Infective or third-stage larvae are transmitted to humans during blood feeding by mosquitoes. The organisms are deposited from the mouthparts of the mosquito in the vicinity of the skin puncture wound, and within several minutes make their way through the dermis to enter the local lymphatics. Several hours later, infective larvae shed their cuticle and develop a new surface (a process referred to as molting) that presents antigens and other molecules to the mammalian host. These fourth stage larvae migrate centrally in the lymphatic vessels and over a period of approximately nine months develop into sexually mature adult male or female worms. The mean life span of the adult worm is five years.

Following copulation with male worms, fecund female parasites release large numbers (often more than 10,000 per day) of embryonic forms, which are referred to as microfilariae. After ingestion in a blood meal taken by a female mosquito, microfilariae exsheath within 24 hours, penetrate the chitinous gut wall of the mosquito, and migrate into the thoracic musculature. Over a period of 10 days to two weeks, the organisms mature to become third stage larvae capable of infecting humans (Southgate 1992).

2.5 Ecological Types of *W. bancrofti*

One of the most remarkable aspects in the problems of intraspecies taxonomy of human filariasis is the occurrence of clearly defined races, each characterized by its pattern of the microfilarial periodicity. In *W. bancrofti*, three races differing in the microfilarial periodicity have been recognized - a nocturnally periodic race distributed widely throughout tropical and sub tropical zones of the world (with the exception of Polynesian sub region), a non-periodic, or more precisely, diurnally subperiodic race restricted to the Polynesian sub region, and a nocturnally subperiodic race reported in the jungle areas in West Thailand (Harinasuta *et al.* 1970a; Harinasuta *et al.* 1970b). These races have different groups of mosquitoes as their intermediate hosts, and the microfilarial periodicity of each coincides with the circadian rhythm of the biting activity of its principal vector mosquitoes.

When the parasite is introduced into an area where transmission can be maintained by the presence of sufficient numbers of vectors the area can become endemic. It has been shown that the same filarial race can develop in different species of mosquitoes that may be ecologically and physiologically distinct. In such cases, filariasis due to the same species and race occurs in areas associated with different ecological conditions. Therefore, the epidemiological or ecological features differ greatly among the endemic areas according to the species of the main vectors. In the case of *W. bancrofti* infection, the following types have been documented.

The *Culex fatigans* type – The nocturnally periodic race of *W. bancrofti* transmitted by mosquitoes of the *Culex pipiens* complex including the races (*pipiens, fatigans* and *molestus*) is the most widely distributed ecological type. *Cx. fatigans* is known as *Cx. quinquefasciatus* (Sasa 1976). This mosquito is highly domestic in nature; and breeds mainly in polluted water bodies adjacent to human dwellings. The adults are usually endophagic, with nocturnal biting habit. Endemic foci of *W. bancrofti* infection transmitted by this mosquito have been found almost all over the tropical and sub tropical regions.

The *Anopheles* type – The mosquito genus *Anopheles* contains a large number of species with different behavioural and ecological characteristics. Because most of the breeding places of anopheline mosquitoes are located in rural environments, this type of filariasis has been referred to as "rural filariasis" by various workers. In tropical Africa, *Anopheles gambiae*, *Anopheles funestus* and related species are the principal vectors of *W. bancrofti* in rural areas. Elsewhere, *Anopheles maculatus*, *Anopheles whartoni*, *Anopheles flavirostris*, *Anopheles punctulatus* have been shown to be the vectors of rural type of filariasis (Sasa 1976).

The *Aedes (Finlaya) poecilus* type – the nocturnally periodic *W. bancrofti* endemic in Philippines are transmitted mainly by *Ae.* (*Finlaya*) *poecilus*, whose larvae breed in the leaf axils of abaca plant. Mosquitoes of the sub genus and with similar breeding habits, called the "*Aedes* (*Finlaya*) *kochi* group" have also been proved to be efficient vectors of the diurnally subperiodic race of *W. bancrofti* in the Polynesian zone.

The *Aedes* (*Ochlerotatus*) *vigilax* type –a day biting mosquito, which breeds in the brackish water swamps has been shown to be the main vector of the diurnally subperiodic race of *W. bancrofti* endemic in the New Caledonian region.

Aedes (*Stegomyia*) *polynesiensis* type – mosquitoes in this group are the principal vectors of the diurnally subperiodic form *W. bancrofti* in the Polynesian region.

2.6 Entomological Aspects of the Vectors of Diurnally Subperiodic and Periodic Filariasis

2.6.1 Ecology

Filariasis due to diurnally subperiodic *W. bancrofti* in Samoa is transmitted mainly by two vectors, *Ae. polynesiensis* and *Ae. samoanus* (Ramalingam and Belkin 1964). Studies on the ecology and bionomics of these two vectors has been reported. Ramalingam (1968) and Suzuki and Sone (1974 & 1978) reported the wide distribution *Ae. polynesiensis* in the South Pacific. While *Ae. polynesiensis* is a container breeder, choosing a range of containers such as water storage drums, discarded receptacles and tree holes to oviposit, *Ae. samoanus* is a leaf axil breeder, restricting itself to axils of plants belonging to the family Pandanaceae. Samarawickrema *et al.* (1987) observed wide variations in biting densities between *Ae. polynesiensis* and *Ae. samoanus.*

2.6.2 Population Dynamics

Service (1976) described various techniques and methods to measure the population size of mosquitoes. Birch (1948) described a method for calculation of the net reproductive rate of an insect population based on the construction of age specific life and fecundity table. Southwood (1966) and Andrewartha and Birch (1954) described a method for calculation of the net reproductive rate of an insect population. Andrewartha and Birch (1954) and Southwood (1966) stated that an innate capacity of increase is a statistic and could be used in the study of population dynamics in assessing the capacity of an insect population to increase under a given physical and biotic environment.

Hayes (1975) studied the seasonal changes in the structure of an isolated population of *Cx. quinquefasciatus* in Texas, USA. Hayes and Downs (1980), from a time series analysis data collected from an isolated population, concluded that temperature influences all the developmental stages in the life history of *Cx. quinquefasciatus*. Rajagopalan *et al.* (1975) stated that the population size in the North Indian town of Faridabad was regulated by temperature and saturation deficiency and the density, survival, net reproductive rate (R_0) and intrinsic rate of increase (r_m) were very low during the hot month of June. De Meillon and Sebastian (1967a) reported that in Rangoon, Myanmar, where the climate is temperate throughout the year, the population of *Cx. quinquefasciatus* was regulated by rainfall. Contrary to this, in areas like Pondicherry, India changes in population size were regulated by physical environment and relative humidity and temperature do not play much role (Rajagopalan 1980).

2.6.3 Vector Implication, Infection and Infectivity Status

Following the classical studies of Bahr (1912) in Fiji, *Ae. pseudoscutellaris*, a day biting mosquito was considered to be the sole vector of subperiodic *W. bancrofti* in the South Pacific Islands. Marks (1951) clearly demonstrated that two species have been confused as *Ae. pseudoscutellaris* in all previous epidemiological studies in Fiji and indicated that the proven vector in most Polynesian areas was probably the new species, which she named *Ae. polynesiensis*. Later, Symes (1955,1960a, 1960b) established that both *Ae. pseudoscutellaris* and *Ae. polynesiensis* were efficient transmitters and that a third species, the night biting *Ae. fijiensis* of the *kochi* group was an equally efficient vector. This was later confirmed by Burnett (1960). Rosen (1955) and Symes (1955, 1960a, 1960b) showed that *Cx. quinquefasciatus*, the vector of periodic *W. bancrofti*, could also transmit subperiodic *W. bancrofti* to a limited extent in the Society islands and Fiji. Iyengar (1955) demonstrated that in New Caledonia subperiodic *W. bancrofti* was transmitted by *Ae. vigilax*. Belkin (1961,1962) pointed out the need for a re-examination of the potential vectors, particularly in the areas where one or more members of the *scutellaris* group and the *kochi* group have been reported.

At least four mosquito species/species groups viz., *Oc. niveus*, *Ae. scutellaris* group, *Mansonia (Mansoniodes) dives* and *Anopheles sundaicus* were reported to bite the aborigine tribes in the jungles of Nancowry group of Nicobar islands (Kalra 1974). Only one specimen of *Oc. niveus* group of mosquitoes was naturally found infected, but none was found with infective stage larva. The role of *Ae. scutellaris*, which is an established vector in some of the south east Asian countries (Gould *et al.* 1982 and Colless 1958), was not ascertained during this study. Russel *et al.* (1975) carried out similar survey, in the same group of islands (Kamorta), found natural infection in *Cx. quinquefasciatus* collected from human dwellings. One out of 150 mosquitoes was found to harbor infective stage larva. This suggests the probable co-existence of both periodic and subperiodic forms of *W. bancrofti* in Nancowry group of islands. During this survey, known vectors of subperiodic form of this species were however not checked. A study carried out by Tewari *et al.* (1995) showed that aborigine tribes who enter the forests are commonly bitten by *Oc. niveus* and *Ae. scutellaris*. *Oc. niveus* was found naturally infected with *W. bancrofti* with infection and infectivity rates of 1.1% and 0.9% respectively. *Cx. quinquefasciatus* was recorded in very low densities and on dissection was found not to be infected. All these studies including the entomological studies of Tewari *et al.* (1995) were based on short-term observations.

Samarawickrema *et al.* (1987) studied the infection and infectivity rates in *Ae. polynesiensis* and *Ae. samoanus* in Samoa. Infection and infectivity rates of *Ae. polynesiensis* were observed to be higher than *Ae. samoanus*. Samarawickrema *et al.* (1987) studied the transmission of subperiodic *W. bancrofti* in certain villages in Samoa, after mass treatment with DEC, and observed reduction in infectivity and infection rates in *Ae. polynesiensis* and *Ae. samoanus*. Rosen (1955) based on experimental transmission studies reported that any density of microfilariae detected in 20 μl of blood could be infective to *Ae. polynesiensis*. Bryan and Southgate (1976) on the contrary reported high infection rates in wild caught *Ae. polynesiensis* fed on carriers with low microfilaria counts.

2.6.4 Transmission Dynamics

The dynamics of transmission of filariasis was studied by various workers. Omori (1958) conducted a series of studies on the effects of temperature on the longevity of filaria larvae and host mosquitoes. Pichon (1974) and

Pichon et al. (1974) discussed with the help of certain mathematical models, the development of microfilariae into infective larval stage in relation to the number of mf ingested by vector mosquitoes. Pichon (2002) discussed the aspect of development of microfilariae into infective larval stage larvae in *Aedes* vectors and its implications in interruption of filariasis in areas where *Anopheles* spp are also involved in the transmission. Rosen (1955) and Bryan and Southgate 1976) reported that the filarial larvae do not cause significant mortality during their development, in vector population. However, Symes (1960) and Zielke (1977) made contrary observations and concluded that a proportion of mosquitoes die of filarial infection. Lardeux and Cheffort (2001) proposed a statistical model of extrinsic cycle duration as a function of temperature to describe three patterns of *W. bancrofti* transmission dynamics transmitted by *Ae. polynesiensis* among the French Polynesian archipelagos. Kartman (1954) formulated the host efficiency index, which is the ratio between the number of microfilariae ingested and the number of infective stages developed in the vector body. Failloux *et al.* (1995) reported variations in vector competences of six geographic strains of *Ae. polynesiensis* for *W. bancrofti* in French Polynesia.

LF due to subperiodic *W. bancrofti* is an important public health problem in the South Pacific. In Samoa the disease has been endemic for a long time and is transmitted by two species of mosquito, the day biting *Ae. polynesiensis* and night biting *Ae. samoanus*. There was a great deal of debate over the sites where the greatest amount of transmission of filariasis occurs in Samoa. From O' Connor's work (1923), it can be inferred that transmission occurred in the villages. Byrd *et al.* (1945) and Iyengar (1959e) stressed that the villages were the hyperendemic foci of infection. Jachowski and Otto (1952,1953), on the other hand, maintained that transmission of subperiodic *W. bancrofti* occurred mainly in a wild ecological niche. They found the transmission potential to be much higher in the plantations and in the bush along the trails to the plantations than in the villages. Jachowski and Otto noted that up to the age of puberty there was little difference in the microfilaria rate between the sexes, but from then onwards the rate increased with a significantly greater percentage in men than in women. They explained this difference as being due to the differences in habits of the Samoans. The women remained in the vicinity of the villages while the men worked in the plantations and were subject to greater exposure. McCarthy and Fitzgerald (1956) working in Samoa were also of the opinion that most of the transmission occurred in the plantations, along the paths leading to the water points, and in similar situations. Ramalingam (1968) was of the opinion that the site of transmission and the vector species are determined, to a large extent, by the particular ecological situation and by socio-economic factors. Zahar *et al.* (1980) reviewed the literature on subperiodic bancroftian filariasis in the South Pacific and emphasized the need to determine the exact association of vectors in different ecosystems where foci of transmission occur, so that appropriate vector control measures could be designed. Samarawickrema *et al.* (1987) reported active transmission of filariasis in Samoa by *Ae. polynesiensis* and *Ae. samoanus*, whose roles differed from village to village. Samarawickrema *et al.* (1987) reported a high Annual Transmission Potential for both these species in certain coastal villages and low potential in the others.

2.6.5 Biting Periodicity

The intensity of transmission of filarial infection in an area depends on the degree of man-vector contact. The biting pattern of *Ae polynesiensis*, a day biting mosquito is documented in the South Pacific Islands. The biting activity of this species was reported to be largely diurnal, though some female mosquitoes bite at night (Ramalingam 1968). Jachowski (1954) reported *Ae. polynesiensis* as being diurnally active with two peaks of activity, a lesser one in the morning, and a greater one in the afternoon.

Various workers have studied the biting habits and host preference of *Cx. quinquefasciatus*. Sasa *et al.* (1965) reported that *Cx. quinquefasciatus* preferred to bite indoors in Bangkok, Thailand, whereas in Rangoon, Burma, it preferred to bite outdoors (De Meillon and Sebastian, 1967b). Rajagopalan *et al.* (1977b) observed that in Delhi, India, the outdoor biting density was higher than the indoor biting density in all months except in September. Studies by Samarawickrema (1967) in Ceylon showed that the overall peak biting activity occurs in the midnight hours and the females of each age group have their own peak biting activity. Sucharit *et al.* (1981) reported that there were two minor peaks of activity, one between 22.00 and 23.00 hrs and the other between 01.00 and 04.00 hrs. Haddow (1960) proposed the geometric mean as modified by C.B. William to analyze the results of long series catches such as all night biting catches. De Meillon and Sebastian (1967b) reported that the peak biting activity occurs in midnight hours and it correlated with the microfilarial periodicity in humans. Subra (1972) concluded that age would affect the biting activity of the endophagous females, particularly during rainy season. Self *et al.* (1969) observed that the legs below knees were the preferred biting sites of *Cx. quinquefasciatus.*

2.6.6 Physiological Age Grading, Parity and Survival

Perry (1912) distinguished the old adults from young ones by the degree of wear and rubbing on the wings. Mer (1932) observed that the ampulla at the anterior end of the common oviduct increased in size during oviposition and did not return to normal size afterwards. Corbet (1960, 1962) reported that the external wear of the abdominal sternites is a useful and reliable method to differentiate the nulliparous and parous mosquitoes. Self and Sebastian (1971) found that a large proportion of newly emerged females exhibit green coloration in thorax and abdomen regions. Detinova (1945) observed that by the presence or absence of "skeins" on ovary the parous mosquitoes could be differentiated from nulliparous mosquitoes. Polovodova (1949) described a method, in which the physiological age of the mosquito can be accurately determined based on the number of ovarian relics on the ovariole pedicels. The age structure of the population of *Ae. polynesiensis* was studied by Samarawickrema *et al.* (1987) in Samoa.

The age structure of the population of *Cx. quinquefasciatus* was studied by Samarawickrema (1967) in Ceylon and Nathan (1981) in Trinidad. Detinova (1962) also reported formation of false dilatation due to degeneration after a blood meal. Nawab Singh and Yasuno (1972) studied the gonotrophic cycle duration in *Cx. quinquefasciatus* in nature during cold, rainy and hot seasons in Delhi, India, using the mark-release capture techniques.

Laurence (1963) calculated the daily survival rate of *Cx. quinquefasciatus* in Vellore, India based on the parity status in adults and the number of mosquitoes infected with various stages of filarial larvae. Samarawickrema (1967) also calculated the daily survival rates based on parous rates for *Cx. quinquefasciatus* in Ceylon. Macdonald (1957) and Gillies (1961) computed the survival rates of anopheline vectors and observed that mosquitoes die rapidly due to various factors also other than old age. Reisen *et al.* (1980) studied the survivorship estimated by vertical age grading methods and daily survivorship based on decline in the recapture of marked females. Muirhead Thomson (1938) found that mosquitoes of different age groups show different responses to temperature and humidity. Hitchcock (1970) studied the age composition and infection rates of various age groups of vector mosquitoes in the South Pacific island of Tonga.

2.7 Taxonomic Status of *Oc. niveus*

This species was originally described as *Aedes* (*Finlaya*) *niveus*. *Ae. niveus* is definitely known to occur only in the Philippines and Vietnam (Knight 1946, Harrison *et al.* 1990). Colless (1958) described a distinct subspecies, *Ae. niveus leonis* , from Singapore. Harrison *et al.* (1990) elevated this to full species status, stating that it occurs in Singapore, Malaysia and Thailand. These nomenclatural changes added to the difficulty in the identification of *Ae. niveus*. However, Tewari and Hiriyan (1995) who collected large number of specimens in the Andaman and Nicobar Islands redescribed *Ae. niveus* and confirmed it to occur as a single species in these islands. There is no need to distinguish *Ae. niveus* from *Ae. leonis* in the Andaman and Nicobar islands because only *Ae. niveus* occurs there (Tewari and Hiriyan, 1995).

Consequent to the elevation of subgenus *Ochlerotatus* to generic rank and the reclassification of the other subgenera by Reinert (2000), *niveus* is now placed in the genus *Ochlerotatus* and is known as *Ochlerotatus* (*Finlaya*) *niveus*.

This species which has been incriminated as a vector of diurnally subperiodic *W. bancrofti* in the Nicobar islands (Tewari *et al.* 1995) has been known as *Ae. niveus* for a long time to the public health specialists and vector borne disease control personnel. This nomenclatural change may be seen as adding to the confusion, to whom this species was known as *Ae. niveus* for a long period. However, to quote Reinert "*I do not highly undertake the division of genus Aedes because many of the species transferred to genus Ochlerotatus are vectors of disease pathogens, have medical and veterinary importance, and have long been known as Aedes. However, I believe the creation of more natural and better defined genera are valid reasons for proposing this change and outweigh the initial inconvenience of the generic change of the affected species*"

2.8 Control of Subperiodic Bancroftian Filariasis

Vector control has traditionally played an important role in the control of LF. Measures designed to reduce vector abundance and/or man-vector contact still provide useful adjuncts to the effects of treating the human population to reduce transmission. In the present section the evolution of filariasis control in the South Pacific islands is discussed.

Vector control was once advocated as the primary tool to control filariasis because effective antifilarial drugs were unknown and MDA campaigns were believed to be too labour intensive. In the 1960s and 1970s, there was a shift in the control strategy to MDA-based campaigns, which often achieved significant reductions in mf prevalence and densities (Ichimori 2001; Esterre *et al.* 2001; Laigret *et al.* 1980). The first two campaigns began in 1966 and 1971 using 12-18 Diethylcarbamazine (DEC) treatments (Ichimori 2001). The DEC treatments consisted of weekly doses of 5mg kg^{-1} bodyweight for six weeks followed by monthly treatments with DEC at 5mg kg^{-1} body-weight. Single, annual doses of DEC at 6 mg kg^{-1} body weight were then administered in 1982, 1983 and 1986. These efforts reduced the mf prevalence from 21% in 1964 to 2.3% in 1987. The mf prevalences had declined to 0.14% in 1974, following the second DEC campaign, but rebounded to 2.1% within two years (Ichimori 2001).

An even more intensive effort was expended on filariasis control in Maupiti, French Polynesia. Since 1955, excluding the years 1960-1967 and 1970 -1974, twice yearly DEC chemotherapy with 6 mg kg^{-1} body weight was administered to an average of 85% of the population in Maupiti (Esterre *et al.* 2001). In addition, mosquito control using DDT from 1955 –1957 and destruction of larval breeding sources from 1955-1970 were implemented. Despite these efforts, 0.4% of residents were positive for mf with 4.6% having antigenaemia in the year 2000 (Esterre *et al.* 2001).

Thus, after cessation of the MDA campaigns in Samoa and French Polynesia, mf prevalence often rose rapidly (Kimura *et al.* 1985; Ichimori 2001; Esterre *et al.* 2001). Whereas these extensive campaigns succeeded in minimizing filariasis temporarily as a public health problem by significantly reducing the number of clinical cases, the elimination of the parasite was not achieved.

In 1997, the World Health Assembly Adopted Resolution (WHA, 1997) which called for the elimination of LF as a global health problem. In March 1999, consecutive meetings between the Ministers and Directors of Health of Pacific island countries and territories endorsed a resolution to develop and implement comprehensive strategy to eliminate LF from the Pacific. Following this resolution, PacELF was formed (Dean 2000) with assistance from the Secretariat of the Pacific Community (funded by the Australian Agency for International Development) and the WHO. PacELF is responsible for the coordination of antifilariasis programmes in the twenty two Pacific island countries and its territories. The twin goals of PacELF are to stop transmission of filariasis and to alleviate the suffering caused by the disease.

The primary strategy of PacELF is mass drug administration (MDA) of DEC (6mg kg $^{-1}$ bodyweight) and albendazole (400 mg per person) in a single, annual dose with health education and clinical care of infected cases. Pacific island countries, particularly Samoa and French Polynesia, have a long history of MDA campaigns using DEC to control LF.

In 2000-2001, the 22 Pacific island countries and territories in the PacELF having a population of over 7.6 million were within the ambit of the global filariasis elimination programme. Similar to earlier DEC based MDA campaigns in Samoa (1966, 1971, 1982, 1983 and 1986) (Ichimori 2001) and French Polynesia (1955 to the present) (Esterre *et al.* 2001), the DEC plus albendazole based PacELF MDA campaign is showing a dramatic immediate impact on filarial prevalence in humans (Burkot and Ichimori 2002).

The challenges to filariasis elimination campaigns based on MDA alone have been reviewed by Burkot and Ichimori (2002). These challenges together with the previous successes of vector control campaign in eliminating filariasis from regions in the Pacific argue for inclusion of entomological components in the control of filariasis and monitoring filariasis elimination programmes.

The control of LF implies both stopping the spread of infection (transmission control) and alleviating suffering caused by the disease (morbidity control). Thus for use throughout the world, with an exception in the loiasis or onchocerciasis zones of sub-Saharan Africa, either of the following two approaches is recommended (Ottesen *et al.* 1997):

I. Once-yearly "single dose" treatment (for 5-6 years) with either:

-a two drug regimen (optimal):ivermectin (200µg/kg body weight) co-administered with either DEC (6mg kg $^{-1}$ body weight) or albendazole (400 mg);

or

-a one drug regimen: DEC (6mg kg $^{-1}$ body weight) alone

II. DEC fortified salt (0.2-0.4% w/w) substituted for regular table/cooking salt for 6-12 months.

Mosquito surveillance and control is already in place in many Pacific island countries. However, the efficacy of anti-vector interventions has rarely been evaluated for its impact at population level. For instance, *Mesocyclops aspericornis*, a predaceous copepod, reduced the number of *Ae. polynesiensis* larvae breeding in treated crab holes (the major breeding habitat of this species) by 98%. Despite the treatment of over 14000 crab holes in one study, there was no measurable impact on the numbers of *Ae. polynesiensis* biting (Lardeux *et al.* 1992). Vector control in the case of *Oc. niveus* has not been attempted due to inaccessibility of the breeding habitats (tree holes) and adult behaviour (exophagic and exophilic).