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2007 ELIMINATION OF LYMPHATIC FILARIASIS IN KOREA

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FORWARD

People in the world nowadays live altogether as a global family. The world becomes narrower and narrower and the tropical diseases, most of which are caused by parasitic organisms are no more endemic diseases limited to certain localities of tropical region, but are of global health problems, which might easily spread over the country. Parasitic diseases such as soil-transmitted helminthiases and water-borne protozoan diseases, which had been prevalent in developing countries due to a poor personal hygiene, have been significantly reduced in several countries. However, parasitic diseases of vector borne parasitic diseases including malaria, trypanosomiasis, leishmaniasis and filariasis still invoke formidable problems worldwide. The diseases have been evidently associated with chronic morbidity and severe mortality in several regions of the world.

The lymphatic filariasis had been prevalent in Korea more than 1,000 years before. Authentic cases of filariasis had been firstly identified in 1927. Thenceforward, Jeju-do, northern part of Gyeongsangbuk-do and remote islands of southwestern parts of had been found to be moderately endemic for lymphatic filariasis in Korea. From the early-1960s, public health officers and scientists of the central government and Universities started to investigate the epidemiological characteristics, clinical manifestations, and other aspects of the lymphatic filariasis including identification and characterization of vector mosquitoes. During this period, Professors in the Department of Parasitology, Seoul National University College of Medicine, performed intensive studies in Jeju-do, area in which the disease had been most highly prevalent in this country. Japanese Scientists also greatly supported us in this period. Scientists also conducted researches for the detection and treatment of the patients during the 1970s-1980s. Centers for Disease Control and Prevention (CDC) has performed central roles during these periods.

Their sincere, dedicated efforts followed by a rapid and remarkable economic growth of Korea, the lymphatic filariasis had been rapidly reduced from the mid-1980s in endemic areas of Jeju-do and Jeollanam-do. Gyeongsangbuk-do inland areas were also found to cease transmission of microfilaria in 1987 by surveillance survey.

CDC carried out a surveillance survey for lymphatic filariasis from 2002 to 2006 in Jeju-do, Gyeongsangbuk-do and Jeollanam-do, areas in which the disease had been endemic. Their clinicoepidemiological surveillance survey confirmed that transmission of lymphatic filariasis in Jeju-do, Gyeongsangbuk-do, and Jeollanam-do had been terminated more than 30 years ago. Occurrence of new case of the lymphatic filariasis including elephantiasis has not been recognized from the late 1980s.

It is hereby my great pleasure and certainly an honor to have this opportunity to report an elimination of lymphatic filariasis in Korea to WHO. In order to make country free of chronic endemic diseases of neglected concerns, our experience has indicated that not only people in our own country but also those in every country should closely and actively cooperated with sincere partnerships, and have coalition and alliance each other.

I extend my sincere gratitude to you and through you to all the colleagues who have been working over a long period of time in first line of filariasis control in the Republic of Korea. Finally, I would like to express my honest condolescence to all of the victims of the lymphatic filariasis in our country as well as in the world.

Jong-Koo Lee, MD, PhD
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PREFACE

It is my great pleasure and certainly an honor to take this opportunity to extend my cordial greetings to all of whom dedicated their sincere efforts on the control and management of the lymphatic filariasis in Korea, once had been prevalent in our country.

Lymphatic filariasis, caused by filarial nematode, *Brugia malayi*, represents one of the most common helminthic infections, and has been shown to be definitely associated with significant mortality and chronic morbidity in several regions in the temperate and tropical zones. When the disease is coupled with chronic elephantiasis, the burden of the disease is substantially exacerbated by the associated social stigma. Therefore, early identification and block transmission of the disease may have great impact not only on the treatment of infected individuals but also on the reduction of the disease burdens in certain communities.

Korea had been endemic for lymphatic filariasis more than 1, 000 years long. However, scientific investigation and control program against the lymphatic filariasis had been launched on the early 20th century. Scientific identification of lymphatic filariasis including elephantiasis was conducted in 1927 for the first time in Korea. During the 1960s, the tropical disease research center of Seoul National University had detected and treated lymphatic filariasis patients in Jeju-do, where the disease had been most prevalent in Korea. They also identified the vector host for filariasis in Jeju-do. National Institute of Health (NIH), as an execute center for elimination of the lymphatic filariasis in inland area in Yeongju-si, Gyeongsangbuk-do, concentrated their efforts on the management of this ancient disease. This systematic and intensive eliminating program for lymphatic filariasis brought to decline the infection rate in this country.

Block transmission of the microfilaria was achieved in the mid-1980s in Gyeongsangbuk-do. In addition, affected patients in Jeju-do had been greatly reduced by end of the 1980s. There had been no authentic case when we performed an epidemiological survey in 2005 as one more surveillance. However, during the mid-1980s, southwestern costal and remote islands areas of Jeollanam-do such as Sinan-gun and Wando-gun were newly found to be moderately endemic for lymphatic filariasis. These patients were treated with diethylcarbamazine combined with ivermectin, and transmission ability was interrupted by surveillance survey during the early-2000s.

Over the past several decades from 1950-2000, we concentrated our efforts on the detection, treatment and follow-up of the lymphatic filariasis patients in highly epidemic areas in Korea. Mass chemotherapy with diethylcarbamazine to microfilaria positive persons and case detection by active intervention and selective treatment not only made them free from microfilaremia but also significantly reduced the microfilarial density in affected patients in the local communities. This resulted in the loss of propagation ability, and undergoes natural cure in Korea, which had been thought to be the most important factors for the elimination of the lymphatic filariasis. Furthermore, improved residential life style of local people is believed to contribute to have decreased the opportunities for residents to be exposed to vector mosquitoes.

The government, university, and concerned health institutes have continuously focused on their efforts to eliminate lymphatic filariasis, which results in stop transmission in Korea. Its occurrence in the human host could not be detected from 2002 to 2006 by surveillance surveys in Gyeongsangbuk-do (594 residents in 8 islands and 16 villages), Jeollanam-do (5,488 people from 63 islands and 101 villages) and Jeju-do (3,344 examinee in 4 islands and 20 villages), where the disease had been prevalent in Korea.

In addition to remarkable economic growth followed by improved personal hygiene and living standard, all of these efforts contributed to the loss of propagation ability of the microfilaria, and fade of this mosquito-borne ancient disease in the Republic of Korea.

Once again, I sincerely appreciate the officers of the Korea National Institute of Health and local government, Professors who belong to the Korean Society for Parasitology and the staffs of the Korea Association of Health Promotion for their active and devoted participation during a long period of time for elimination of lymphatic filariasis in the Republic of Korea.

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8. 27. 2007

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2007 ELIMINATION OF LYMPHATIC FILARIASIS IN KOREA

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Part I

HISTORICAL REVIEW OF LYMPHATIC FILARIASIS IN KOREA

1. Introduction

Historically, Korea was endemic area for lymphatic filariasis, which had been caused by the nematode parasite, *Brugia malayi*, more than 1, 000 years before. Elephantiasis of the lower extremities was also found in certain localities in Korea. Elephantiasis of the lower extremities was traditionally called "Soojongdari (leg dropsy)" or "Darijeongeung (king leg)". In addition, when lymphangitis and lymphadenitis associated with fever and transient joint swelling, it had been called "Pinaerim (blood down flow)", "Pijeong (blood disease)" or "Gakmomsal (malaise with arthralgia)" (Seo, 1978).

Scientific identification of lymphatic filariasis including elephantiasis was conducted in 1927 for the first time in Korea (Yun, 1927). Subsequent epidemiological studies in middle-south areas of Korean peninsula showed that 2.1-18% of the persons examined were microfilaria positive cases in their peripheral blood smear (Oh, 1929; Moon, 1939). An intensive study revealed 12.1% microfilaria positive cases (604/5,001 cases) throughout South Korea (Senoo and Lincicome, 1951). During the period, the patients had been thought to be infected with *Wuchereria bancrofti* and secondarily with *Streptococcus* spp (Yun, 1927). However, clinical manifestations of these patients were substantially different from those observed with bancroftian filariasis. Neither chyluria nor scrotal involvement could be observed even in the cases with advanced stages. Senoo (1943) indeed identified the microfilaria affected with these patients were associated with *B. malayi*, but not with *W. bancrofti*.

It is not well described and is still curious that when lymphatic filariasis became prevalent in the Korea. According to the scientific literature (Seo, 1978), it seems likely that, at least, filariasis was not endemic in this peninsula prior to the Koryo Dynasty (935-1392 AD, Korea). During the Koryo Dynasty, the import/export transportations and communications between the Koryo and the Song (960-1279 AD, China) or Yuan Dynasty (1280-1368 AD, China), and south-east and middle Asian countries were substantially increased by via sea routes from central coastal areas of China (e.g., Shanghai) through southwestern islands (the Heuksan Islands) to Yeongam-gun, Jeollanam-do, Korea. In addition, some castaways arrived from southern China as well as other southeast Asian countries such as Sri Lanka, Indonesia, the Philippines and Malaysia where lymphatic filariasis might be endemic. Based on these descriptions, lymphatic filariasis is thought to be an imported disease in Korea.

Japanese scientists (Fujimori, 1924; Murakami, 1925) reported a presence of elephantiasis in Korea for the first time. Yun (1927) subsequently demonstrated a filarial worm in a sectioned left inguinal lymph node at autopsy of an elephantiasis patient who had been born in Chungcheongnam-do (middle part of Korea). Oh (1929) also observed microfilariae in the peripheral blood of 24 Koreans and described nocturnal periodicity. An epidemiological survey of 527 elephantiasis cases in Chungcheongnam-do demonstrated that 12 patients were microfilaria positive in their blood. A series of epidemiological survey in Chungcheongnam-do, Jeollabuk-do and Jeju-do observed that hydrocele or chyluria were hardly associated with these patients. It was later found that Korean elephantiasis mainly affected with the lower extremities and occasionally with the arms but never involved in the external genitalia (Moon, 1940).

Senoo (1943) recognized that the microfilariae found in southern Korea to be identified as Microfilaria *malayi*. Nelson et al. (1946) also reported the occurrence of *Wuchereria malayi* in 8.5% of 570 Korean prisoners of the World War II. Senoo and Lincicome (1951) reported the distribution of brugian filariasis in Korea by examining 5,001 patients representing 25 villages from South Korea. They found that 604 of the patients were microfilariae positive in their peripheral blood, all of the causative agent has been identified as *W. malayi*. Their epidemiological survey concluded that the highest incidence of *W. malayi* had occurred in Jeju-do, the next in the southwestern areas, and the lowest in the southeastern areas of the Korean peninsula. The mosquito vectors responsible for the transmission of lymphatic filariasis, however, could not be identified by this time.

2. *Launching of epidemiological survey and control strategies against lymphatic filariasis in Korea during the post-Korean War to the late 1970s*

An epidemiological survey for endemic filariasis conducted in the 1950s demonstrated 9.2% of positive rate (19/206 cases) (Paik et al., 1957) in Chungcheongnam-do. Subsequent surveys reported that 11.4% (26/229 schoolchildren) and 22.2% (79/356 inhabitants) (Lee et al., 1961, 1964). Night blood specimens collected from 2,139 inhabitants who resided in 15 villages in Jeju-do showed 8.6% of microfilaria positive rate (Seo et al., 1965). It was later found that filariasis distributed throughout the southern Korea except Gyeonggi-do and Gyeongsangnam-do. A total of 601 cases out of 30,534 persons examined (2.0%) were found to be infected with *B. malayi*. They reported that there were three major endemic foci of brugian filariasis in Korea, including the northeastern part (inland) of Gyeongsangbuk-do, the western coastal areas of Jeollanam-do and Jeju-do. Jeju-do was found to be highly endemic, while other two localities were found to be moderate to low endemic.

Several investigators thereafter plotted out endemic areas in Namwon-myeon and Pyosun- myeon which were the most highly endemic areas in Namjeju-gun, Jeju-do (data not shown). In these areas, mass chemotherapy with diethylcarbamazine had been extensively conducted during 1968 and 1973. In the inland of the northeastern areas of Gyeongsangbuk-do, the prevalence of lymphatic filariasis was reported to be in the range of 3.1 to 13.4% (Hwang et al., 1965; Seo et al., 1968; Kim et al., 1971,1977; Soh et al., 1974). In the endemic areas of Yeongju-gun, Gyeongsangbuk-do (one of these inland areas), a mass and selective treatment with diethylcarbamazine was carried out to *B. malayi* microfilaria positives (Soh et al., 1977). In contrast, the western coastal and plain areas were found to be relatively low endemic; 1.5% at Daedeok-gun, Chungcheongnam-do, and 2.0% in Jindo-gun of Jeollanam-do (Table 1).

Chemotherapy of the lymphatic filariasis conducted in Jeju-do during the 1960s and the early 1970s. The conventional dosage of diethylcarbamazine had been applied in the initial stage of the control program (Seo et al., 1973). Unfortunately however, many of the treated cases had severe side reactions with febrile attacks for the first several days of the drug administration and this had seriously hampered further implementation of the filariasis control programs. This problem had been overcome after introduction of low dosages daily or with a gradual increase of daily dosages after several days of initial administration, totaling 36 mg/kg in a full course during the early 1970s. In Yeongju area of Gyeongsangbuk-do, microfilaria positives were medicated with diethylcarbamazine 1 mg/kg of body wt, daily for 36 days (Soh et al., 1977).

According to Lee (1978), there were 9 genera of mosquitoes such as *Anopheles, Culex, Aedes, Armigeres, Mansonia, Heizmannia, Tripteroides, Culiseta and Tozorhynchites* in Korea. *Aedes togoi* was recognized as the vector mosquito of *B. malayi* in Jeju-do, Korea (Lee et al., 1964; Kim et al., 1973). In addition, *An. sinensis* was also found to be the vector mosquito responsible for transmission of *B. malayi* in inland areas (Kim et al., 1974, 1977). In experimental infection, both *Ae. togoi* and *An. sinensis* were highly susceptible to *B. malayi*.

3. *Control of lymphatic filariasis in Korea since the 1980s*

Jeju-do had long been known as the highest endemic area of lymphatic filariasis in Korea with the highest microfilaremiae 19.5% in Taeheung-ri, Namjeju-gun until the 1970s. The microfilarial density was 3.63/µl blood (Seo et al., 1965). The prevalence of filariasis decreased to a significantly low level of 0.5% following mass and selective treatments conducted since 1968 (Kim, 1994). A survey done in 1988 in four villages of Jeju-do that were formerly well known endemic areas observed that microfilaremia among the inhabitants was 0.3% out of a total of 357 persons (Paik et al., 1988). On the other hands, in the eastern inland area (Gyeongsangbuk-do), the moderate endemicity of lymphatic filariasis during the early 1970s was considered to be almost eliminated in the 1980s with selective treatments. The average microfilariae positive rate of this area in the late 1960s and early 1970s were 3.1% and 8.1%, respectively. Long term evaluation surveys with two 7 year intervals conducted in the 7 sample villages have revealed that the microfilariae rates decreased from 12.4% in 1973 to 2.2% in 1980 and 0% in 1987 (Kim, 1994).

The transmission of the filariasis in the formerly known endemic areas in Korea had been thought to be almost ceased around the middle of the 1980s (Kim et al., 1980, 1994; Lee et al., 1985, 1987). However, in a series of extended investigation conducted in the 1980s, groups of islands including Daeheuksan-do of Heuksan-myeon, located in the southwestern part of the Korean peninsula were belatedly found to be moderately endemic with *B. malayi* filariasis (Lee et al., 1986, 1987, 1988, 1989, 1992, 1995). Surveys in these areas demonstrated relatively high microfilaria rate among inhabitants with 11.2% on the average out of a total of 2,159 persons examined by 120$\mu\ell$ of nightblood in the 29 villages of the 15 small islands from 1985 to 1988 (Lee et al., 1986, 1987, 1988). All of the islands surveyed were found to be endemic and the microfilaria rates ranged from 2.2% to 22.4% by island. The positive cases were found in all age groups, being increased gradually in older age groups. Microfilarial density of the positive cases was relatively low. The average microfilaria count for 198 positive cases was 33.4 per 120 µl of night blood. In Wando-gun, Jindo-gun, and Yeosu-si of Jeollanam-do in the southern areas, the microfilaria rate was 2.5% with a moderate density in 1990 to 1992 (Lee et al., 1992). In Yeongju area, the microfilaria positives found on the islands in Sinan-gun were treated with diethylcarbamazine with the low dosage schedule from 1986 to 1992, and these treatments reduced microfilaria rate in this area from 12.3% to 1.4% in 2000 (Chai et al., 2003).

Most recently, we performed a large scale antibody test in 3,049 school children aged 10-13, in areas where *B. malayi* had been prevalent, using BRUGIArapid™ (MBDr, Malaysian Bio-Diagnostics Research), and found that no case was positive. This data may reflect the transmission of filariasis in the Republic of Korea probably has already terminated. Mass and selective chemotherapy with diethylcarbamazine conducted on and off by area since the 1960s, and remarkable economic growth followed by improved living standards, improvement of housing conditions, and elevated life-style of inhabitants seem to have contributed to the disappearance of this mosquito-borne disease in the Republic of Korea.

The important factors that contributed to block the transmission of lymphatic filariasis in inland Korea might include selective chemotherapy with diethylcarbamazine, as well as improvement of the quality of life including housing (Kim et al., 1980; Lee et al., 1987). The situation was similar in remote islands. In addition, changes of the out-door environment , improvement of personal sanitation and decrease in the number of residents in remote areas in these islands may have contributed to block the transmission of filariasis in the Republic of Korea.

4. Vector mosquitoes of lymphatic filariasis in Korea

With regard to *B. malayi,* which had been endemic in Korea, two species of the mosquitoes, *Ae. togoi* and *An. sinensis* had been served as the main vector.

In Jeju-do, *Ae. togoi* caught in 4 local villages were found to be infected with *B. malayi* third-stage larva, which is an infective to human (Lee et al., 1964). Subsequently, a lot of studies have demonstrated that *Ae. togoi* served as the main vector for lymphatic filariasis in the Republic of Korea (Chun, 1968; Lee et al., 1989). The infection rate of the mosquitoes varied from 0.3% to 8.8%. The third-stage larva of *B. malayi* was identified from *Ae. togoi* mosquitoes caught in Manje-do (Island), Sinan-gun, by rearing the fed mosquitoes for 10 days. *An. sinensis* and *Ae. togoi* were shown to be highly susceptible to the filarial infection, while *Ae. koreicus* had poor susceptibility. It was impossible to infect *Culex pipiens* (Kim et al., 1971). High susceptibility of *Ae. togoi* to *B. malayi* infection was repeatedly reported in Korea (Seo and Lee, 1973). In a blood feeding experiment with *Ae. togoi* mosquitoes caught in Manje-do, Heuksan-myeon, a total of 70 third-stage larvae of *B. malayi* were obtained in 25 of 313 blood-fed mosquitoes (Lee et al., 1989).

The vector efficiency of *Ae. togoi* mosquitoes under natural conditions was found to become lowered when compared to that of artificially cultivated mosquitoes (Lee, 1969), however, the mosquitoes could still serve as a vector for *B. malayi* filariasis. *Ae. togoi* also served as a vector for the dog heart worm, *Dirofilaria immitis.* Its third-stage larva was found in 1 of 9 experimentally infected mosquitoes.

An. sinensis was shown to have high susceptibility, which suggested that this species would serve as a vector mosquito in inland Korea (Kim et al., 1971). Kim et al. (1973) identified

128 third stage infective larvae from 14 mosquitoes by examining 4,351 *An. sinensis* in Yeongju-gun (Kim et al., 1974, 1977) *Ae. togoi* is known to be the dominant species in remote islands of Korea. In Heuksan-do (Island), *Ae. togoi* was caught by light traps indoors (90.8% of the total mosquitoes trapped) as well as outdoors (75.7% of the total). Among the mosquitoes caught in the daytime, resting places, *Ae. togoi* was the dominant species (78.0%). All these results indicated that *Ae. togoi* was the most important vector mosquito that could transmit filariasis in remote islands in the Republic of Korea (Lee et al., 1986; Lee et al., 1992). *An. sinensis* was the main vector species in inland korea where *Ae. togoi* does not exist (Tables 3 and 4) (Kim et al., 1971, 1973).

Ae. togoi was shown to suck blood from sunset to sunrise; they suck blood from 7:00 - 8:00 pm (30 minutes after sunset) to 05:00 - 06:00 am (30 minutes before sunset), with the peak period of 10:00 pm - 02:00 am (Ree et al., 1987). These results showed that an occurrence of microfilariae in the peripheral blood was closely related with the active feeding time of *Ae. togoi*, implying that *Ae. togoi* could play the role of a highly susceptible vector host for lymphatic filariasis. It was shown that *Ae. togoi* bite humans more actively indoors than outdoor (1:0.63). *Ae. togoi* could mature an initial egg batch without feeding a blood meal. The autogeny rate among the natural populations was 3.1% at Heuksan-do and Wan-do and 24.8% in Jeju-do in May (Ree et al., 1988).

The relationship between the periodicity of microfilariae in the peripheral blood and the blood sucking time of the mosquitoes was analyzed (Lee et al., 1992). The periodicity of microfilaremia was observed in 6 patients from 9:00 pm to 07:00 am in the next morning by 2-hour intervals, employing 50 µl of the peripheral blood. They showed a typical nocturnal periodicity (Lee et al., 1988). The lowest microfilaremia was observed from 11:00 am to 3:00 pm. It gradually increased from the evening to mid-night (9:00 pm), and reached a plateau approximately 01:00 am (1.6 microfilariae/µl). The highest microfilaremia in the patient blood was observed during 11:00 pm - 05:00 am (1.1-1.4 microfilariae/µl). Human biting mosquitoes actively sucked the blood from 7:00 pm to sun-rise in the next morning. Their peak human biting was observed during 01:00 am - 03:00 am. The results demonstrated that the occurrence of microfilaremia in the peripheral blood was highly correlated with the time of high activity of mosquitoes.

5. Pathobiology and clinical manifestations of lymphatic filariasis in Korea

It has long been suggested that there are three major pathogenetic factors responsible for pathobiological alterations in lymphatic filariasis; an allergic reaction elicited by metabolites of the worms, mechanical blockage of lymphatics due to the existence of immature or adult worms, dead or alive, and fibrosis and blockage of the lymphatics due to secondary microbial infections. A sudden onset of lymphangitis with pain, urticaria, swelling and regional lymphadenopathy is considered to be provoked by allergic reactions during the early acute stage of filariasis. This early allergic reaction is usually accompanied by proliferative and granulomatous changes in the lymphatic wall and lymph node structures.

Clinical manifestations observed in Korean patients were found to be fairly different from those of bancroftian type reported in Kyushu, Japan (Moon, 1939, 1940; Ewert et al., 1972). One of the unique characteristics included that most of elephantiasis patients in Korea did not reveal microfilaremia in their peripheral blood smear, while *Streptococcus haemolyticus* was isolated from erysipeloid skin lesion of the patient. It was later found that when the isolated streptococci were subcutaneously inoculated into normal adults and the microfilaria positive or elephantiasis cases, only the latter showed strong local or generalized reactions which resembled the recurrently found symptoms during the clinical course of lymphatic filariasis (Moon, 1940). On the other hands, after inoculation of streptococci mixed with the saline extract of *Dirofilaria immitis*, very strong reactions were observed even in the normal human skin or subcutaneous tissues, as well as in the scrotal tissues of experimental rabbits. These data strongly suggested that frequent episodes of lymphangitis with filarial fever were caused by the parasites, in association with bacteria such as *S. haemolyticus* (Moon, 1940). Many investigators, however, agreed with the following pathogenetic mechanism that the initial tissue responses are provoked by the parasites and their metabolic products, but not by supervening secondary bacterial infections such as *S. haemolyticus* (Ewert et al., 1972; Beaver et al., 1984). This hypothesis became more evident, and it might be accepted that in early stages of filariasis, allergic reaction of the host tissues to the filarial worms and their metabolites are the main factor for the pathogenesis of lymphangitis, and in later stages mechanical blockage of the lymphatics by the degenerating parasites causes extension of the lesion and fibrous tissue repair which are responsible for the development of elephantiasis.

The episodic febrile attacks accompanied by acute lymphadenitis and lymphangitis are the clinical manifestations characteristic to the early stage of lymphatic filariasis. This allergic lymphangitis is caused by the introduction of fresh infective larvae. The attacks are usually recurrent, and known as "Momsal"in filariasis endemic areas including Jeju-do. When lymphangitis is associated with febrile attack and transient swelling of the extremities, it is traditionally called "Pinaerim" or "Pijong" in these endemic areas. This clinical manifestations, "Pinaerim" or "Pi-Momsal" (combines "Momsal" with "Pinaerim"), lasts several days and recurrently occurs several times in a year. However, the "Bagu", a small itching erythematous edema, a term described as an initial skin lesion of lymphatic filariasis in Hachijo-Koshima, Japan, was hardly recognized in Korean patients. The recurrent febrile attacks, "Momsal" and the repeated occurrence of lymphangitis, "Pinaerim", seemed to be important factors that may consequently result in elephantiasis in some of the infected cases. Enlargement of lymph nodes was also found in some cases; large in size, not hard, rather rubbery in consistency and movable. The most commonly affected site is the inguinal lymph nodes. In few cases, hard cord-like lymphatics and varicose nodes were also observed. No case of lymphangitis of the spermatic cord or lymph-scrotum, which was commonly seen in bancroftian filariasis, was recognized in lymphatic filariasis patients in Korea (Seo, 1978). However, two cases of scrotal hypertrophy were observed in Jeju-do, albeit it was unclear whether these changes might have originated from a filarial infection (Soh et al., 1966). Clinical signs such as chyluria, haematochyluria or chylous effusions were not usually observed in Korean patients, but elephantiasis of the extremities, locally termed as "Soojongdari", was frequently observed. However, most of cases demonstrated relatively mild symptoms, including only slightly enlarged legs and arms with smooth surface. The episode of recurrent febrile attack, lymphangitis, and elephantiasis are the most important clinical signs of lymphatic filariasis found in Korea.

To figure out the clinical manifestations of lymphatic filariasis in Korea, field surveys were conducted in Nonsan and Buyeo, Chungcheongnam-do (Moon, 1939) and Jeju-do (Moon, 1939) during the earlier period between 1939 and 1940. The reports demonstrated that males showed a higher prevalence than females. In Chungcheongnam-do, out of 161 cases examined, the proportions of males and females were 85.1% and 14.9%, respectively (Moon, 1939). The onset age of "Momsal" fever was between 15 and 25 years old, and more than 100 cases were found in the age between 40 and 60 years. The febrile attack occurred most frequently in October and the symptoms were exacerbated when external wounds are accompanied. Three type of elephantoid changes of the skin including dermatosclerosis, being the most common type (68/161 patients), papillomatous type, and sclerodactylic type, with less common ones, could be classified. The most commonly affected sites were the dorsal side of the foot or the right lower leg (83/161 cases). In particular, varicose changes of the vein in lower extremities or in the popliteal fossa (73/161 cases) caused by phlebitis, were frequently observed. The lymph-scrotum or chyluria was recognized from none of the patients (Moon, 1939). Other investigators (Lee et al., 1964) observed the clinical manifestations of 15 cases of filarial elephantiasis in Jeju-do; one involved in the upper extremities, seven in the lower extremities, and seven in both extremities. They also found a higher prevalence of microfilaremia in females (24.4%) than in males (20.5%), as well as more elephantiasis cases in females (37 cases) than in males (six cases). Another epidemiological study in Jeju-do reported a total of 84 elephantiasis cases, four microfilaremia patients, and two cases of scrotal hypertrophy (Soh et al., 1966). The most predilection site for elephantiasis was lower extremities (77%), followed by upper extremities (6%). Involvement of both extremities was found to be 16.7%. Other extensive epidemiological studies were subsequently carried out to observe clinical aspects of lymphatic filariasis in some villages of the southeastern area of Jeju-do (Seo, 1975, 1978). These reports showed that most of the patients (86.6%, 155/179 cases) experienced febrile attacks and 57.7% (101/175 patients) of the patients suffered from episodic lymphangitis. The rate of elephantiasis cases to the whole population of these endemic villages reached approximately 2.0% (Seo, 1975). The clinical symptoms, such as febrile attacks and lymphangitis, demonstrated a peak frequency distribution at their ages between 10-19 years. In the case of elephantiasis, the peak frequency was observed at the age of 40- 49 years. The onset of febrile attack and lymphangitis started at the age of less than 19 years, while the onset of elephantiasis was approximately 29 years (Seo, 1975, 1978). In eastern inland of Gyeongsangbuk-do, where lymphatic filariasis had also been prevalent, four cases of elephantiasis were reported (Soh et al., 1966); three patients were males and one was female. They exhibited elephantiasis in their lower extremities, which manifested at their 4^{th} decades. Other investigation on lymphatic filariasis in this area described the clinical manifestations 72 filariasis cases; a total of 58 cases (80.5%) revealed various clinical complains, which included lumbago, limb pain, cold sensation, lymphedema or elephantiasis, fever attack, urticaria, cough, palpitation, nausea, fatigue, dizziness and asthma, in the decreasing order. However, 14 cases (19.5%) did not show any clinical presentations (Soh and Kim, 1974). The microfilarial densities were not correlated with the clinical signs. Elephantiasis of the lower extremities was more common (82.1%) than that of the upper extremities (17.9%).

The average age of onset, frequency, and duration of filarial febrile attack was observed 8.4 years, 2.7 times a year and 2.2 days, respectively. The fever was usually accompanied by various signs such as headache, muscle pain, and chill. The attack seems to be initiated by severe exercise, especially in summer (Seo, 1976). Episodic lymphangitis was also an important clinical manifestation. Its average onset age, frequency and duration were 7.8 years, 1.7 times in a year and 1.1 days in an episode, respectively. The lymph nodes, which had been most commonly affected, were inguinal lymph nodes with painful swelling. This lymphangitis spread into the adjacent areas as diffuse, reddish streaks centrifugally from the inguinal lymph nodes. The swelling increased in the leg and dorsal foot with painful erythematous reactions. Elephantiasis was observed as mild swellings of the leg or arm in its early stage. The swellings gradually increased in size with repeated febrile attacks of "Momsal" and episodic lymphangitis of "Pinaerim". The affected part swelled and subsided repeatedly and the pitting edema was gradually replaced by the elephantoid skin. Elephantiasis of the lower extremities was almost three times more common than that of the upper extremities. There were some cases affected in both extremities.

Surveys on the clinical observation of lymphatic filariasis in Korea were carried out on Heuksan-do (islands) comparing with a control group on an island free from the filarial infection (Yong et al., 1988). They divided these patient groups into two categories of microfilaremia cases (151 cases) and lymphedema-elephantiasis cases (36 patients). The clinical symptoms associated with microfilaremia cases included fever, chill, fatigue, headache, dizziness, and myalgia. Females complained more clinical presentations with a higher mean microfilarial density (39.1/120 μl) than males (23.4/120 μl), while the microfilarial density was not necessarily correlated with the clinical manifestations. The most frequently observed clinical manifestations in these patients were episodic fever attacks or lymphangitis in their extremities (37.7%, 57/151 cases). The elephantiasis cases were composed of 36 patients; five males and 31 females. The upper extremities were involved in eight patients, the lower extremities were involved in 23 cases, and remaining five cases both upper and lower extremities were involved. The plausible inducing factors of recurrent lymphangitis of the extremities were found to be injuries (36%) and fatigue (28%). No particular reasons were noted in the remaining cases (36%). The frequency and duration of lymphangitis varied according to each patient. Lymphangitis occurred most frequently in autumn. The mean age of the onset of clinical symptoms including episodic fever attacks or lymphangitis was 26.4 years, and that of lymphedema or elephantiasis was 35.4 years. There was an interval of nine years between the onsets of these symptoms.

The first authentic case of lymphatic filariasis was found at autopsied materials of a Korea resident in Kyoto, Japan, who was born in Buyeo-gun, Chungcheongnam-do and had lived there until emigration to Kyoto (Yun, 1927). The patient visited Kyoto University-Hospital complaining of swollen legs and enlargement of both inguinal nodes since several years earlier. The history of the patient revealed that he incidentally recognized swelling of the left inguinal node about eight years before. This swelling became gradually enlarged up to the hen's egg size. lower extremities were also enlarged with fever attack. Those symptoms subsided within about one month, while several minor attacks of these symptoms recurred 5-6 times a year, particularly in autumn. Approximately 8 months before his death, swelling of both legs with varicose veins and enlarged inguinal lymph nodes at both sides were noticed. The blood smear specimens revealed no microfilaria. The histopathological findings showed lymphangiectasis, thickening of the lymphatic walls, disappearance of adipose tissues, and atrophic changes of the lymph follicles in hilar, mesenteric, and retroperitoneal lymph nodes. In another study (Seo, 1975), histopathological characteristics of the lymphatic filariasis were analyzed in nine patients resided in Jeju-do using lymph node biopsy specimens. The histopathological findings could be grouped into two patterns. One was composed of chronic hyperplastic lymphadenitis and chronic exudative inflammatory processes. Hyperplasia of germinal centers was most prominently observed which was characterized by capsular thickening, fibrosis, and infiltration of lymphocytes. The lymphoid follicles were distorted. The lymphatic ducts were dilated and thickened. The medullary sinuses and hilar lymphatics were rather obliterated. The vascular wall was thickened due to a proliferation of endothelial cells. Although histiocytic sequestrations were recognized in some focal areas, necrotic lesions were hard to observe. In one case, fragments of an adult male worm were found in the necrotic center of the granulomatous lesion. The parasite was completely surrounded by fibrosis and hyalinization of the infected node, and infiltrated with a group of plasma cells. The other exudative type was characterized by diffuse sinusoidal dilatation and infiltration of inflammatory cells, principally consisted with lymphocytes, plasma cells, histiocytes, and occasional eosinophils. In some cases, typical angiomatous transformation of the sinusoids was found. Lymphostasis was also noticed in the medulla and hilum.

6. Chemotherapy and control of lymphatic filariasis in Korea

***Brugia malayi*, a filarial nematode causing lymphatic filariasis, had been endemic in southern parts and remote islands of Korea for a long period of time; especially Jeju-do and Yeongju-gun in Gyeongsangbuk-do were highly endemic areas (Kim et al., 1971; Seo, 1978). The positive rate of microfilaremia in Jeju-do was approximately 20% in the 1960s (Lee, 1961; Lee et al., 1964; Seo et al., 1965, 1968). However, it drastically decreased to below 1% in the mid-1980s due to an extensive control program (Kim et al., 1973; Lee et al., 1985; Lee et al., 1986). The microfilaria positive rate in Yeongju-gun also decreased from 8.1% in the 1970s to 2.2% in the early 1980s (Kim et al., 1977, 1980). In 1985, there were no authentic cases of lymphatic filariasis patient among 328 randomly selected persons in Yeongju-gun, which suggested that the transmission of filariasis was blocked and the infection has almost been ceased in this area (Kim, 1985; Lee et al., 1987).**

The effective control of filariasis in the Republic of Korea was accomplished mainly by an effective medication followed by intensive surveillance, elevation of residing environmental conditions and life qualities, and control of mosquitoes. Diethylcarbamazine is a highly effective drug against lymphatic filariasis; however, severe untoward reactions occur. To minimize the untoward effects of diethylcarbamazine, an alternative chemotherapeutic regimen was recommended (Seo and Lee, 1973); decreasing the total dosage to 37.5 mg/kg and a gradual increase of the dosage from 0.5 mg/kg to 6 mg/kg (a low dosage schedule). The conventional regimen of diethylcarbamazine is 72 mg/kg in a total dose by treating 6 mg/kg/day for 6 days and several repeated medications for 1-2 months. In addition, alternative regimen, low dose medication (5 mg/kg/day for 6 days) was also found to be effective in Jeju-do. In addition to the therapeutic efficacy of diethylcarbamazine, reduction of microfilaria count in the medicated population is essential to reduce the infection rate in endemic regions.

Several consecutive surveys were conducted on filariasis of the residents in Sinan-gun and Jindo-gun (County), Jeollanam-do (Province), southern parts of Korea, during 1986-1990 (Lee et al., 1987, 1988, 1989, 1992). In these surveys, 212 of 2,574 subjects (8.2%) were found to be positive with the microfilaria of *B. malayi*. One of the important findings was that microfilaremia was observed in three children aged under 10 years, which suggested that filariasis was locally transmitted in those days in these areas although the transmission rate was seemed to be fairly low (Lee et al., 1986, 1987, 1988, 1989, 1992; Yong et al., 1988). However, a recent survey demonstrated that microfilaremia was observed only in 6 of 380 cases (1.6%) in 2000 (Chai et al., 2003) and 2 of 1,393 cases (0.2%) in 2002 (Lee et al., unpublished data) in older ages over 60s with low microfilarial densities of 1-2 per 120 µl peripheral blood. These results strongly suggested that the possibilities of filariasis transmission became negligible in these areas. In Jindo-gun, the positive rate was 1.7% (5/296 cases) (Lee et al., 1992) and 0% (0/631 cases) in 2002. Of the 4 positive cases in the previous examination, 3 were re-examined and none was found to be positive for microfilariae.

During 1986-1992, microfilaria positive cases in Sinan-gun and Wando-gun were treated with diethylcarbamazine with the low dosage schedule as recommended by Soh et al. (1977). A total of 36 mg/kg of diethylcarbamazine was used administering 1 mg/kg body weight. daily for 36 days. Prior to the treatment, the microfilaremia positive rate was 8.2% (212/2,574 cases) in 11 islands of Sinan-gun with an average microfilarial density of 31.8 per 120 µl blood. After the treatment, 142 of 212 positive cases, having the average microfilarial density of 29.6 (n = 142), were followed-up. Among 142 cases, 110 (77.5%) revealed no microfilaria and the average microfilaria count in the remaining 32 patients dropped from 29.6 to 17.9. In Bogil-do (Wando-gun), three of four positive persons turned out to be negative after treatment. In two islands of Jindo-gun, all of these three followed-up cases later than 2 years of post-treatment were found to be free of microfilaria. Among 142 re-examined persons in Sinan-gun, the negative conversion rate within 5 months of treatment was 17.6%; the rate in 1 year was 24.7% and that in

2 years was 34.5%. Two positive cases in 1986 (Lee et al., 1986) were also found to be positive in 2000 (Chai et al., 2003). A total of six persons including the above two persons were treated with a single dose of albendazole (400 mg) and ivermectin (150 μg/kg), which resulted in successful treatment (Chai et al., 2003).

Against 43 microfilaremia cases, diethylcarbamazine was administered as a standard course and their night blood was examined 3 months after the medication. Prior to the follow-up blood examination, 1 pill of diethylcarbamazine was administered again, and blood examination was done after 30 minutes. The negative conversion rate 3 months after the initial treatment was 32.6% (14/43) and the rest of the patients (67.4%, 29/43) remained with microfilaria positive in their blood smear. The average microfilarial density of 29 positive people was 10.9, and the microfilarial reduction rate was 74.5%. After treatment with 1 pill of diethylcarbamazine, the average microfilarial density was 9.2 and the reduction rate was 83.6%. Four patients showed a positive conversion after the treatment and 7 cases showed a negative conversion after the treatment. However, there was no significant difference between the pre- and post-treatment data when 1 pill of diethylcarbamazine was administered. The results shown here suggest that low levels of transmission occurred continuously on the islands around Heuksan-do as a newly found endemic area in the 1980s. However, even in this area, filariasis seems to have been nearly eradicated by active case finding and medication, long-term natural extinction, and improvement of environmental conditions.

In 2006, a seroepidemiological survey was conducted by NIH team for 3,049 school children aged 10-13, in areas where *B. malayi* filariasis had been prevalent. None of them was found to be positive with anti-*B. malayi* antibody. This result may further reflect that the transmission of filariasis in the Republic of Korea probably has been terminated. Finally, remarkable growth in economic status which brought improved environment and personal hygiene, and elevated life-style of inhabitants contributed to the fading of this mosquito-borne disease in the Republic of Korea.

Part II

EPIDEMIOLOGY OF LYMPHATIC FILARIASIS IN KOREA

1. Introduction

Lymphatic filariasis in Korea had been solely caused by *B. malayi* (Seo, 1978). The first authentic case was found to be infected with an inguinal lymph node (Yun, 1927). Thenceforward, epidemiological studies in Jeju-do, Jeollanam-do and Gyeongsangbuk-do demonstrated that these areas were main foci for lymphatic filariasis in Korea (Oh, 1929; Moon, 1939; Lee et al., 1961, 1964; Kim et al., 1971, 1973, 1977; Seo, 1978).

During the early 1970s, mass chemotherapy was implemented in several endemic foci with satisfactory results. In Yeongju-si, one of the main foci in Gyeongsangbuk-do, a remarkable decrease of the prevalence was achieved, which resulted in complete disappearance during these periods (Lee et al., 1987). On the other hands, western remote islands such as Heuksan-do, were found as new endemic foci of lymphatic filariasis during the 1980s (Lee et al., 1986). A recent epidemiological study, however, revealed that this area is now also free of lymphatic filariasis (Chai et al., 2003). Resurgence of lymphatic filariasis is hardly expected in Korea.

The episodic febrile attacks with an acute lymphadenitis and lymphangitis are characteristic to early stage lymphatic filariasis in Korea. This allergic lymphangitis is caused by the newly infected larvae, which was traditionally called "Momsal" in Jeju-do. When lymphangitis is associated with febrile attack and transient swelling of the extremities, it had been called "Pinaerim" or "Pijong. This kind of clinical manifestations lasted several days and recurrently occurred several times in a year. The recurrent febrile attacks, "Momsal" and the repeated lymphangitis, "Pinaerim", might be important factors that lead elephantiasis in Korea. The most commonly affected site is the inguinal lymph nodes. No case involving scrotal region was observed in Korea (Seo, 1978). The clinical signs such as chyluria, haematochyluria or chylous effusions were not observed in Korean patients. Instead, elephantiasis of the extremities, locally termed as "Soojongdari", was frequently observed. However, most of cases demonstrated relatively mild symptoms, including only slightly enlarged legs and arms with smooth surface. The episode of recurrent febrile attack, lymphangitis, and elephantiasis are the most prominent clinical signs of lymphatic filariasis found in Korea.

2. *Parasites (Brugia malayi), vectors, reservoirs, and life cycle*

The adult worms are minute and thread-like in shape, and harbored a smooth cuticula. The parasites thrive in lymphatic vessels. Mature females and males vary in length from 43 to 55mm and from 13 to 23mm, and in width ranged from 130 to 170 µm and from 70 to 80µm, respectively. The microfilariae are crowded together in coiled masses within the uterus of the mature female worm. These larvae are expelled from the adult females and move into the visceral and the peripheral blood.

The microfilaria of *B. malayi* is different from that of other species. The most distinctive morphological character of the *B. malayi* microfilaria is the presence of two discrete nuclei in the top of the tail part. The microfilariae exhibited typical nocturnal periodicity in the patients' peripheral blood. When the mosquitoes take blood meal, the microfilaria transmit to the vector host, and mature into 3rd stage larva. This infective-form larva lives in the salivary gland of the mosquitoes. Human infection results from introduction of the infective larvae into the puncture wound when an infected mosquito takes blood meal. The larvae invade the lymphatic vessel and begin to mature. Approximately 10 months after infection of the 3rd stage larvae, the parasites fully mature to adults and continue to produce larvae.

Filariasis *malayi* had been prevalent on Jeju-do, remote islands in southern parts of Korean peninsula, and Gyeongsangbuk-do of inland area. The mosquito vectors mainly involved in the transmission of *B. malayi* in Korea is *Ae. togoi* and *An. sinensis. Ae. togoi* played major role as vector in the formerly endemic area on Jeju-do and on the inlands. While *An. sinensis* played vector role in the inland area. None of the animals were reported to the reservoir host of *B. malayi* in Korea. In experimental infection, the parasite can be matured into adults in cats and gerbils. Life cycle of *B. malayi*, Yeongju strain of inland Korea had been maintained for many years here in NIH using *Ae. togoi* as vector and gerbil (*Meriones unguiculatus*) as definitive host.

Ae. togoi was found to suck blood during night-time, from sunset to sunrise; they suck blood actively from 10:00 pm to 04:00 am (peak time; 01:00 am - 03:00 am). The number of mosquitoes caught indoors was 60.7 and that outdoors was 50.3. *Ae. togoi* may bite humans more actively indoors during midnight. These data demonstrated that an occurrence of microfilaria in the peripheral blood was closely related to the active feeding time of *Ae. togoi*, and further suggested that *Ae. togoi* could play the role of a highly susceptible vector for *B. malayi* filariasis in Korea.

In inland Yeongju area in 1970s, *An. sinensis* was proven to be the vector of *B. malayi* by finding the natural infection with infective 3rd stage larvae of *B. malayi* through an investigation conducted in 1973 (Kim, 1974, 1977). *An. sinensis* was one of the predominant species in the mosquito population density in the inland area. Quite a variation was seen in the population density of adult mosquitoes by species, depending on the village areas. The most predominant species was *An. sinensis* which accounted for 69.5% of the total number of mosquitoes collected. *Culex pipiens pallens* was next at 15.7% followed by *Aedes vexans* 7.7%, *Culex tritaeniorhynchus* 3.4%, *Anopheles yatsushiroensis* 2.0%, *Anopheles sineroides* 1.5%, *Culex bitaeniorhynchus* 0.1%, and *Culex orientalis* 0.1% . The population density of *An. sinensis* tended to increase more in the village located in hilly areas than those in open areas (Kim et al., 1977).

The prevalence of mature larvae of *B. malayi* in *An. sinensis* in the inland area seemed to be very low (Table 3). Such a result was contrasted sharply with the finding that *An. sinensis* was highly susceptible to *B. malayi* in artificial infection. The cause of such a low infective rate might be the aspects of zoophilic biting preference of *An. sinensis,* existence of animals such as cattle which were favored over humans for biting by the species, and the environment, and gradual improvement and changes in living habits of inhabitants which affect the transmission of the parasite. That is, *An. sinensis* prefers animal bait to human, and most were found in abundant numbers feeding or resting in cow sheds or in pig stiles. Only a few were biting man. A relatively high number of *An. sinensis* or *Ae. vexans* was caught in indoors collection. This was because the cow sheds were located so close to the house structure that some of the mosquitoes used to fly into the kitchen, living room or veranda and rest there after feeding on the cattle.

In considering the susceptibility of mosquitoes to *B. malayi* infection, *Ae. togoi*, a known vector of *B. malayi* on Jeju-do, was also susceptible to the parasite of Yeongju strain. However, better recovery of the infective of 3rd stage larvae was seen in *An. sinensis* at dissection than in *Ae. togoi*. This was perhaps because *An. sinensis* was more susceptible than *Ae. togo* to *B. malayi* of this area, although such a fact could be the result of the difference in the average amount of blood meal in different mosquito species. *Cx. pipiens pallens* is thought not to be related to the transmission of *B. malayi,* though this species shows the most active biting on human bait. *An. sinensis* was considered to be the vector most responsible in the transmission of *B. malayi* in this area from its predominance in the relative population density and its greater susceptibility to the parasite infection (Kim et al., 1977).

Considering the mosquito season and period *An. sinensis* prevails, the transmission of *B. malayi* in inland Korea could have occurred for approximately four months a year from June to September with a peak in the warmer months. The rest of the cooler months function as a natural barrier against transmission of the infection.

3. Epidemiological characteristics of human infection

During the early period between the 1920s and 1940s, several investigators have observed the clinical and epidemiological characteristics of lymphatic filariasis in Korea (Yun, 1927; Oh, 1929; Moon, 1939). The first wide survey was conducted in the 1950s, in which 5,001 night blood smears in 25 randomly selected villages in Jeju-do were analyzed (Senoo et al., 1951). The result showed that 12.1% (604/5,001 cases) of the samples were positive for microfilaria of *B. malayi*. An epidemiological study subsequently demonstrated 9.2% of positive rate (19/206 cases) (Paik et al., 1957), 11.4% (26/229 schoolchildren), 22.2% (79/356 inhabitants) (Lee et al., 1961, 1964) and 8.6% (184/2,139 inhabitants) (Seo et al., 1965). These collective data suggested strongly that there were three major endemic foci for lymphatic filariasis in Korea, such as northeastern part (inland) of Gyeongsangbuk-do, the western coastal areas of Jeollanam-do and Jeju-do. Jeju-do was found to be highly endemic, while two others were found to be moderate to low endemic.

A large-scale based field surveys were carried out in 1965 and 1968 to figure out the nationwide distribution of filariasis. In these series of surveys, they examined the presence of microfilaria in the peripheral blood smear specimens from newly conscripted soldiers from over the country and of local residents (Seo et al., 1965, 1968). A total of 24,816 specimens were microscopically examined. It was found that 0.63% (155/24, 816 cases) were observed to have microfilaria in the blood smears. The highest positive rate was recognized in draftees from Jeju-do (3.5%) followed by Gyeongsangbuk-do (1.2%). These investigators also examined the night blood specimens obtained from local residents in Jeju-do (2,308 samples), Gyeongsangbuk -do (974 cases), and Jeollanam-do (451 cases) (Seo et al., 1968). The microscopic examination revealed positive rate of 17.6% (407 cases), 3.1% (30 samples), and 4% (18 cases) in Jeju-do, Gyeongsangbuk-do, and Jeollanam-do, respectively. A nationwide survey done during the 1960s demonstrated 2.4% (784/32,673 cases) of microfilaria positive rate (Seo et al., 1965, 1968). The lymphatic filariasis had been prevalent throughout South Korea except for Gyeonggi-do and Gyeongsangnam-do until the early 1970s (Seo, 1978).

In 1970s, the distribution of *B. malayi* filariasis in the inland Korea around Yeongju seemed to be extended widely, although the prevalence was low on the average based upon the prevalence rate of microfilaremia by village. Among the village surveyed then, all the villages had microfilaremia cases, showing 8.1% on the average with the lowest 5.0% by 20μl night blood. In some isolated villages located in pocket areas surrounded by hills, the prevalence rate of microfilaremia reached moderate level showing 17.9% or 18.0%. The prevalence rate of microfilaremia among inhabitants would certainly be higher to some extent than the above figures when a more sensitive method such as millipore concentration technique was applied. Therefore, it would seem that transmission of the disease occurred more frequently or easily among the villagers in the narrow closed areas in relation to the bionomics of the vector mosquito (Kim et al., 1977).

Microfilaria rate by age group revealed an increase by age group, i.e., from 2.6% in 5-9 years to a peak at an average of 18.2% in the over 70s age group. This was considered to be resulted by a cumulation of cases of microfilaremia by increased chance of exposure of inhabitant populations to the infection. These results were quite different from those observed in high endemic areas on Jeju-do where the microfilaria rate in the children's group was almost as high as in the adult group and the peak was seen in the 29-38 age group (Senoo et al., 1951 ; Kim et al., 1973). Such results indicated that the transmission of *B. malayi* infection in the Yeongju area seemed to be rather slow and more difficult than in the high endemic area on Jeju-do. By sex, the microfilaria rate was similar in both sexes in the young age groups but after middle age the rate became higher in male than in female. The peak of microfilaria rate in males was seen in the 40-49 age group. Microfilaria density was relatively low in relation to the low rate of microfilaremia and increased slightly by age groups.

An. sinensis was confirmed to be the vector of *B. malayi* infection in the Yeongju area through the vector search investigation (Kim, 1974; Kim et al., 1977). *An. sinensis* was a predominant species of mosquitoes in this area and highly susceptible to *B. malayi* infection. However, the prevalence of natural infection with 3rd stage larvae of *B. malayi* in *An. sinensis* was extremely low, i.e., 0.3% out of 4,403 examined. The average number of larvae in the positive mosquitoes was 9 (Table 3).

With all the data obtained, such as microfilaria rate and microfilaria density of the inhabitants, prevalence of elephantiasis, and infective rate of vector mosquitoes, the transmission in this area seemed to be generally low. However, through interviews with the inhabitants, elephantiasis had been recognized as occurring in this area since long ago. The introduction of filariasis to this area was now presumed that it had occurred at least nearly a century ago, based on comments of the villagers at that time. Some reported having contracted the disease at an early age; others recalled cases of swollen legs or feet among their parents or ancestors; finally some reported that such manifestation of the disease as swollen legs or feet, which they call "Soojongdari" or " Kaggi", were seen more frequently in the past. From such results, the endemicity of filariasis in this area probably had a peak of prevalence in the past and then had shown in general a slow but continuing transmission with retarding tendencies, though it seemed to be widely prevalent. Such assumptions were also supported by the data of the prevalence rate of microfilaremia by age group. However, it was noteworthy that the filariasis was persistently prevalent even to moderate level in certain hilly pocket areas. Man seemed to be the only natural host of filariasis *malayi* as carrier in Yeongju area (Kim et al., 1977).

The low endemicity of the filariasis *malayi* in the 1970s was also understood from the relatively short period of transmission throughout a single year. The efficient transmission period for the parasite is approximately 4 months of warm season when the mosquitoes are prevalent and active in biting. Mosquito population decreases in autumn from a peak in summer and some of them hibernate in winter. Thus the climatic condition functioned as a natural barrier against the transmission. People were easily exposed to mosquitoes in summer time, since the farmers usually returned home from farming at dusk and often had their dinner on veranda or in door yards of the house enjoying comfortable atmosphere after dark. This time roughly coincides with time of mosquito emergence; thus there was ample opportunities to be bitten by mosquitoes both indoors and outdoors, though mosquito nets and insecticides had widely been used by village people before going to bed.

In spite of such exposure of the village people to mosquito bite and the abundance of vector mosquito population, biting preference of the *An. sinensis* is in principle zoophilic and only a minor fraction bite man. A tremendously high number of the population were biting cattle in cow sheds particularly in the warmer month. Many of the households in the villages surveyed own their own cattle. It was peculiar at that time that cow sheds were located very close to the house or were even connected to the house structure. Such close existence of man and cattle during the night from the time of mosquito emergence in the evening helped vector mosquitoes to distinguish their favorite animal baits more easily, being attracted by cow sheds and animals. This long standing habits of raising cattle in the villages seemed to result in a reduction of risk from infection as the cattle became a kind of decoy. This was in spite of the fact that the conditions were relatively unhygienic (Kim et al., 1977).

During the mid-1980s, the western remote islands such as Heuksan-do (islands) of Sinan-gun, Jeollanam-do were found to be endemic foci in Korea (Lee et al., 1986). A large scale epidemiological survey in these areas demonstrated moderate endemicity of *B. malayi* with clinical elephantiasis cases (Lee et al., 1988, 1989; Yong et al., 1988). Surveys in these areas revealed moderate microfilaria rate among inhabitants (10.6%) out of a total of 1,862 persons examined in the 21 villages of the 11 small islands from 1985 to 1987 (Lee et al., 1986, 1988). The people resided in these islands were found to be lightly to moderately infected with the parasite (range: 4.0 - 22.4%). The positive cases were found in all age groups, but showed increasing tendency according to their ages with the peak at 17.3% in the 40-49 year age group. It was noteworthy that microfilaremia was observed in three children aged under 10 years, which suggested that filariasis was locally transmitted in the these days in this area. However, microfilarial density of the positive cases was relatively low. The average microfilaria count for 198 positives was 33.4/120 μl night blood. A recent epidemiological survey in these areas showed six microfilariae positive cases (1.6%), all of them were females aged 57-72 years, and from only two villages of the Daeheuksan-do (Chai et al., 2003).

In 2005, NIH team carried out a large scale anti-*B. malayi* antibody test for 3,049 school children aged 10-13, in areas where lymphatic filariasis had been prevalent, using commercially available BRUGIArapid™ (MBDr). There was no case that showed positive reaction. Mass and selective chemotherapy with diethylcarbamazine conducted in the latter half of the part century, as well as remarkable economic growth followed by improved living standards and elevated life-style of inhabitants contributed to the elimination of lymphatic filariasis in the Republic of Korea.

In conclusion, there had been four endemic foci of lymphatic filariasis in Korea including Jeju-do, eastern inland of Gyeongsangbuk-do, costal areas and inlands of Jeollanam-do, and western remote islands of Jeollanam-do during the 1960s. The south-western remote islands including Daeheuksan-do(islands) remained to be the only areas where malayan filariasis did exist by 2000. However, all of these microfilaria positives were aged persons (57-72 years) with quite low microfilarial densities. In 2005, NIH team performed seroprevalence survey for 3,049 school children aged 10-13, where lymphatic filariasis had been prevalent and found no positive case. This result indicated that the transmission of filariasis in the Republic of Korea was terminated sometime in the past.

4. Clinical and pathobiological characteristics

The first authentic Korean case of lymphatic filariasis was found at autopsied materials of inguinal lymphs of a man, who was born in Buyeo-gun, Chungcheongnam-do (Yun, 1927). The patient visited Kyoto University-Hospital with the chief complaints of swollen legs and enlargement of both inguinal nodes, which had developed several years earlier.

Yun (1927) had experienced incidentally recognized swelling of the left inguinal node during the past 8 years. This swelling became gradually enlarged up to the hen's egg size. lower extremities were also enlarged with fever attack. The symptoms subsided within approximately one month, while several minor attacks of these symptoms recurred 5-6 times in a year, particularly in autumn. Approximately 8 months before he died, swelling of both legs with varicose veins and engorgement of inguinal lymph nodes at both sides were noticed. His blood smear revealed no microfilaria. On the histopathological examination, lymphangiectasis, thickening of the lymphatic walls, disappearance of adipose tissues, and atrophic changes of the lymph follicles in hilar, mesenteric, and retroperitoneal lymph nodes were observed.

The histopathological findings of the Korean patients could be grouped into two patterns (Seo, 1975). One consisted with chronic hyperplastic lymphadenitis and chronic exudative inflammatory processes. Hyperplasia of germinal centers was most prominently observed which was characterized by capsular thickening, fibrosis, infiltration of lymphocytes, and distortion of the lymphoid follicles. The lymphatic ducts were shown to be dilated and thickened. The medullary sinuses and hilar lymphatics were obliterated. The vascular wall was thickened due to a proliferation of endothelial cells. Although histocytic sequestrations were recognized in some focal areas, necrotic lesions were hard to observe. In one case, fragments of an adult male worm were found in the necrotic center of the granulomatous lesion. The parasite was completely surrounded by fibrosis and hyalinization of the infected lymph node, and infiltrated with a group of plasma cells. The other exudative type was characterized by diffuse sinusoidal dilatation and infiltration of inflammatory cells, principally composed of lymphocytes, plasma cells, histiocytes, and occasionally of eosinophils. Typical angiomatous transformation of the sinusoids was also noticed. In the medulla and hilum, lymphostasis was also recognized.

Three major pathophysiological factors are known to be profoundly involved in the clinical manifestations and pathological alterations in lymphatic filariasis. These included an allergic reaction induced by the parasite metabolites, mechanical blockage of lymphatics occupied by the parasites and subsequent fibrosis, and blockage of the lymphatics due to secondary microbial infections. The allergic reactions during the early acute stage of filariasis caused a sudden lymphangitis with pain, urticaria, swelling and regional lymphadenopathy. This early allergic reaction is usually accompanied by proliferative and granulomatous changes in the lymphatic wall and lymph node.

One of the unique clinical manifestations observed in Korean patients was most of elephantiasis patients did not reveal microfilaremia in their peripheral blood smear, while *Streptococcus haemolyticus* was frequently isolated from erysipeloid skin lesion. However, when the isolated streptococci were subcutaneously inoculated into normal adults and the microfilaria positive or elephantiasis cases, only the elephantiasis patients showed local or generalized reactions (Moon, 1940). Therefore, he concluded that frequent episodes of lymphangitis with febrile attack were mainly caused by the parasites, not by bacteria such as *S. haemolyticus* (Moon, 1940). Many investigators also insisted that the initial tissue responses are provoked by the parasite metabolites but not by supervening secondary bacterial infections (Ewert et al., 1972; Beaver et al., 1984). It was found that allergic reaction of the host tissues against the filarial worms and their metabolites are the principal factors involved in the pathogenesis of lymphangitis in its early stage. In later stages, recurrent blockage of the lymphatics by the degenerating parasites provoked lesional extension and fibrosis in wax and wane pattern, which are responsible for the elephantiasis.

The episodic febrile attacks with an acute lymphadenitis and lymphangitis are characteristic to early stage lymphatic filariasis. This allergic lymphangitis is caused by the newly infected larvae, which was traditionally called "Momsal" in Jeju-do, where filariasis was endemic. When lymphangitis is associated with febrile attack and transient swelling of the extremities, it had been called "Pinaerim" or "Pijong" in these endemic areas. This kind of clinical manifestations lasted several days and recurrently occurred several times in a year. However, the "Bagu", a term described as an initial skin lesion of lymphatic filariasis (a small itching erythematous edema) in Japan was not observed in Korean patients. The recurrent febrile attacks, "Momsal" and the repeated lymphangitis, "Pinaerim", might be important factors that lead elephantiasis in these cases. Engorgement of lymph nodes, but not hard, rather rubbery in consistency and movable, was found in some cases. The most commonly affected site is the inguinal lymph nodes. In addition, hard cord-like lymphatics and varicose nodes were observed in few cases. No case involving scrotal region was observed in Korea (Seo, 1978). Although two cases of scrotal hypertrophy were observed in Jeju-do, it was not clear whether these changes might have been associated with a filarial infection (Soh et al., 1966). In addition, clinical signs such as chyluria, haematochyluria or chylous effusions were not observed in Korean patients. Instead, elephantiasis of the extremities, locally termed as "Soojongdari", was frequently observed. However, most of cases demonstrated relatively mild symptoms, including only slightly enlarged legs and arms with smooth surface. The episode of recurrent febrile attack, lymphangitis, and elephantiasis are the most prominent clinical signs of lymphatic filariasis found in Korea.

In earlier period during 1939 and 1940, field surveys were conducted in Nonsan and Buyeo, Chungcheongnam-do (Moon, 1939) and Jeju-do (Moon, 1939) to characterize the clinical manifestations of lymphatic filariasis in Korea. The reports found that males showed a higher prevalence than females. In Chungcheongnam-do, the proportions of males and females were 85.1% and 14.9%, respectively, when a total of 161 cases were examined (Moon, 1939). The "Momsal" fever was shown to start between 15 and 25 years old, and more than 100 cases were found in the age between 40 and 60 years. The febrile attack occurred most frequently in October and the symptoms were exacerbated by external injuries. Three type of elephantoid changes of the skin such as dermatosclerosis, being the most common type (68/161 patients), papillomatous lesions, and sclerodactylic type, with less common ones, could be classified. The most commonly affected sites were the dorsal side of the foot or the right lower leg (83/161 cases). Particularly, varicose changes of the vein in lower extremities or in the popliteal fossa (73/161 cases), which had been caused by phlebitis, were frequently observed. However, chyluria or lymph-scrotum was not observed in these patients (Moon, 1939). Other investigators (Lee et al., 1964) observed the clinical manifestations of 15 cases of filarial elephantiasis in Jeju-do; one involved in the upper extremities, seven in the lower extremities, and seven in both extremities. They also found a higher prevalence of microfilaremia in females (24.4%) than in males (20.5%), as well as more elephantiasis cases in females (37 cases) than in males (6 cases). An epidemiological study in Jeju-do also reported a total of 84 elephantiasis cases, four microfilaremia patients, and two cases of scrotal hypertrophy (Soh et al., 1966). The most predilection site for elephantiasis was lower extremities (77%), followed by upper extremities (6%). Involvement of both extremities was found to be 16.7%. Subsequent extensive epidemiological studies were conducted to figure out the clinical aspects of lymphatic filariasis in some villages of the southeastern area of Jeju-do (Seo, 1975, 1978). These reports showed that most of the patients (86.6%, 155/179 cases) experienced febrile attacks and 57.7% (101/175 patients) of the patients suffered from episodic lymphangitis. The rate of elephantiasis cases to the whole population of these endemic villages reached approximately 2.0% (Seo, 1975). The clinical symptoms, such as febrile attacks and lymphangitis, exhibited a peak frequency of distribution at their ages, 10-19 years. In the case of elephantiasis, the peak frequency was observed at the age of 40-49 years. The onset of febrile attack and lymphangitis started at the age of less than 19 years, while the onset of elephantiasis was approximately 29 years (Seo, 1975, 1978). In eastern inland of Gyeongsangbuk-do, four cases of elephantiasis were reported during the 1960s (Soh et al., 1966); three patients were males and one was female. These patients demonstrated elephantiasis in their lower extremities, which manifested at their 4th decades. Other investigation in this area described the clinical manifestations 72 filariasis cases; a total of 58 cases (80.5%) revealed various clinical complaints including lumbago, limb pain, cold sensation, lymphedema or elephantiasis, fever attack, urticaria, cough, palpitation, nausea, fatigue, dizziness and asthma, in the decreasing frequency. However, 14 cases (19.5%) did not show any clinical presentations (Soh and Kim, 1974). Interestingly, the microfilarial counts were not correlated with the clinical signs. Elephantiasis was more commonly found in the lower extremities (82.1%).

The febrile attacks were shown to be started at 8.4 years old, 2.7 times in a year, and lasted for 2.2 days in a single attack, respectively. The fever was likely to be associated with various signs such as headache, muscle pain, and chill. The symptoms were shown to be worsened by heavy physical exercise, especially in summer (Seo, 1976). Recurrent lymphangitis was also an important clinical manifestation, which started from 7.8 years old. Its frequency and duration were 1.7 times in a year and 1.1 days in an attack, respectively. The inguinal lymph nodes were found to be most frequently involved. The symptoms included painful engorgement and tenderness. This lymphangitis spread into the adjacent areas as diffuse, reddish streaks centrifugally from the inguinal lymph nodes. The lymphedema together with painful erythematous reactions were frequently found in the leg and dorsal foot. Elephantiasis was also observed with mild swellings of the leg or arm in its early stage. The swellings gradually increased in size accompanied by recurrent febrile attacks of "Momsal"and episodic lymphangitis of "Pinaerim". The affected part swelled and subsided as wax and wane pattern, and the pitting edema was gradually replaced by the elephantoid skin. Elephantiasis of the lower extremities was almost three times more common than that of the upper extremities. Occasionally, elephantiasis of the both extremities was also observed.

Clinicoepidemiological surveys of lymphatic filariasis in Korea were conducted in Heuksan-do (Yong et al., 1988). They classified the patient groups according to the presence of microfilaremia (151 cases) and lymphedema-elephantiasis (36 patients). The clinical symptoms associated with microfilaremia cases were found to be fever, chill, fatigue, headache, dizziness, and myalgia. Females complained more clinical manifestations with a higher microfilarial density in the peripheral blood smear (39.1/120 µl) than that of males (23.4/120 µl). However, microfilarial density was not shown to be necessarily correlated with the clinical presentations. The most frequently observed clinical manifestations in these patients were recurrent febrile attacks or lymphangitis in their extremities (37.7%, 57/151 cases). The elephantiasis cases consisted with patients; five males and 31 females. Eight patients were found to be affected with the upper extremities, 23 cases were found to be affected in the lower extremities, and remaining five cases were found to be affected in both upper and lower extremities. The possible predisposing factors of recurrent lymphangitis of the extremities were thought to be injuries (36%) and fatigue (28%). No specific reasons were found in the remaining cases (36%). The frequency and duration of lymphangitis varied according to the individual patient. Lymphangitis was shown to be most frequently occurred in autumn. The mean age of the onset of clinical symptoms including episodic fever attacks or lymphangitis was 26.4 years, and that of lymphedema or elephantiasis was 35.4 years. Interval between the onsets of these symptoms was nine years.

5. Diagnosis, treatment and follow-up surveillance

The diagnosis of lymphatic filariasis included microscopic examination of peripheral blood specimens, serological tests which are directed to detect specific antibodies/antigens, ultrasonographic demonstration, and molecular biological examinations. However, non-specific general abnormality in blood tests gave rise to a clue. The most common non-specific finding in blood tests from infected individuals is eosinophilia, which may exceed 3,000/μl. The exact frequency of eosinophilia due to filariasis in infected individuals is difficult to determine partly because other helminth infections often coexist in these people and partly because eosinophilia seemed to be observed either early in infection or following therapy. Microscopic hematuria and proteinuria may be present in individuals with renal system involvement.

The specific laboratory diagnosis of lymphatic filariasis depends either on the demonstration of circulating microfilaria in the peripheral blood or various stages of the parasite in biopsied tissue sections. Blood examination for detection of microfilariae should be performed in all individuals in whom the diagnosis of filariasis is suspected. *B. malayi* in Korea tends to show nocturnal periodicity of microfilaria. Therefore, blood should be taken in the night time, between 10:00 p.m. and 02:00 a.m. because the greatest number of microfilariae can be found in blood around midnight. The pattern of periodicity can be reversed by changing the patient's sleep-wake cycle. Various morphological characteristics of the parasite will normally assist in its identification to the genus and specific level. Concentration techniques, especially those using the polycarbonate membrane filtration of a ml or more of heparinized blood, can detect the parasite in those with very low microfilaria counts.

Serological techniques using the indirect fluorescent assay with microfilaria and adult worm antigens can assist in confirming a clinical suspicion of filaria infection when the parasite is not demonstrable. The development and application of specific monoclonal antibodies for the detection of circulating antigens in the enzyme-linked immunosorbent assay will probably increase the specificity of the assay. In epidemiological studies of lymphatic filariasis, ELISA has been used to detect anti-parasite IgG4. ELISA is cheaper, easier to application and less time-consuming method. In addition, immunoglobulin E (IgE) is thought to play an important role in protective immunity and pathogenesis of helminth infections. The initial indication that IgE may correlate with disease pathology for lymphatic filariasis and the demonstration that patients with tropical pulmonary eosinophilia and elephantiasis had high levels of IgE antibodies. It is also thought that the ratio of IgG4 to IgE in particular is important in disease progression following infection. A modified Th2 response characterized by high IgG4/IgE seems to be associated with asymptomatic helminth infections (Atmadja et al., 1995).

Ultrasonography is accepted as a suitable and sensitive diagnostic tool to detect living adult filaria in the lymphatic ducts. The adult filarial worms can be detected by their typical movement pattern. The worm nests are stable over time and can be observed at regular intervals under treatment conditions. Presently available specific DNA probes for filariasis are probably not as useful for patient diagnosis as they are for epidemiological purposes.

The effective eradication of filariasis in the Republic of Korea was accomplished principally by a mass chemotherapy followed by intensive surveillance, improvement of socio-economic conditions and living standard, environmental hygiene through reconstruction of villages and houses, together with elimination of mosquito vectors (Kim, 1985). Diethylcarbamazine, a drug of choice for treatment of lymphatic filariasis was used to treat the patients. The conventional regimen of diethylcarbamazine was 72 mg/kg in total dose by administering 6 mg/kg/day for 6 days and several repeated medications for 1-2 months. Although diethylcarbamazine is a highly effective drug against lymphatic filariasis, it also revealed severe untoward effects. Therefore, an alternative therapeutic regimen was introduced (Seo and Lee, 1973). This low dosage schedule included decreasing the total dosage to 37.5 mg/kg with a gradual increase of the dosage from 0.5 mg/kg to 6 mg/kg. Another low dose regimen (5 mg/kg/day for 6 days) was also found to be effective in Jeju-do. In addition to the therapeutic efficacy of diethylcarbamazine, reduction of microfilarial density in the medicated population was essential to reduce the infection rate in endemic areas.

The patients in Sinan-gun and Wando-gun were treated by using a low dosage schedule (Soh et al., 1977). A total of 36 mg/kg of diethylcarbamazine was administered (1㎎/㎏ daily for 36 days). Before treatment, the microfilarial rate was 8.4% (213/2, 533 samples) in the 24 villages on the 12 islands of Sinan-gun with an average microfilarial density (31.7/120 μl of blood). However, 2-year follow-up examination revealed that 110 patients were found to be free of microfilaria (77.5%, 110/142 cases). The microfilarial density dropped from 29.6 to 17.9 as well (n = 32). The reduction rate of the total number of microfilaria reached 86.3%. In Bogil-do (Wando-gun), all of three positive cases turned out to be negative after treatment. In two islands of Jindo-gun, all of three re-examined persons later than 2 years were found to be free from microfilaria. Changes in microfilarial positive rate after treatment were also observed. Among 114 re-examined persons in Sinan-gun, the negative conversion rate within 5 months was 21.9% (25 cases); the rate in 1 year was 76.0% (38/50) and that in 2 years was 86.4% (57/66), including 6 positives of Wando-gun and Jindo-gun. However, two positive cases in 1986 (Lee et al., 1986) remained to be microfilaremia positive until 2000 (Chai et al., 2003).

Although *B. malayi* in Korea has nocturnal periodicity, a low-level microfilaremia is still observed in the daytime (Lee et al., 1988). Therefore, day-time blood smear and diethylcarbamazine provocation test were compared three months after treatment in order to evaluate drug efficacy. Without diethylcarbamazine provocation test, the negative conversion rate was 32.6% (14/43 cases), while 67.4% (29/43 cases) retained microfilaria in their blood in their day-time blood smear. In the following provocation test, 10 microfilarial negative persons remained negative and 22 microfilarial positives remained as positive. Four negative cases turned tout to be positive by the provocation, and seven positives turned negative. The microfilarial densities in these persons who showed positive conversion were very low (1 to 4 microfilariae/120 μl). No significant difference between the results with and without diethylcarbamazine provocation test was observed in the post-treatment follow-up evaluation.

Part III

LAUNCHING AND OPERATION OF CONTROL PROGRAM OF LYMPHATIC FILARIASIS IN KOREA(FROM THE 1960S AND THE 1990S)

1. Status of lymphatic filariasis in Korea since the 1920s to the 1960s
2. Nationwide control program of lymphatic filariasis during the period of the 1960s to the late 1970s

2-1. Epidemiological studies of lymphatic filariasis during the 1960s and the 1970s

2-2. Clinical manifestations of lymphatic filariasis in Korea

2-3. Nationwide control program

3. Check-up for the efficacy of the control program and finalizing the elimination program during the 1980s and the 1990s

1. Status of lymphatic filariasis in Korea since the 1920s to the 1960s

The microfilariae found in the cattle were firstly described in Korea by Yamada et al. (1912) and Kawamura (1915). They examined the blood specimens of Korean cattle and identified microfilaria of the *Setaria* species. Nakagawa (1914) also observed some kinds of microfilaria in the blood samples of Korean sparrows, but he did not identify the exact species.

Japanese scientists (Fujimori, 1924; Murakami, 1925) reported a presence of elephantiasis in Korea for the first time. A Korean male visited Murakami laboratory in Kyoto Imperial University Hospital in Kyoto, Japan with the chief complaint of left lower leg swelling which had been developed for 8 years. Kondoleon's operation was recommended as a palliative surgical therapy of elephantiasis. He died approximately one month after the operation. A post-mortem examination of this patient was carried out by the pathologist. The pathologist found a male filarial worm in his sectioned left inguinal lymph node, and stated that filaria worm is the causative agent of elephantiasis in Korea (Yun, 1927). This is the first authentic record of the presence of adult filaria worm in a sectioned left inguinal lymph node at autopsy of an elephantiasis patient who was born in Chungcheongnam-do.

Oh (1929) observed microfilariae in the peripheral blood of 24 Koreans and described nocturnal periodicity. An epidemiological survey of 527 elephantiasis cases in Chungcheongnam-do showed that 12 patients were confirmed to be infected with microfilaria in their blood. However, hydrocele or chyluria were not associated with the microfilaremia or elephantiasis patients in a series of epidemiological survey in Chungcheongnam-do, Jeollabuk-do and Jeju-do. Later, it was found that Korean elephantiasis mainly affected lower extremities and occasionally arms, but never involved the external genitalia. This observation was confirmed in Jeju-do as well as in the mainland (Moon, 1940).

The first epidemiological and clinical survey of 1,638 cases of elephantiasis in Chungcheongnam-do was carried in 1930 (Oh, 1929). At his microfilarial survey, only 12 out of 527 cases were found to be microfilaria positive. Therefore, he considered the etiology of elephantiasis might not to be associated with filariasis but with certain bacterial infections. Subsequently, Moon (1939) conducted an epidemiological survey on endemic elephantiasis in Nonsan and Buyeo in Chungcheongnam-do and Namwon myeon in Jeju-do. He analyzed the clinical symptoms observed from a total of 204 cases, and particularly he observed that there was no case with hydrocele and/or chyluria.

The microfilariae found in southern Korea were identified as *M. malayi* Brug at this time (Senoo, 1943). Nelson et al. (1946) reported that, among 570 samples from Korean prisoners of the war, *W. malayi* microfilaremia was found to be 8.5%. Senoo and Lincicome (1951) reported the distribution of brugian filariasis in Korea by examining a total of 5,001 patients representing 25 villages from South Korea. They found that 604 (12.1%) of the patients were microfilariae positive in their peripheral blood, all of which have been identified as *W. malayi*. In addition, microfilaremia was detected 15.4% in Chungcheongnam-do, 11.2% and 9.3% in Jeollanam and Jeollabuk-do, and Gyeongsangnam and Gyeongsangbuk-do respectively. These results clearly demonstrated that, until the 1950s, many filariasis patients existed in southern parts of Korean peninsula.

2. Nationwide control program of lymphatic filariasis during the period of the 1960s to the late 1970s

2-1. Epidemiological studies of lymphatic filariasis during the 1960s and the 1970s

An extensive epidemiological survey on the detection of microfilaremia was carried out in Korea in 1951 (Senoo and Lincicome, 1951). They have examined a total of 5,001 persons in

25 villages on the mainland and Jeju-do. Of these, 604 cases were shown to be infected with *B. malayi*. The highest incidence of filariasis occurred in Jeju-do, the next highest in the southwestern area and the lowest in the southeastern area. Thereafter, several independent investigations focused on the epidemiological points of view including incidence rate were carried out in Korea (Paik, 1957; Lee, 1961; Hwang et al., 1965; Lee et al., 1964). During this period, epidemiological investigations also reported that 11.4% - 22.2% of elementary school children were found to be infected with microfilaria of *B. malayi* in Jeju-do (Lee, 1961 and 1964). He surveyed a total of 229 school children and found the 26 were to be infected (Lee, 1961). He subsequently reported that 14.7% of the examined persons were microfilaria positive in their blood smears (79/536 cases) (Lee, 1964).

According to Seo et al. (1965, 1968), 784 cases out of 32,673 persons were found to be infected with *B. malayi* in Korea. From 1964 to 1967, 30,534 persons were examined for the presence of microfilaria in their blood smears. A total of 24,816 night blood specimens were collected from the drafted young man aged 20 - 29 just before being conscript in the army recruitment camp where they assembled from various localities of the Korea (Seo et al., 1968). The additional blood smears were also drawn from 2,308 inhabitants in six villages of Jeju-do, 974 inhabitants of Gyeongsangbuk-do, 165 inhabitants of Namhae-gun, Gyeongsangnam-do and 2,287 inhabitants of Jeollanam-do. Among 24,816 draftees from all over the country in the army recruitment camp, 155 (0.63%) have been proved infected with *B. malayi*. Microfilaria positive cases were found to be 0.05% (1/2,102 cases) from Seoul, 2 0.9% (2/1,409 cases) Gangwon-do, 0.3% (8/3,320 cases) from Chungcheongnam-do, 0.1% 2/2,118 persons) from Chungcheongbuk-do, 1.2% (27/2,287 cases) from Jeollanam-do, 0.4% (9/2,201 cases) from Jeollabuk-do, 1.4% (69/5,008 cases) from Gyeongsangbuk-do and 3.5% (27/769 cases) from Jeju-do. A single microfilaria positive case, however, was not found in the draftees from Gyeonggi-do and Gyeongsangnam-do, when a total of 1,960 and 3,642 persons were subjected to the studies. Based on these results, Jeju-do was found to be the highest microfilaremia area (3.5%), followed by Gyeongsangbuk-do (1.4%) and Jeollanam-do (1.2%), in order of frequency. Among the draftees from Jeju-do, those from Namjeju-gun were found to be 5.4% (19/331 cases). In addition, 7 (2.3%) out of 309 from Bukjeju-gun, and 1 (0.8%) out of 129 from Jeju-si were found to be infected with *B. malayi* microfilaria. Among the draftees from Gyeongsangbuk-do, those from Yeoungdeok-gun showed the highest microfilaria positive rate (8.0%), followed by Bonghwa-gun (5.1%). Besides, those from Yeongju-gun showed 3.8%, Andong-gun 2.9%, Uljin-gun 1.5%, Gunwi-gun 0.9% and Uiseong-gun 0.4%. positive rates. On the other hands, the microfilarial positive rates from those in several counties in Jeollanam-do showed 2.9% in Yeongam-gun, 2.3% in Boseong-gun, 2.1% in Wando-gun, 1.6% in Jangheung-gun, 1.1% in Haenam-gun, 0.3% in Goheung-gun and 0.4% in Gangjin-gun. In Gangwon-do, 6 (1.0%) out of 599 in Samcheok-gun were found to be infected, 1 out of 20 in Jeonseon-gun, 1 out of 39 in Wonju-si, 1 out of 52 in Wonseong-gun, 2 out of 262 in Myeongju-gun, and 1 out of 42 in Chuncheon-si. In Jeollabuk-do, 3 out of 199 in Imsil-gun, 2 out of 122 in Namwon-gun, 2 out of 369 in Gochang-gun, 1 out of 83 in Jangsu-gun and 1 out of 19 in Muju-gun were found to be infected. In Chungcheongnam-do, 2 out 499 in Daejeon-si, 2 out of 182 in Daedeok-gun, 1 out of 190 in Gongju-gun, 1 out of 195 in Buyeo-gun, 1 out of 340 in Boryeong-gun, and 1 out of 36 in Asan-gun were found to have microfilariae in their blood specimens.

The age and sex distributions of microfilaria positive cases in Jeju-do were investigated. There was no distinct relationship between the incidence of positive cases of microfilariae and age or sex of the cases. However, the highest rate of 24.0% in the 30-39 age group and next of 20.6% in the 50-59 age group were observed.

Another microscopic examination was carried out from the inhabitants in nine different counties of Gyeongsangbuk-do. Of these, 3.1% (30/974 inhabitants) were found to be infected by *B. malayi*. Microfilaria positive cases were detected in the persons from Uljin-gun (4.2%), Bonghwa-gun (10.5%), Andong-gun (6.3%), Yeoungdeok-gun (3.0%) and Cheongsong-gun (1.5%). The mean microfilarial density was 12.2/20 μl of blood with the range of 3.0 to 14.0/20 μl of blood.

Lymphatic filariasis was found to be distributed mainly in north-eastern parts of Gyeongsangbuk-do. The microfilaria rate of the male group (7.0%) was higher than the female group (4.1%) of the inhabitants of Gyeongsangbuk-do. In the age distribution, the highest rates of microfilaremia were observed 13.2% in 20-29 age group of male, and 7.6% in 15-19 age group of female. The microfilaria positive rates were 0 to 3.2% for 400 inhabitants examined in four villages of Jindo-gun in Jeollanam-do. The average microfilarial density was 27.3/20 μl of blood. Only 1 out of 51 inhabitants in a small village of Haenam-gun was found to be infected with the microfilaria. Microfilaremia cases were not found in the inhabitants (1,820 persons) in Goguem-do in Wando-gun, while there were three cases of elephantiasis of the lower extremities. In Jindo-gun, the microfilaria rates of male (2.4%) is a little higher than that of the female (1.6%), and the highest rate of microfilaria was shown in 40-49 age group (9.1%).

2-2. Clinical manifestations of lymphatic filariasis in Korea

The episodic febrile attacks with an acute lymphadenitis and lymphangitis are characteristic to early stage lymphatic filariasis in Korea. In later stage, most prominent clinical presentation observed in Korean patients was most of elephantiasis cases did not have microfilaria in their peripheral blood smear.

The allergic lymphangitis is caused by the newly infected larvae, which was traditionally called "Momsal"in Jeju-do. When lymphangitis is associated with febrile attack and transient swelling, it had been called "Pinaerim" or "Pijong". The recurrent febrile attacks, "Momsal" and the repeated lymphangitis, "Pinaerim", might be important to lead elephantiasis in these elephantiasis cases. Smooth enlargement of the lymph nodes was found in some cases. The most commonly affected site is the inguinal lymph nodes. The hard cord-like lymphatics and varicose nodes were observed in few cases as well. No case involving scrotal area was observed in Korea (Seo, 1978). In addition, clinical signs such as chyluria, haematochyluria or chylous effusion were not observed in Korean patients. However, elephantiasis of the lower extremities, locally termed as "Soojongdari", was frequently observed, although most of cases manifested relatively mild symptoms, such as slightly enlarged legs and arms with smooth surface. The episode of recurrent febrile attack, lymphangitis, and elephantiasis are the most prominent clinical findings of lymphatic filariasis in Korea.

A survey was done to observe the clinical manifestations employing 15 cases of filarial elephantiasis in Jeju-do; one involved in the upper extremities, seven in the lower extremities, and seven in both extremities (Lee et al., 1964). He also reported that a higher prevalence of microfilaremia in females (24.4%) than in males (20.5%), as well as more elephantiasis cases in females (37 cases) than in males (6 cases). An epidemiological study in Jeju-do also reported a total of 84 elephantiasis cases, four microfilaremia patients, and two cases of scrotal hypertrophy (Soh et al., 1966). The most predilection site for elephantiasis was lower extremities (77%), followed by upper extremities (6%). Involvement of both extremities was found to be 16.7%. Subsequent epidemiological studies were conducted to figure out the clinical aspects of lymphatic filariasis in some villages of the southeastern area of Jeju-do (Seo, 1975, 1978). These reports showed that most of the patients (86.6%, 155/179 cases) experienced febrile attacks and 57.7% (101/175 patients) of the patients suffered from episodic lymphangitis. The rate of elephantiasis cases to the whole population of these endemic villages reached approximately 2.0% (Seo, 1975). The clinical symptoms, such as febrile attacks and lymphangitis, exhibited a peak frequency of distribution at their ages, 10-19 years. In the case of elephantiasis, the peak frequency was observed at the age of 40-49 years. The onset of febrile attack and lymphangitis started at the age of less than 19 years, while the onset of elephantiasis was approximately 29 years (Seo, 1975, 1978). In eastern inland of Gyeongsangbuk-do, four cases of elephantiasis were reported in the 1960s (Soh et al., 1966); three patients were males and one was female. These patients demonstrated elephantiasis in their lower extremities, which manifested at their 4th decades. Other investigation in this area described the clinical manifestations of 72 filariasis cases; a total of 58 cases (80.5%) revealed various clinical complaints including lumbago, limb pain, cold sensation, lymphedema or elephantiasis, fever attack, urticaria, cough, palpitation, nausea, fatigue, dizziness and asthma, in the decreasing frequency. However, 14 cases (19.5%) did not show any clinical presentations (Soh and Kim, 1974). Interestingly, the microfilarial counts were not correlated with the clinical signs. Elephantiasis was more commonly found in the lower extremities (82.1%).

The febrile attacks were shown to be started at 8.4 years old, 2.7 times in a year, and lasted for 2.2 days in a single attack, respectively. The fever was likely to be associated with various signs such as headache, muscle pain, and chilling sensation. The symptoms were shown to be worsened by heavy physical exercise, especially in summer (Seo, 1976). Recurrent lymphangitis was also an important clinical manifestation, which started from 7.8 years. Its frequency and duration were 1.7 times in a year and 1.1 days in an attack, respectively. The inguinal lymph nodes were found to be most frequently involved. The symptoms included painful engorgement and tenderness. This lymphangitis spread into the adjacent areas as diffuse, reddish streaks centrifugally from the inguinal lymph nodes. The lymphedema together with painful erythematous reactions were frequently found in the leg and dorsal foot. Elephantiasis was also observed with mild swellings of the leg or arm in its early stage. The swellings gradually increased in size accompanied by recurrent febrile attacks of "Momsal" and episodic lymphangitis of "Pinaerim". The affected part swelled and subsided as wax and wane pattern, and the pitting edema was gradually replaced by the elephantoid skin. Elephantiasis of the lower extremities was almost three times more common than that of the upper extremities. Occasionally, elephantiasis of the both extremities was also observed.

2-3. Nationwide control program

There were three major endemic foci of lymphatic filariasis in Korea the northeastern inland part of Gyeongsangbuk-do, the south-western coastal areas of Jeollanam-do and Jeju-do. Jeju-do was found to be the most highly endemic, whereas two other localities were found to be moderate to low endemic. Several investigators plotted out endemic areas in Namwon-myeon and Pyosun- myeon, which were the highest endemic areas in Namjeju-gun, Jeju-do. In this area, mass treatment with diethylcarbamazine was extensively conducted during 1968 and 1973.

In the inland of the northeastern areas of Gyeongsangbuk-do, the prevalence of *B. malayi* filariasis was reported to be in the range of 3.1 to 18.0% (Hwang et al., 1965; Seo et al., 1968; Kim et al., 1971, 1973, 1977; Soh et al., 1974). In high endemic areas of Yeongju-gun, Gyeongsangbuk-do (one of these inland areas), the microfilaria rate reached 18.0% in a village. In contrast, the western plain and coastal areas were found to be relatively low endemic; 1.5% at Daedeok-gun, Chungcheongnam-do, and 2.0% in Jin-do of Jeollanam-do.

Several studies have been focused on the application of optimal dosage for the treatment of lymphatic filariasis (Santiago-Stevenson et al., 1947; Wilson, 1950; Endesom and Whartom, 1958). However, many of the treated cases in the hyperendemic groups of lymphatic filariasis had severe side reactions, such as febrile attacks for the first several days of administration. This untoward effect seriously hampered further implementation of the filariasis control programs. This problem had been overcome after the early 1970s by administration of daily low dosages or with a gradual increase of daily dosages. Briefly, a low dosage schedule starts from the small initial dose, 0.5 mg/kg with increasing amount up to 6 mg/kg once a day for 5 days. Thereafter, 6 mg/kg dose was added every day, totaling diethylcarbamazine citrate 36 mg/kg in a full course, until disappearance of the microfilariae in the blood was achieved (Seo et al., 1973; Soh et al., 1977). Mass treatment has been known to provoke side reactions, such as headache, dizziness, nausea, vomiting, febrile reaction and local reactions (lymphangitis and lymphadenitis), which were not occurred by 0.5 mg/kg of the initial dose, but administration of this dosage could destruct the both microfilaria and adult worms. The febrile reaction was most frequently observed in 80.5% in the conventional, 43.9% in the low dosage schedule. The principal untoward effects usually appeared within 6 to 10 hours and lasted 48 to 72 hours in the former treatment, but these untoward symptoms occurred in 7 to 8 hours and lasted 24 to 43 hours in the latter dosage schedule. The chemotherapeutic response to low dosage schedule within shorter length of treatment was equal to that of larger doses in long term medication from the point of the reduction in microfilaria, and, in particular, the resulting side-reactions were reduced when the low dosage schedule was followed. Mass treatment was carried out on the basis of the high endemic area, where microfilaria positive rate reached 20.7% (Wimi-ri in Jeju-do). The use of 6 mg of diethylcarbamazine citrate/kg of body weight once daily at monthly internals for 12 times (totaling 72 mg/kg in a course) has been chosen as a standard chemotherapeutic course of the mass treatment. This treatment regimen was repeated year over year on the all positive cases detected for four years from 1970 to 1973. As a result, the positive rate was remarkably decreased to 2.7% from 20.7 (Seo, 1975). With this extensive eradication program, the positive rate was drastically dropped out below 1% in the middle 1980s (Lee et al., 1985; Lee et al., 1986).

The microfilaria positive rate in Yeongju-si, Gyeongsangbuk-do also decreased from

8.1% in the 1970s to 2.2% in the early 1980s. There was no positive case among 328 randomly selected persons in high endemic area of Yeongju-si, which suggested that transmission of filariasis was blocked and the infection had been almost completely controlled in this area (Kim et al., 1977,1980,1985,1994; Lee et al., 1987).

3. *Check-up for the efficacy of the control program and finalizing the elimination program during the 1980s and the 1990s*

An epidemiological survey performed in 1988 in four villages of Jeju-do that were formerly well known endemic areas has observed that microfilaremia among the inhabitants was 0.3% out of a total of 357 persons (Paik et al., 1988). On the other hands, Gyeongsangbuk-do, the moderately endemic area of *B. malayi* filariasis during the early 1970s was found to be completely controlled in the 1980s (Kim et al., 1985; Lee et al., 1987). The average microfilaria rate of this area in the late 1960s and early 1970s were 3.1% and 8.1%, respectively. Long term evaluation surveys with two 7-year intervals conducted in the 7 sample villages have confirmed that the microfilaria rate decreased from 12.4% in 1973 to 2.2% in 1980 and 0% in 1987 (Kim et al., 1980, 1985, 1994; Lee et al., 1987).

After the mid-1980s, groups of islands including Daeheuksan-do of Heuksan-myeon, located off the southwestern part of the Korean peninsula, were newly found to be moderately endemic with lymphatic filariasis (Lee et al., 1986). Surveys in these areas demonstrated relatively high incidence among inhabitants with 10.6% in the average out of a total of 1,862 persons examined in the 21 villages of the 11 small islands from 1985 to 1987 (Lee et al., 1986, 1988). All of the islands were found to be endemic and the positive rates ranged from 4.0% to

22.4%. The positive cases were found in all age groups, being increased gradually in older age groups with the peak at 17.3% in the 40-49 year age group, although microfilarial density of the positive cases was relatively low. In Wando-gun, Jindo-gun, and Yeosu-si of Jeollanam-do, the microfilarial rate was 2.5% in 1990 to 1992 (Lee et al., 1992). The infected people in Sinan-gun were treated with diethylcarbamazine during 1986 to 1992 with the low dosage schedule, and finally these treatments resulted in below 2% positive rate. A small-scale survey was conducted in this area in 2000. A total of 378 people, 151 male and 227 female, living in 8 villages (6 on Daeheuksan-do, 1 on Daejang-do, and 1 on Yeongsan-do) were subjected to a night blood survey for microfilaremia, and physical examination for elephantiasis on the extremities. There were 6 (1.6%) microfilaria positive cases, all in females aged 57-72 years, and from only two villages of the Daeheuksan-do. There were 4 patients with lower leg elephantiasis, but they showed no microfilaremia (Chai et al., 2003).

Part IV

CURRENT STATUS OF LYMPHATIC FILARIASIS IN REPRESENTATIVE ENDEMIC AREAS

1. Microfilaria positive rate in local population of Jeju-do

In Jeju-do, Senoo and Lincicome (1951) reported the high infection rate of 26.6% in Wimi-ri, Namwon-myeon, of which rate varied from 0.8 to 47% in the 1960s to 1970s (Lee,1961; Lee et al., 1964; Seo et al., 1965, 1968; Moon, 1968; Kim et al, 1973). In Namjeju-gun, microfilaria positive rate was 12% - 16.8% during the 1960s (Lee, 1961, 1964; Soh et al., 1966; Kim et al., 1968; Seo et al., 1968). The highest endemic area was found to be Namwon-myeon. During the 1970s, the infection rate ranged between 3.4 and 7.8%. However, the infection rate dropped out approximately 1% during the 1980s, when examined a total of 5,554 residents (ranged between 0.6 and 1.5%). Most recently we collected blood specimens from a total of 1,801 dwellers in 9 different villages in these areas and microscopically examined the presence of microfilaria in their blood, but found no positive case for microfilaremia in 2005 (Table 6).

In Bukjeju-gun, microfilaria positive rate was shown to be 10.2% (0.8-17.7%) among 1,298 investigated people during the 1960s. However, the infection rate reduced below 1.0% in the 1980s. When a total of 370 local residents were examined for their microfilaremia in 1980, 8 persons were found to have microfilaria in their blood specimens. During the 1990s, no more new cases were reported from this area. In 2005, we surveyed peripheral blood smears from a total of 1,543 resident people in 11 different local villages in these areas and found no positive cases (Table 7).

2. Jeollanam-do

2-1. Microfilaria positive rate in local population of Sinan-gun areas

Until the early 1980s, positive rate of microfilaremia in respective islands of Sinan-gun was found to be 12.3% (47/382 dwellers)in 6 villages of Daeheuksan-do, 8.9% (27/304 residents) in Hong-do, 10.8% (29/269 dwellers)in Daedun-do, 22.4% (15/67 residents) in Daejang-do, 20.0% (9/45 dwellers) in Youngsan-do, 7.2% (9/125 dwellers) in Damul-do, 4.0% (13/322 dwellers) in Gageo-do, 21.7% (18/83 dwellers) in Sangtae-do, 17.9% (10/56 residents) in Joongtae-do, 15.0% (15/100 dwellers) in Hatae-do, and 5.5% (6/109 dwellers) in Manjae-do, respectively. All of these positive persons were administered 36 mg/kg dose of diethylcarbamazine 1mg/kg body wt. daily for 36 days from the early 1980s to the mid-1980s.

As a consequent result, the microfilaremia positive rate considerably decreased from 12.5 % of 761 dwellers in 1986-1989 to 1.3% in 2000. Another epidemiological survey done during 1986 to 1992 also revealed that 198 cases of 2,027 dwellers (9.8%) were found to be microfilaria positive in their blood. When the follow up survey was done again in 2000, all of these positive cases except two cases (0.2%, 2/1,251 dwellers) were conversed to negative. In addition, independent survey done in some other areas in these islands disclosed 0.1% (2 of 1,393 dwellers, which was composed of 569 males and 824 females) of positive rate in two villages. However, microfilaria positive cases could not be detected any more in these areas. In 2006, we carried out a seroepidemiological study in these areas using more than 100 serum samples from elementary school children, but found no positive case. These results strongly suggested that the transmission of lymphatic filariasis might be completely blocked and the infection reached a phase of extinction in the islands of Sinan-gun (Table 8).

2-2. Microfilaria positive rate in local population of Jindo-gun areas

In 1992, the positive rate of microfilaria in these regions were shown to be 3.7% in Donggeocha-do (2/54 people), 7.1% in Cheongdeung-do (2/28 dwellers), and 1.1% (1/94 residents) in Gwanmae-do. These areas were found to be relatively low endemic areas when compared to other remote islands areas among Jeollanam-do.

An epidemiological survey done in ten years later in 2002 has revealed no microfilaria positive cases in these areas. The study subjects were composed of 248 people in Donggeocha-do, Cheongdeung-do, and Gwanmae-do, and 631 residents (246 males and 358 females) in 18 village of 15 islands in Jindo-gun.

In 2006, we investigated a total of 383 people resided in 11 villages in eight different islands in Jindo-gun and found no positive case. This result indicated that the lymphatic filariasis appeared to be eradicated in Jindo-gun islands (Table 9).

2-3. Microfilaria positive rate in local population of Wando-gun areas

Wando-gun is located in the southwestern part of Jeollanam-do. During the mid-1980s, Wando-gun area was belatedly found to be an endemic area (0 to 1.6% positive rate) (Lee et al., 1992). However, Wando-gun has been shown to have lowest infection rates compared to other endemic areas in Jeollanam-do including Sinan-gun (9.8% - 21.6%), Jindo-gun (1.7% - 7.1%), Yeosu-si (0.9% - 2.4%) during 1985 to 1992 (Lee et al., 1986, 1987, 1988, 1989, 1992). When we examined a total of 500 inhabitants (245 male and 255 female) in four villages in Bogil-do, Wando-gun, three microfilaria positive cases were detected in 1992. The positive rate was 0.6%. They were all aged male cases. However, recent survey carried out in the same areas in 2003 revealed that, among 465 examinees, no positive case could be detected. This result strongly suggested that transmission of lymphatic filariasis was terminated in these areas. Table 10 summarized changes of microfilaremia in these areas.

2-4. Microfilaria positive rate in local population of population of Yeosu-si, Tongyeong-si and Yeonggwang-gun areas

An epidemiological survey of 723 blood specimens, which were collected from 312 males and 411 females, from 10 villages and 5 islands in Yeosu-si during the mid-1990s revealed no positive case with microfilaria. This number accounted for 58.6% of whole dwellers in this area. A total of 230 samples collected from 97 males and 133 females from three village inhabitants of Geomun-do revealed 0.9% of positive rate of microfilaria (1.0% for male and 0.3% for female). However, no positive case was detected in 2004 when 423 people (178 men and 245 women) from four villages were subjected to the examination (Table 11).

We investigated a total of 594 people, which consisted of 270 males and 324 females, from 16 villages in eight different islands of Tongyeong-si in 2004.We found no positive case. This number accounted for 78.4% of whole inhabitants of the areas covered (Table 12). An investigation for microfilaria of 76% of whole inhabitants, which included 266 people (127 males and 139 females) from five villages in four islands which belong to Yeonggwang-gun revealed no positive case of microfilaria in their blood specimens in 2005 (Table 13).

3. Microfilaria positive rate in local population of Gyeongsangbuk-do

During the 1960s, Seo et al. (1965, 1968) examined a total of 974 blood specimens for the presence of microfilaria. The microscopic observation revealed positive rate of 3.1% (30 samples). Microfilaria positive cases were detected in the persons from Uljin-gun (4.2%), Bonghwa-gun (10.5%), Andong-gun (6.3%), Yeongdeok-gun (3.0%) and Cheongsong-gun (1.5%), respectively. The mean microfilarial density was 12.2/20 μl of blood with the range of 3.0 to 14.0/20 μl of blood. During the 1970s to 1980s, the infection rate decreased below 1%. In 2005, NIH team collected a total of 1,369 blood samples from these areas and examined for their positive rate of microfilaria, but found no positive case (Table 14) (Kim et al., 2006).

4. Ecology of vector mosquitoes

The variation of seasonal distribution of *Ae. togoi* larvae was observed. It showed 65.3 in March, when water temperature was approximately 5.8℃. Their appearance increased gradually and plateaued after June, at which 93.5 larvae were collected in a night in southern coastal area of Jeollanam-do. When the larva was collected per quadrat from March to October in Maemul-do, the average number of the larvae were 24.9 and 72.9 in March and June, respectively, but these numbers continually decreased after August. In Jeju-do, average numbers of the collected mosquitos were 9.2 in April. Of these, 1st to 2nd week age constituted with 70.7%, and 4th week age constituted with 9.8%. It reached peak in June (Tables 16-21) (Lee et al., 1995).

Lee et al. (1995) also observed the appearance of *Ae. togoi* larvae according to the salt concentration of the rock pool in southern costal area of Jeollanam-do. As the salt concentration of rock pool increase after July by climate condition such as temperature or typhoon, occurrence of the larvae had greatly decreased. In reproductive place of larvae, 68.6% of the larvae were observed in 0.5% salt concentration.

An increase of the salt concentration in water for rearing larvae might reduce the susceptibility of *Ae. togoi* mosquitoes to *B. pahangi* infection (Sucharit et al., 1982). The mosquitoes were cultured under salt concentrations of 0, 0.5, 1.0, 2.0 and 4.0% (Lee, 1992). Five days after the final molting, the adult mosquitoes were subjected to feed on gerbil having a microfilarial count of 13. 76/μl of blood. Mosquitoes grown at > 2.0% salt concentrations seemed to be less susceptible to the filarial infection. The average numbers of filarial larvae/mosquito were 1.75, 1.95, 1.74, 1.36 and 1.33, when the mosquito larvae were grown in 0, 0.5, 1.0, 2.0 and 4.0% salt concentrations, respectively. The average number of microfilariae was less than 5 in 80% of the mosquitoes. However, some mosquitoes were found to be infected with up to 37 microfilariae.

Ae. togoi was found to suck human blood during night-time. They suck blood actively from 9:00 pm to 04:00 am with peak time at 02:00 am. *Ae. togoi* might bite humans more actively indoors during midnight. The number of the mosquitoes caught indoors was 60.7 and that of outdoors was 50.3. The relationship between the microfilarial periodicity in the peripheral blood and the blood sucking time of the mosquitoes was analysed (Lee et al., 1988). The microfilarial periodicity of *B. malayi* on the island of south-western part of Korea was typically nocturnal. The highest microfilaria count in the patient blood was observed during 11:00 pm - 5:00 am (1.1-1.4/µl). The pattern of nocturnal periodicity of microfilaria in the peripheral blood observed on the south-western island was quite similar to that observed in the inland Korea (Kim et al., 1971, 1977) as well as on Jeju-do (Seo, 1974). Human biting mosquitoes actively sucked the blood during 1:00 am - 3:00 am. These results collected clearly demonstrated that the occurrence of microfilariae in the peripheral blood was highly correlated with the time of high activity of mosquitoes.

Part V

EFFICACY EVALUATION OF ELIMINATION PROGRAM IN 2006

1. Necessity and method of the evaluation
2. Filarial antibody test for the elementary school children and residents who have had inhibited in the endemic areas of lymphatic filariasis prior to the elimination

2-1. Filarial antibody test for the elementary school children

2-2. Filarial antibody test for the resident people

3. Vector mosquito surveys to examine the infective filarial larvae in previously endemic areas

1. Necessity and method of the evaluation

In order to properly evaluate the filariasis control program, establishment of comparative criteria, technical indicators, and reliable methods for evaluation is prerequisite. Effective control and prevention of *B. malayi* filariasis should be accompanied with trials on a large scale of administration of anthelmintics with extensive geographical coverage over a long period. Blockage of the transmission of the lymphatic filariasis should cover up the whole endemic areas.

When a total of 32, 673 people in eight different provinces in Korea were subjected to microscopic examination for *B. malayi* from 1964 to 1970, 784 cases revealed microfilaremia in their blood specimens. All of these people were treated with diethylcarbamazine. From 1960-1969, a total of 8,713 local residents in Jeju-do was examined. Of these, a total of 1,110 people were shown to be positive with the microfilaria or they were found to be an acquaintance of the patients. All the positives were subjected to prescription of diethylcarbamazine. The number of positive cases was drastically dropped in the 1980s. When a total of 6,124 people were subjected to microscopic examination, 58 cases were found to be positive with microfilaria. Those with microfilaria were also treated with diethylcarbamazine.

On the other hands, an investigation in a control area of Yeongju-si, Gyeongsangbuk-do demonstrated that a total of 73 microfilaria positives were found when 557 persons were subjected to the microscopic examination in 1973; number of positives cases were significantly decreased to 8 out of 370 persons examined in 1980. In 1987, No microfilaria positive case was found when a total of 125 persons were examined in this area. This result indicated that the transmission of filariasis *malayi* was almost ceased in inland Korea.

In the case of Jeollanam-do, microfilaria positive rate was found to be 8.2% (212 positive cases when a total of 2,574 inhabitants were examined) between 1986 and 1990 in Sinan-gun; the rate decreased to 1.6% in 2000 (6 positive cases/380 examinee), and to 0.14% (2 cases/1,393 people) in 2002, respectively. In Jindo-gun, 5 people was shown to be microfilaria positive in their peripheral blood smears when a total of 296 inhabitants were examined in 1992 (1.7%), but when we performed epidemiological survey in 2003, no more positive case could be detected (0 case/631 examinee). In addition, we found a total of 3 cases among 500 inhabitants in 1991 (0.6%) in Wando-gun. However, no positive with microfilaria was found among reexamined 2,488 persons in 2003 by NIH team. Also the occurrence of the microfilaria cases could not be found from these areas from 2002 to 2005. These data indicate that transmission of *B. malayi* has ceased in Gyeongsangbuk-do, Jeollanam-do and Jeju-do areas where *B. malayi* had been prevalent in Korean peninsula.

Furthermore according to consultation of WHO filariasis elimination regional committee, specific antibody test using BRUGIArapid™ (MBDr) and peripheral blood smear examination were executed for the 10 ~ 13 years old children (elementary school 3rd ~ 6th grade) and the inhabitants of the former filariasis endemic areas from 2005 to 2006.

2. Filarial antibody test for the elementary school children and residents who have had inhibited in the endemic areas of lymphatic filariasis prior to the elimination

2-1. Filarial antibody test for the elementary school children

For the detection of anti-*B. malayi* antibodies in young age groups, primary school children of 3rd to 6th grade (10 to 13 years old), BRUGIArapid^{TM} dipstick test kit was used as recommended by WHO in 2005. In short, the dipstick is prepared with a goat anti-mouse antibody control line and *B. malayi* recombinant-antigen test line. Anti-filarial antibodies in patient sera react with this antigen, followed by binding of this complex with monoclonal anti-human IgG4 conjugated to colloidal gold. The overall results of the evaluation for brugian filariasis showed 97% sensitivity, 99% specificity, 97% positive predictive value and 99% negative predictive value (Rahmah et al., 2001). Further evaluations of the test were reported (Rahmah et al., 2003; Lammie et al., 2004; Fischer et al., 2005).

We selected 11 primary schools in Jeju-do, 18 places in Jeollanam-do, and two sites in Gyeongsangbuk-do, where *B. malayi* filariasis had been endemic. In Jeju-do, Aewol-eup, Gujwa-eup, Chuja-myeon (Daeseo-ri and Sinyang-ri), Namwon-eup (Harei, Sillea, Wimi, Namwon, and Taeheung), Seongsan-eup (Sinsan), and Pyoseon-myeon (Tosan) were chosen. In Jeollanam-do, a total of 18 places were selected; Nohwa-do (Ipo-ri), Bogi-ldo (Buhwang-ri and Jungtong-ri), Jin-ri, Hong-do, Heuksan-myeon (Yeongsan-ri, Heuksanbuk, Heuksanseo, Heuksandong, Heuksanhatae, and Heuksan Gageo), Gwanmae-do Gwanmae, Donggeocha-do Donggeocha, Seogeocha-do Seogeocha, Geomundo Geomun-ri, Seo-do (Seodo-ri and Deokcheon-ri), and Geomun (Dong-do). In Gyeongsangbuk-do, Yeongju-si (Hamang-dong and Hyucheon 1-dong) was included.

Out of a total tested of 1,329 children (720 males and 609 females) in Jeju-do, of 1,369 children (739 males and 630 females) in Gyeongsangbuk-do, and of 351 children (191 males and 160 females) in Jeollanam-do, none were found positive.

2-2. Filarial antibody test for the resident people

For this study, a total of 1,526 residents were randomly selected from formerly endemic areas of Jeollanam-do, Gyeongsangbuk-do, and Jeju-do. In brief, people reside in Wimi 2-ri, Gueom-ri, Tosan 2-ri, Taehung1-ri, Hare1-ri, Gimnyeong-ri, Samdal2-ri, Yecho-ri, Sinyang 2-ri, Yongheung-ri, Deaseo-ri were subjected to the test in Jeju-do, In Jeollanam-do, dwellers in Seodo-ri, Geomun-ri, Yuchon-ri, Seonchang-ri, Beakdo-ri, Jeongdong-ri, Yesong-ri, Jukchon-ri, Hongdo1-gu, Hongdo 2-gu, Jin-ri 2-gu, Ma-ri, Bi-ri, Wqanchon-ri, Sip-ri, Sa-ri, Cheondeung-do, Seogecha-do, Gwanmea-do, Gage-do, Damul-do, Deadun-do, Yongsan-do, and Tea-do were subjected to antibody test. People in Yeongju-si (Yongsang 2-ri, Yongsang1-ri, Sincheon 2-ri, Manbang 2-ri, Jidong 2-ri) in Gyeongsangbuk-do were also selected for the specific antibody test. Out of a total tested of 446 persons (162 males and 284 females) of five different areas in Jeju-do, of 865 persons (335 males and 535 females) of 25 remote island areas in Jeollanam-do, and of 215 persons of five areas in Gyeongsangbuk-do, none were found to be positive.

3. *Vector mosquito surveys to examine the infective filarial larvae in previously endemic areas*

The mosquitoes discovered in the west Pacific area are known to be 37 species which belong to four genera. *Ae. togoi* has been recognized as an important vector for transmission of *B. malayi* on Jeju-do, southern coastal areas and on islands. *An. sinensis* was importantly involved in local transmission of *B. malayi* in inland Korea (Kim et al,. 1977).

Ae. togoi is a dominant species in Jeju-do among all 14 species of mosquitoes identified in this area (Wada et al., 1973). From 2002 to 2005, NIH team had caught the mosquitos using Yoshisawa Black light trap, and classified their species. *Ae. togoi* constituted a major population, of which proportion had been reached 41.2% of the total mosquito population. In Namwon-eup Jeju-do, the collected mosquitos were a total of 76 individuals classifiable to four species, three genera. These included *Cx. pipiens* (53.9%), *Ae. togoi* (40.1%), *Cx. tritaeniorhynchus*(5.3%), and *An. sinensis* (0.7%). In Wando-gun, eight species belonging to four genera were collected from May to October and *Ae. togoi* constituted a dominant species in this area. In the mosquito densities in two places of Geomun-do, Yeosu-si, *Ae. togoi* occupied 85.4% of the whole mosquito population. In Maemul-do, Tongyeong-si, *Ae. togoi* also constituted a dominant species (98.6%) from May to October during 2002-2005. *An. sinensis*, a vector species in the inland areas was not detected.

It had been quite curious that the vector host for lymphatic filariasis in inland Korea had not been identified (Cha, 1969). Kim et al. (1971) reported that *An. sinensis* was a dominant species occupied 69.5% of the collected mosquitoes in Yeongju-si. Although, *An. sinensis* had been thought to be involved in the transmission of *B. malayi* in this area, dissection of the local mosquitoes carried out in 1971 did not reveal the third stage *B. malayi* larvae. However vector potential test revealed that *B. malayi* microfilariae develope favorably to the 3rd stage infective larvae in *An. sinensis.* In an extended investigation conducted in 1973, out of a total of 4,351 *An. sinensis* dissected, 14 of them (0.3%) were found harboring *B. malayi* 3rd stage infective larvae. *An. sinensis* was thus confirmed to be the main vector of *B. malayi* filariasis in the inland Korea (Kim et al., 1971, 1977).

Part VI

ASSESSMENT ON THE SUCCESS OF FILARIASIS ELIMINATION PROGRAM

1. Brief review of the elimination program

The lymphatic filariasis was first recorded in Korea in 1927 by identifying the *B. malayi* worm sections from an autopsied specimen of an elephantiasis patient. Thereafter, investigators demonstrated that filariasis had also been found in Chungcheongnam-do and Jeju-do (Oh, 1929). During the 1930s, microfilaria positive rate among 5,001 residents in 25 villages in the southern region of Korea and Jeju-do had been described (604 cases/5,001 samples) (Senoo & Lincicome, 1951). The highest positive rate in Jeju-do reached by 26.6%, and all the affected species were found to be *B. malayi*. Since then, many researchers reported about the endemic distribution of lymphatic filariasis in Korea including Jeju-do.

Seo et al. (1968) investigated the regional distribution of 784 persons who were found to be microfilaria positive from a night blood sample survey of 32,673 persons. They reported that these people were from coastal and inland areas of Jeollanam-do, northeast region of Gyeongsangbuk-do, and Jeju-do. Among them, Jeju-do was the largest epidemic foci in Korea because 78% (617 persons) of the positive persons resided in Jeju-do. Prior to the nationwide survey, Seo et al. (1965) examined a total of 2,139 persons from all over Jeju-do, and reported that the larva positive rates ranged from 0.8 to 19.5%, and the average number of larvae was 1.9/1 µl of blood.

To review the changing patterns of microfilaria positive rate in Bukjeju-gun, Jeju-do, where the lymphatic filariasis was highly epidemic during the 1960s, Seo et al. (1965, 1968) reported the positive rate of 10.2% from 1,298 inhabitants. However, this positive rate conspicuously decreased to below 1.0% during the 1980s (Lee et al., 1985, 1989). In 2005, epidemiological survey done by the filariasis team of the National Institute of Health did not find microfilaria positive persons from 1,543 subjects by microscopic examination. For Namjeju-gun, the positive rate was reported to be ranged from 12 to 16.8% according to the investigators during the 1960s (Lee, 1961; Lee et al., 1964; Moon, 1968; Seo et al., 1965, 1968). During the 1970s, however, it considerably decreased to 3.7 to 4.0% (Kim et al., 1973; Seo et al., 1973). It decreased to 1.5% in the first half and further down to 0.6% in the second half during the 1980s (Lee et al., 1985, 1986). In 2005, no microfilaria positive people were found from 1,801 people, which clearly indicated that the microfilaria completely disappeared from Jeju-do island where once was an endemic area.

In inland Korea, Hwang et al. (1965) examined 378 persons in Yeongju, Gyeongsangbuk-do, and observed a total of 29 microfilaria positive persons (7.7%) for the first time. In 1970s, through an epidemiological investigation conducted in 1970 to 1973, the prevalence rate of microfilaremia was shown to be 8.1% on the average out of a total of 2,178 persons examined from 32 villages with the range of microfilaria rate 2.6 to 18.0% (Kim et al., 1971, 1974, 1977). Clinical and physical observations of Malayan filariasis cases of Yeongju area were carried out as well (Soh et al., 1974, 1977). To reduce the severe side reactions induced by the conventional regimen of diethylcarbamazine (72mg/kg) maintaining its efficacy, efficacy of diethylcarbamazine citrate against Malayan filariasis was evaluated with three modified low dosage schedule prior to mass treatment in this area (Kim et al., 1974;Soh et al., 1977). Mass chemotherapy with diethylcarbamazine was carried out with low dosage schedules (36mg/kg) of 1mg/kg body wt. daily for 36 days, which showed the most acceptable result. For an evaluation of the transmission of *B. malayi* in the villages in this area, transition of prevalence rate of microfilaremia was determined for 14 years period with 7 years interval in a control area from 1973. The prevalence rate was 12.4% out of 621 persons examined from 6 villages in 1973. The prevalence rate in 1980 was 2.2% out of 370 persons examined, and in 1987, none were found positive out of 328 persons examined (Kim et al., 1980, 1994: Lee et al., 1987). These results indicated that the transmission of *B. malayi* filariasis was probably terminated in this area.

On the other hands, the south-western remote islands including Heuksan-do (islands) of Sinan-gun, Jeollanam-do were belatedly found to be endemic foci in Korea during the mid-1980s (Lee et al., 1986). Large scale-based epidemiological surveys in these areas were extensively carried out by several investigators (Lee et al., 1988, 1989; Yong et al., 1988). From 1986 to 1990, a total of 213 cases of microfilaria positive persons were detected out of 2,533 subjects (8.4%) in Sinan-gun. However, microfilarial density of the positive cases was relatively low.

The average microfilaria count for 198 positives was 33.4/120 µl night blood. In this region, three (0.1%) positive cases were found even among young age group under 10, which strongly suggested that there was propagation although the transmission was minimal. An epidemiological survey done in 2000 found 6 positive cases among 380 persons (1.6%) (Chai et al., 2003). In addition, two positive cases among 1,393 samples tested (0.2%) were found in 2002 from an examination by National Institute of Health. However, all of these people were older than 60, and the microfilarial density was 1.5/120 µl. These results clearly demonstrated that there was almost no possibility of transmission of filariasis in these areas.

The microfilaria positive rate in Jindo-gun, Wando-gun, and Yeosu-si, was estimated as low as 0.6-1.7% in 1992. Chemotherapy with diethylcarbamazine together with ivermectin greatly contributed to the reduction of lymphatic filariasis in these areas. No positive person was detected in 2002 and 2004 in these areas.

2. Implementation of nationwide filariasis elimination programs

Although diethylcarbamazine has been shown to have more killing effect against *B. malayi* filarial worms than it did against *W. bancrofti*, administration of first dose of diethylcarbamazine to the lymphatic filariasis patients often caused fever and other serious untoward effects. In addition, there were carriers whose microfilaria count rapidly decreased by successive administration of diethylcarbamazine in a short time but gradually increased again. In this case, good results could be achieved when they took the medicine once every week or month for a long time. Based on this finding, it was recommended for the patients to take 2 mg/kg once every day for the first five days and then 6 mg/kg every week or month.

When Jeju-do was found to be highly epidemic area for lymphatic filariasis, many researchers conducted epidemiological surveys and administered the patients with diethylcarbamazine to microfilaria positive people to exterminate filariasis (Seo et al., 1973, 1974; Kim et al., 1973). Paik (1986) administered diethylcarbamazine with the dose of 5 mg/kg/day for six days (total 30 mg/kg) to 34 persons among 52 microfilarial positive cases as a short-term concentration method. The total microfilarial count in blood prior to administration was found to be 3,558 and the average count was 104.6. Two weeks after the treatment, the total microfilarial count decreased to 2 with an average count of 0.07. Although the microfilarial count increased slightly to 16 with an average count of 0.5 four months after medication, administration of diethylcarbamazine was found to have relatively excellent microfilariacidal effect. The negative conversion rate of microfilaremia was determined to be 93% at two weeks of administration, and 74.2% at four months post-treatment, respectively. More conspicuous finding other than the negative conversion rate of microfilaremia was the decrease of microfilarial density in the administered group. The successful treatment of the patients based on individual microfilarial negative conversion rate was important, however, sharp decrease of microfilarial density would have great impact on the removal and/or reduction of local transmission of filariasis in community based endemic areas. Many investigators insisted that the decrease of microfilarial density in a certain group is more conspicuous than the negative conversion rate of microfilaremia. Conclusively, it is believed that the decrease of microfilarial density in the administered group has profound impact on the removal of filariasis in certain local endemic areas.

One remarkable finding was that microfilaria negative conversion rate and reduction rate reached a plateau when 1 mg/kg of diethylcarbamazine was administered for 36 days (total 36 mg/kg) for *B. malayi* positive persons in Sinan-gun, Jindo-gun, and Wando-gun in Jeollanam-do between 1986 and 1992. The average microfilarial density of 213 positive persons in Sinan-gun was initially found to be 31.7. Among these 213 positive persons, 142 persons were subjected to re-examination three months after medication. Their average microfilaria density was found to be decreased to 29.6 of them. Among these people, 110 persons (77.5%) showed negative conversion and the remaining microfilaria positives also showed a decreased microfilarial density from 29.6 to 17.9, resulting in 86.4% of microfilarial reduction rate. The reason why some people did not respond to the drug, thus resulting in a failure of drug treatment. This result might be ascribed to the fact that different physiological reaction of individuals to the drugs. It might partly due to an improper administration of the drug by the carriers who did not feel the need for medication. Chai et al. (2003) administered a mixture of albendazole (400 mg) and ivermectin (150 µg/kg) to six microfilarial positive persons found in Sinan-gun, Jeollanam-do as a single therapy. They were all found to have negative conversion. The microfilaria positive persons identified in 2002 were also cured by the same regimen.

3. *Environmental changes that shrink mosquito breeding rock pools along the sea shores by construction of new towns (Saemaeul movement) and villages*

It is known in Korea that the vector hosts of *B. malayi* is *Ae. togoi* in the coast and islands and that of inland is *An. sinensis*. Since discovery of the infectious larvae of *B. malayi* from *Ae. togoi* in Jeju-do in 1960 (Lee, 1964), many researchers examined the presence of the larvae within the mosquito and confirmed that the mosquito involved in the transmission of *B. malayi* in Jeju-do was *Ae. togoi* (Chun, 1968; Kim et al., 1973; Wada et al., 1973; Seo 1978). Seo et al (1965) reported that there are many holes in rocks in the coast of Jeju-do, and they provided the optimum unhabitual conditions for the larvae of *Ae. togoi*, because they found that the more holes the rocks had, the higher was the infection rate. Lee (1969) found that *Ae. togoi* was the most prevalent species in Jeju-do. Its prevalence reached as high as 70 to 90% according to the villages. In natural status, the infection rate of the larvae to the *Ae. togoi* is proportional to the infection rate of residents. Therefore, the natural infection of mosquitoes is directly associated with human infection, which implies that transmission of lymphatic filariasis could successfully be controlled through the mass chemotherapy of humans.

The improved life standard of residents is believed to have greatly decreased the opportunities for residents to be exposed to the blood sucking of vector mosquitoes. In the past, there were many agricultural and fishing villages that did not have electricity and many of the residents slept outside during the hot summer and easily exposed to mosquito biting. However, this is no longer the case with the supply of electricity, and the use of mosquito net and pesticides such as mosquito repellent and aerosols have created a situation that is unfavorable to the spread of mosquito-borne diseases.

Furthermore, all the residences in farm villages and islands now have protection nets on windows to block insects including mosquitoes, and most houses in islands have installed chassis at the end of the eaves to shut the always strong wind, so the inside of the house is not directly exposed to the outside, further preventing the intrusion of mosquitoes.

4. Changes in human behaviors: avoiding mosquito bites, seeking medical attentions and etc

The improvement of living standards, residences and villages by the modernization and economic development that began from the 1970's, the gradual urbanization of farm villages and industrial development, wide use of agricultural pesticide, and chemical extermination of insects to prevent the mosquito mediating diseases, especially during summer season, have significantly reduced the habitats and the population density of mosquitoes. Moreover, the heightened health consciousness of individuals accompanied by economic affluence partly contributed to the extermination of endemic diseases. The virtual active period of mosquitoes is six to seven months in Korea, which is shorter than the tropical and subtropical zones. These various environmental causes are also believed to minimize the exposure to mosquitoes and contributed to the prevention of propagation of the disease in Korea.

Most importantly, the microfilarial positive patients were continuously searched for and should be treated, and this resulted in free of microfilaremia in these persons. Although they were not converted to microfilaremia negative, the microfilarial density was greatly decreased, which was the principal factors responsible for the extermination of filariasis. In particular, Jeju-do and other islands were turned into tourist destinations, and the improved residential environment and development of the community decreased the habitats of mosquitoes. Another cause was the increased interest of people in self-protection against mosquitoes, which decreased the opportunities for people to be exposed to mosquitoes. In these areas, the positive people decreased greatly since the 1980s and most of them are now adults in their sixth decades or older. The population of farm villages and islands is continuously decreasing. The young people migrate from islands to inland and cities for education and employment, which resulted in almost no natives in these areas. Some of the positive people are naturally decreasing with movement or death. Such complex causes as movement to other regions, death, and natural cure have contributed together to the extermination of filariasis in the endemic areas in Korea.

Part VII

CONCLUDING REMARK

Elimination of lymphatic filariasis in Korea

References

Elimination of lymphatic filariasis in Korea

The lymphatic filariasis had been prevalent in Korea more than 1,000 years before. The episodic febrile attacks accompanied by acute lymphadenitis and lymphangitis are the clinical manifestations characteristic to the early stage of lymphatic filariasis in Korea. This allergic lymphangitis is caused by the introduction of fresh infective larvae. The attacks are usually recurrent, and traditionally known as "Momsal" in filariasis endemic areas in Korea. When lymphangitis is associated with febrile attack and transient swelling of the extremities, it is traditionally called "Pinaerim" or "Pijong"in these endemic areas. These clinical manifestations, "Pinaerim" or "Pi-Momsal" (combines "Momsal" with "Pinaerim"), lasts several days and recurrently occur several times in a year. The recurrent febrile attacks, "Momsal"and the repeated occurrence of lymphangitis, "Pinaerim", seemed to be important factors that may consequently result in elephantiasis in some of the infected cases. Enlargement of lymph nodes was also found in some cases; large in size, not hard, rather rubbery in consistency and movable. The most commonly affected site is the inguinal lymph nodes. In few cases, hard cord-like lymphatics and varicose nodes were also observed. No case of lymphangitis of the spermatic cord or lymph-scrotum, which was commonly seen in bancroftian filariasis, was recognized in lymphatic filariasis patients in Korea (Seo, 1978). Clinical signs such as chyluria, haematochyluria or chylous effusion were not usually observed in Korean patients, but elephantiasis of the extremities, locally termed as "Soojongdari", was frequently observed. The episode of recurrent febrile attack, lymphangitis, and elephantiasis are the most important clinical signs of lymphatic filariasis found in Korea.

Jeju-do had long been known as the highest endemic area of lymphatic filariasis in Korea with the highest microfilaremia 19.5% in Taeheung-ri, Namjeju-gun until the 1970s (Soh et al., 1977). The microfilarial density was 3.63/µl of blood (Seo et al., 1965). The prevalence of filariasis decreased to a significantly low level of 0.5% following mass and selective treatments conducted since 1968 (Kim, 1994). The prevalence further dropped out in 1998. A survey done in four formerly well known endemic areas revealed that microfilaria positive rate of 0.3%, when a total of 357 persons were subjected to microscopic examination (Paik et al., 1988). In the southeastern inland area, Gyeongsangbuk-do, where lymphatic filariasis had been moderately endemic during the early 1970s, the disease had been eradicated in the 1980s by extensive case detection and selective treatments. The average microfilaria rate of this area during the late 1960s and early 1970s were 3.1 % and 8.1 %, respectively. Long term evaluation surveys with two 7-year intervals conducted in seven sample villages have revealed that the microfilaremia rates decreased from 12.4% in 1973 to 2.2% in 1980 and 0% in 1987 (Kim, 1994).

Lymphatic filariasis had been thought to be almost disappeared before middle of the 1980s in Korea. However, a groups of islands including Daeheuksan-do of Heuksan-myeon, which located off the southwestern costal area of the Korea peninsula, were belatedly found to be moderately endemic with lymphatic filariasis during the mid-1980s (Lee et al., 1986). Surveys in these areas during 1985-1987 demonstrated relatively high incidence (10.6%) among inhabitants. When we examined a total of 1,862 persons in 21 villages of the 11 small islands, all of these islands were found to be endemic, and the positive rates ranged from 4.0% to 22.4% (Lee et al., 1986, 1988). The positive cases were found in all age groups, being increased gradually with age, and reached its peak in the 40-49 year age group (17.3%), although the microfilarial density of the positive cases was relatively low (33.4/120 μl of night blood). After the treatment with diethylcarbamazine with the low dosage schedule, however, infection rate had been dropped to 1.4% in 2000.

The successful eradication of filariasis in the Republic of Korea was accomplished mainly by an effective medication followed by intensive surveillance, elevation of residing environmental conditions and life qualities, and control of mosquito vectors. Diethylcarbamazine is a highly effective drug against lymphatic filariasis; however, severe untoward reactions occur. To minimize the untoward effects of diethylcarbamazine, an alternative chemotherapeutic regimen was introduced (Seo and Lee, 1973); decreasing the total dosage to 37.5 mg/kg and a gradual increase of the dosage from 0.5 mg/kg to 6 mg/kg (a low dosage schedule). The conventional regimen of diethylcarbamazine is 72 mg/kg in a total dose by treating 6 mg/kg/day for 6 days and several repeated medications for 1-2 months. This alternative regimen, low dose medication (5 mg/kg/day for 6 days), was also effective in the patients in Jeju-do. In addition to the therapeutic efficacy of diethylcarbamazine, reduction of microfilaremia in the medicated population is essential to minimize the infection rate in endemic regions. The successful treatment of the patients based on individual microfilarial negative conversion rate was important, however, sharp decrease of microfilarial density would have great impact on the removal of local transmission of filariasis in community based endemic areas. Many investigators insisted that the decrease of microfilarial density in a certain group is more conspicuous than the negative conversion rate of microfilaremia. It is believed that the decrease of microfilarial density in the administered group has profound impact on the removal of filariasis in certain local endemic areas.

Most recently, we performed a large scale antibody test using BRUGIArapid™ for 3,049 school children aged 10-13, in areas where *B. malayi* filariasis had been prevalent, and found that no case was positive. This data may reflect the transmission of filariasis in the Republic of Korea was terminated.

In conclusion, over the past several decades from 1950s to 2006, many investigators paid their efforts to the detection, treatment, follow-up of the lymphatic filariasis patients in endemic areas and to the control of the filariasis in Korea. Mass combined with selective treatment with diethylcarbamazine to microfilaria positive persons had been made them free from microfilaremia and contributed to the significant reduction of the microfilarial density. Significant reduction of microfilaria positives in an area influenced eventually to the endemicity of the filariasis in the locality. Together with remarkable economic growth followed by improvement of environment personal hygiene and living standard, these factors stated above contributed to blocking the transmission cycle of *B. malayi* and led to the disappearance of this mosquito-borne ancient disease in the Republic of Korea.

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Annex 1

Important Events

1927 Identification of first authentic case of lymphatic filariasis in Korea.

1929-1930 First epidemiological survey was carried out in Chungcheongnam-do and Jeju-do.

1930-1940 Analysis of the clinical manifestations observed in Korean patients. The episodic febrile attacks accompanied by acute lymphadenitis and lymphangitis are the clinical manifestations characteristic to the early stage of lymphatic filariasis. The recurrent febrile attacks, and the repeated occurrence of lymphangitis seemed to be important factors that may consequently result in elephantiasis in some of the infected cases. Enlargement of lymph nodes was also found in some cases; large in size, not hard, rather rubbery in consistency and movable. The most commonly affected site is the inguinal lymph nodes. No case of lymphangitis of the spermatic cord or lymph-scrotum was recognized in lymphatic filariasis patients in Korea. Clinical signs such as chyluria, haematochyluria or chylous effusions were not usually observed, but elephantiasis of the extremities was frequently observed. The episode of recurrent febrile attack, lymphangitis, and elephantiasis are the most important clinical signs of lymphatic filariasis found in Korea.

1951 Survey in southern region of Korea and Jeju-do revealed 12.1% of positive rate for microfilaria (604 cases/5,000 examinee). The highest positive rate in Jeju-do reached 26.6%. All the affected species were identified as *Brugia malayi*.

1953	Launching of nationwide epidemiological survey. There were three major endemic foci of the lymphatic filariasis in Korea, including the northeastern part of Gyeongsangbuk-do, the western coastal areas of Jeollanam-do and Jeju-do.
1964	Start mass chemotherapy with diethylcarbamazine in endemic areas. Identification of *Aedes togoi* as a vector mosquito for *B. malayi* filariasis on Jeju-do.
1973	Introduction of low dosage regimen with diethylcarbamazine. Administration of low dosages daily or with a gradual increase of daily dosages after several days of initial administration, totaling 36 mg/kg in a full course.
1974	Identification of *Anopheles sinensis* as a vector mosquito responsible for local transmission of *B. malayi* in inland areas of Korea.
1980	Epidemiological surveys in Jeju-do, where the lymphatic filariasis was most endemic, revealed that the microfilaria positive rate reduced to a significantly low level of 0.5% following mass and selective treatments. In inland Korea, there has also been marked decrease of microfilaremia from 12.4% in 1973 to 2.2% in 1980.
1986	The epidemiological surveys in four villages of Jeju-do showed 0.3% of microfilaria positive rate in their peripheral blood smears. In inland Korea, microfilaria positive case was not detected.
1986	A groups of remote islands of Jeollanam-do, including Daeheuksan-do of Heuksan-myeon (Sinan-gun), which is located off the southwestern part of the Korean peninsula, were newly found to be endemic areas of *B. malayi* filariasis. Surveys in these areas demonstrated relatively high microfilaria rate among inhabitants with 10.6% on the average out of a total of 1,862 persons examined in the 21 villages of the 11 small islands from 1985 to 1987. The average microfilaria count for 198 positive cases were 33.4/120 µl night blood.

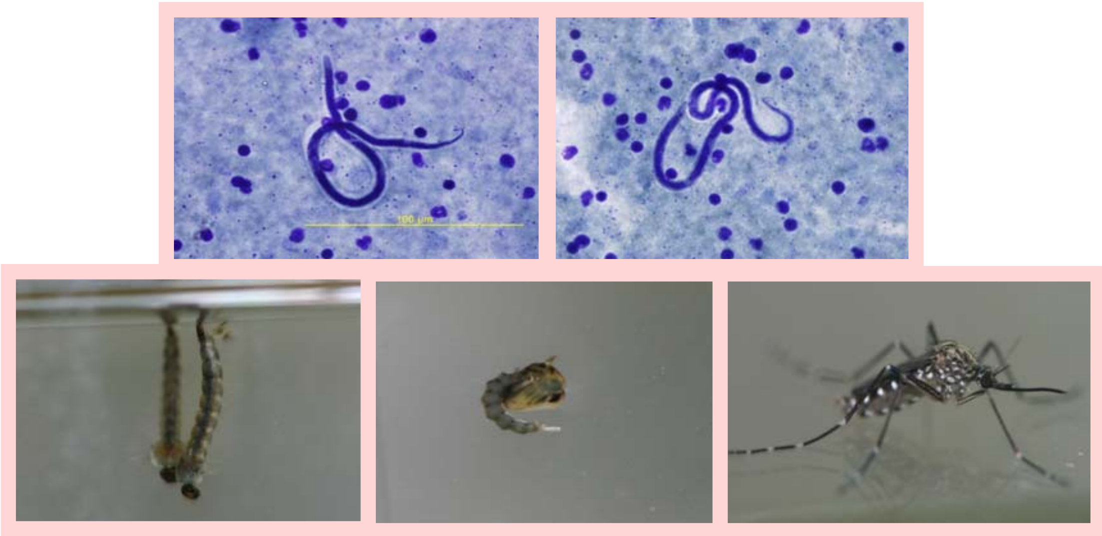
1988 Analysis of the relationship between the nocturnal periodicity of microfilariae of *B. malayi* in the peripheral blood and the blood sucking time of the vector mosquitoes. The lowest microfilaria count was seem between 11:00 am and 3:00 pm. It gradually increased in the evening, with a significant increase at night around 9:00 pm and reached a plateau around 1:00 am (1.6 microfilariae/μl). The highest microfilaremia was observed during 11:00 pm - 5:00 am (1.1-1.4 microfilariae/μl). The mosquitoes showed a typical nocturnal activity. Their peak human biting time was between 1:00 am - 3:00 am.

1992-2000 The infected people in Sinan-gun were treated with diethylcarbamazine from 1986 to 1992 with the low dosage schedule. In 2000, epidemiological survey revealed 1.4% of positive rate (2 cases). A total of six persons including these two persons were treated with a single dose of albendazole and ivermectin, which resulted in successful treatment. In 2003, no positive case was found in these areas.

2002-2005 Microfilaria surveys were done in three endemic areas of Jeju-do, Jeollanam-do including Sinan-gun and Gyeongsangbuk-do. No case was found to be positive with microfilaria by microscopic examination (0 case/9,426 examinee).

2006 A seroepidemiological survey was carried out for 3,049 school children aged 10-13, in areas where *B. malayi* filariasis had been prevalent . No case was positively reacted. This result may further reflect that the transmission of filariasis in the Republic of Korea has already probably terminated more than three decades ago.

Annex 2: Photographs (Case and control)



Brugia malayi microfilaria from positive cases of Sinan-gun, Jeollanam-do (Kim et al., 2002) and *Aedes togoi* being reared in insectary (2007)

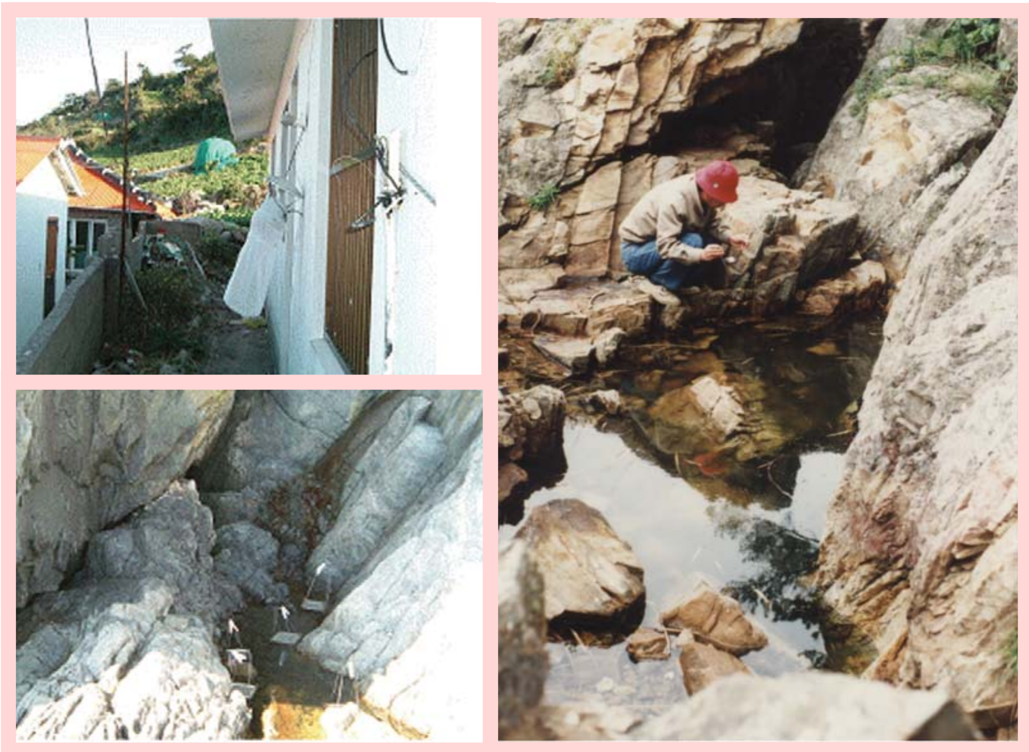
Visiting to a village in endemic areas and residents waiting for blood collection (Sinan-gun, 1986, 1987)

Education of filariasis to the residents in endemic areas and distribution of DEC tablets (Sinan-gun Jeollanam-do, 1987)

Elephantiasis of upper extremities of filariasis *malayi* cases (Sinan-gun, Jeollanam-do, 1986 and 1988)

Elephantiasis of lower extremities of filariasis *malayi* cases

(Sinan-gun, Jeollanam-do, 1986 and 1989)



Yoshisawa black light traps hanged under the eaves of a house and around rock pools on the seashore of Maemul-do as *Aedes togoi* breeding places (Sinan-gun, Jeollanam-do, 1988)

Anti-*Brugia* specific antibody test for elementary school children in Jeollanam-do, Gyeongsangbuk-do, and Jeju-do in 2006

Anti-*Brugia* specific antibody test by BRUGIArapid™ (MBDr) in the former endemic areas of Jeollanam-do, Gyeongsangbuk-do and Jeju-do in 2006

Past view of a village and a house in an endemic area of Jeollanam-do (1986)

Recent view of a village and a house in an endemic area of Jeollanam-do (2006)

Past view of a village and a house in an endemic area of Gyeongsangbuk-do (1987)

Recent view of a village and a house in an endemic area of Gyeongsangbuk-do (2006)

Past view of a village of an endemic area of Jeju-do (1986)

Recent view of a village of an endemic area of Jeju-do (2006)

Appendix I

LIST OF TABLES

Table 1. Microfilarial survey of night blood specimens collected from army recruitment camp in 1964 to 1967.

Areas	No.exam.	No.pos. (%)
Seoul	2,102	1 (0.005)
Gyeonggi-do	1,960	0
Gangwon-do	1,409	12 (0.9%)
Samcheock-gun	599	6 (1)
Chuncheon-si	42	1 (2.4%)
Myeongju-gun	262	2 (0.8)
Wonseong-gun	52	1 (1.9)
Wonju-si	39	1 (2.6)
Jeongseon-gun	20	1 (5)
Chungcheongnam-do	3,320	8 (0.3)
Daejeon-si	499	2 (0.4)
Gongju-gun	190	1 (0.5)
Daedeock-gun	182	2 (1.1)
Buyeo-gun	195	1(0.5)
Boryeong-gun	340	1 (0.3)
Asan-gun	36	1 (2.8)
Chungcheongbuk-do	2,118	2 (0.1)
Cheongwon-gun	408	1 (0.2)
Okcheon-gun	207	1 (0.5)
Jeollabuk-do	2,201	9 (0.4)
Namwon-gun	122	2 (1.6)
Imsil-gun	199	3 (1.5)
Jangsu-gun	83	1 (1.2)
Muju-gun	19	1 (5.3)
Gochang-gun	369	2 (0.5)
Jeollanam-do	2,287	27 (1.2)
Wando-gun	380	8 (2.1)
Haenam-gun	419	5 (1.1)
Yeongam-gun	34	1 (2.9)
Boseong-gun	298	7 (2.3)
Jangheung-gun	259	4 (1.6)
Gangjin-gun	228	1 (0.4)
Goheung-gun	303	1 (0.3)
Gyeongsangbuk-do	5,008	69 (1.4)
Yeoungdeok-gun	112	9 (8)
Bonghwa-gun	568	29 (5.1)
Yeongju-gun	160	6 (3.8)

Table 1. Microfilarial survey of night blood specimens collected from army recruitment camp in 1964 to 1967 (continued)

Areas	No. exam.	No.pos. (%)
Andong-gun	757	21 (2.9)
Uljin-gun	67	1 (1.5)
Uiseong-gun	262	1 (0.4)
Gunwi-gun	108	1 (0.9)
Daegu-si	541	1 (0.2)
Gyeongsangnam-do	3,642	0
Jeju-do	769	27 (3.5)
Jeju-si	129	1 (0.8)
Namjeju-gun	331	19 (5.4)
Bukjeju-gun	309	7 (2.3)
Total	24,816	155 (0.63)

(Seo et al., 1968)

Table 2. List of Korean mosquitoes

I Anophelinae

Genus 1. *Anopheles*

1. *Anopheles sinensis* Wiedemann
2. *Anopheles sineroides* Yamada
3. *Anopheles koreicus* Yamada & Watanabe
4. *Anopheles yatsushiroensis* Miyazaki
5. *Anopheles lindesayi japonicus* Yamada
6. *Anopheles pullus* Yamada

II. Culicinae

Genus 2. *Culex*

7. *Culex (Neoculex)hayashii* Yamada
8. *Culex (Neocules) rubensis* Sasa et Takahashi
9. *Culex (Lutzia) fuscanus* Wiedemann
10. *Culex (Lutzia) vorax* Edwards
11. *Culex (Culiciomyia) kyotoensis* Yamaguti et La Casse
12. *Culex (Culex) bitaeniorhynchus* Giles
13. *Culex (Culex) sinenesis* Theobald
14. *Culex (Culex) whitmorei* Giles
15. *Culex (Culex) orentalis* Edwards
16. *Culex (Culex) mimeticus* Noe
17. *Culex (Culex) jacksoni* Edwards
18. *Culex (Culex) tritaeniorhynchus* Dyar
19. *Culex (Culex) vishnui* Theobald
20. *Culex (Culex) sitiens* Wiedemann
21. *Culex (Culex) vagans* Wiedemann
22. *Culex (Culex) pipens pallens* Coquillett
23. *Culex (Culex) pipiens quinquefasciatus* Say

Genus 3. *Aedes*

24. *Aedes (Stegomyia) albopictus* Skuse
25. *Aedes (Stegomyia) chemulpoensis* Yamada
26. *Aedes (Stegomyia) flavopictus* Yamada
27. *Aedes (Stegomyia) galloisi* Yamada
28. *Aedes (Finlaya) nipponicus* La Casse et Yamaguti
29. *Aedes (Finlaya) oreophilus* Edwards
30. *Aedes (Finlaya) hatorii* Yamada
31. *Aedes (Finlaya) japonicus* Theobald
32. *Aedes (Finlaya) koreicous* Edwards
33. *Aedes (Finlaya) togoi* Theobald
34. *Aedes (Finlaya) seoulensis* Yamada
35. *Aedes (Finlaya) kobayashii* Nakata
36. *Aedes (Aedimorphus) vexans nipponii* Theobald
37. *Aedes (Aedimorphus) alboscutellatus* Theobald
38. *Aedes (Ochlerotatus) dorsalis* Meigen
39. *Aedes (Neomelaniconion) lineatopennis* Ludlow
40. *Aedes (Aedes) esoensis* Yamada

Genus 4. *Armigeres*

41. *Armigeres (Armigeres) subalbatus* Coquillett

Genus 5. *Mansonia*

42. *Manonia (Mansonia) uniformis* Theobald
43. *Mansonia (coquilletidia) ochracea* Theobald

Genus 6. *Heizmannia*

44. *Heizmannia lii* Wu

Genus 7. *Tripteroides*

45. *Tripteroides bambusa* Yamada

Genus 8. *Culiseta*

46. *Culiseta (culiseta) kanayamenisis* Yamada
47. *Culiseta (Culiseta) nipponica* Yamaguti et La Casse

III Toxorhynchitinae

Genus 9. Toxorhynchites

48. *Toxorhynchites (Toxorhychites) towadensis* Matsumura
49. *Toxorhynchites (Toxorhynchites) aurifluus koryoensis* Osasawara

(Lee, 1978)

Table 3. Natural infection of *Anopheles sinensis* with *Brugia malayi* 3rd stage infective larvae in Yeongju-si, Gyeongsangbuk-do

Authors (Year)	village	Microfilaria rate (%)	No. of dissected	No. pos.
Kim et al. (1971)	Sangmang-2ri	6.3	2,304	0
Kim et al. (1973)	Unmun-1ri & Sincheon-2ri	12.4	4,351	14

(Kim et al., 1971, 1974, 1977)

Table 4. The rate of natural infection of *Aedes togoi* in Jeju-do (1960~1975)

Authors (Year)		Village							
		Wimi-2ri	Taeheung-ri	Tosan-ri	Biyang-ri	Haye-ri	Heonggan Is.	Kapa Is.	Wimi-1ri
Lee (1964)	Mf rate (%)	22.2	-	-	-	-	-	-	-
	No. of dissected	464	-	-	-	-	-	-	-
	No. pos.	2	-	-	-	-	-	-	-
	Infect. rate (%)	0.7	-	-	-	-	-	-	-
Chun (1968)	Mf rate (%)	-	28.6	27.2	27.3	13.4	17.1	6.2	-
	No. of dissected	-	157	-	130	139	-	19	-
	No. pos.	-	10	-	11	5	-	1	
	Infect. rate (%)	-	6.4	-	8.5	3.6	-	5.2	-
Kim et al. (1973)	Mf rate (%)	-	30.1	12.4	17.7	-	25.2	7.1	-
	No. of dissected	-	127	126	98	-	78	67	-
	No. pos.	-	9	4	4	-	6	1	-
	Infect. rate (%)	-	7.1	3.2	4.1	-	7.7	1.4	-
Kim et al. (1973)	Mf rate (%)	-	4.3	6.4	2.7	15.2	26.1	0.9	-
	No. of dissected	-	96	64	30	-	28	64	-
	No. pos.	-	0	0	0	-	3	0	-
	Infect. rate (%)	-	0	0	0	-	10.7	0	-
Seo (1976)	Mf rate (%)	-	-	-	-	-	-	-	19.2
	No. of dissected	-	-	-	-	-	-	-	299
	No. pos.	-	-	-	-	-	-		1
	Infect. rate (%)	-	-	-	-	-	-	-	0.3

Table 5. Transition of microfilaria rate in inhabitants of Yeongju-si in 1973, 1980 and 1987

Area	Village	1973			1980			1987		
		No. exam.	No. pos.	% pos.	No. exam.	No. pos.	% pos.	No. exam.	No. pos.	% pos.
Yeongju-si	Baranggol	61	11	18.0	34	2	5.9	34	0	0
	Ganuni	66	4	6.1	-	-	-	48	0	0
	Guitonggol	41	3	7.3	30	0	0	33	0	0
	Alseonggol	86	15	17.4	72	3	4.2	50	0	0
	Jangjagol	91	5	5.5	65	0	0	38	0	0
	Saehae	276	39	14.1	169	3	1.8	125	0	0
Total		**621**	**77**	**12.4**	**370**	**8**	**2.2**	**328**	**0**	**0**

(Kim, 1994; Kim et al., 1973, 1980; Lee et al., 1985, 1986, 1987, 1988, 1989; Paik et al., 1986, 1988)

Table 6. Reduction of microfilaria rate in Namjeju-gun

Year		Village					
		Namwon-eup	Pyoseon-myeon	Seongsan-eup	Andeok-myeon	Daejeong-eup	Total
1963-'65	No. exam.	317	162	201	150	0	830
	No. pos.	59	22	7	12	0	100
	% pos.	18.6	13.6	3.5	8	0	12
1968-'70	No. exam.	1,301	800	0	0	1,239	3,340
	No. pos.	326	174	0	0	60	560
	% pos.	25.1	21.8	0	0	4.8	16.8
1970-'73	No. exam.	5,415	3,289	4,980	0	0	13,684
	No. pos.	257	119	168	0	0	544
	% pos.	4.7	3.6	3.4	0	7.8	4
1978	No. exam.	312	365	0	0	360	1,037
	No. pos.	18	20	0	0	0	38
	% pos.	5.8	5.5	0	0	0	3.7
1982-'84	No. exam.	1,133	488	1,892	0	0	3,513
	No. pos.	22	13	17	0	0	52
	% pos.	1.9	2.7	0.9	0	0	1.5
1985-'89	No. exam.	1,448	172	115	241	65	2,041
	No. pos.	8	1	4	0	0	13
	% pos.	0.5	0.6	3.5	0	0	0.6
2005	No. exam.	1,059	516	90	0	136	1,801
	No. pos.	0	0	0	0	0	0
	% pos.	0	0	0	0	0	0

(Kim et al., 1968; Kim et al., 1968, 1970, 1973; Kim et al., 2005; Lee, 1961, 1964; Moon, 1968; Seo et al., 1965, 1969, 1973, 1974, 1976; Soh et al., 1966)

Table 7. Reduction of microfilaria rate in Bukjeju-gun

Year		Village						
		Aewol-eup	Hallim-eup	Gujwa-eup	Hangyeong-myeon	Jocheon-eup	Chuja-myeon	Total
1963-'68	No. exam.	63	542	174	201	119	199	1,298
	No. pos.	10	96	3	2	1	20	132
	% pos.	15.9	17.7	1.7	1	0.8	10.1	10.2
1985-'89	No. exam.	117	136	165	0	147	513	1,078
	No. pos.	1	0	1	0	0	9	11
	% pos.	0.9	0	0.6	0	0	1.8	1
2005	No. exam.	105	302	410	189	0	537	1,543
	No. pos.	0	0	0	0	0	0	0
	% pos.	0	0	0	0	0	0	0

(Kim et al., 1968; Kim et al., 1968, 1987; Kim et al. 2005; Lee, 1961, 1964; Lee et al., 1985, 1986, 1987, 1988, 1989; Moon, 1968; Paik, 1986, 1988; Seo et al., 1965, 1968, 1969; Soh et al., 1966)

Table 8. Reduction of microfilaria rate on the islands in Sinan-gun, Jeollanam-do in 1986 to 2002

Island	Village	1986-1992			2000			2002		
		No. Exam.	No. Pos.	% Pos.	No. Exam.	No. Pos.	% Pos.	No. Exam.	No. Pos.	% Pos.
Daeheuksan-do	Jin-ri 2gu	90	2	2.2	73	0	0	89	0	0
	Bi-ri	60	10	16.7	46	0	0	57	1	1.8
	Sa-ri	55	5	9.1	76	2	2.6	111	0	0
	Sim-ri	78	9	11.5	44	4	9.1	63	1	1.6
	Ma-ri	51	11	21.6	27	0	0	33	0	0
	Gonchon-ri	48	10	20.8	24	0	0	-	-	0
	Ye-ri 2gu	-	-	-	-	-	-	69	0	0
Subtotal		**382**	**47**	**12.3**	**290**	**6**	**2.1**	**422**	**2**	**0.5**
Daedun-do	Su-ri	124	15	12.1	-	-	-	89	0	0
	Domok-ri	61	7	11.5	-	-	-	48	0	0
	O-ri	84	7	8.3	-	-	-	32	0	0
Subtotal		**269**	**29**	**10.8**	**-**	**-**	**-**	**169**	**0**	**0**
Hong-do	Hongdo 1gu	162	12	7.4	-	-	-	142	0	0
	Hongdo 2gu	142	15	10.6	37	0	0	40	0	0
subtotal		**304**	**27**	**8.9**	**37**	**0**	**0**	**182**	**0**	**0**
Gageo-do	Gageo 1gu	235	7	3	-	-	-	96	0	0
	Gageo 2gu	44	4	9.1	-	-	-	20	0	0
	Gageo 3gu	43	2	4.7	-	-	-	16	0	0
Subtotal		322	13	4	-	-	-	132	0	0
Daejang-do	Jangdo-ri	67	15	22.4	45	0	0	56	0	0
Yeongsan-do	Yeongsan-ri	45	9	20	45	0	0	-	-	0
Damul-do	Damul-ri	125	9	7.2	49	0	0	84	0	0
Sangtae-do	Sangtaedo-ri	83	18	21.7	-	-	-	31	0	0
Jungtae-do	Jungtaedo-ri	56	10	17.9	-	-	-	-	-	-
Hatae-do	Hataedo-ri	100	15	15	-	-	-	43	0	0
Manjae-do	Manjaedo-ri	109	6	5.5	-	-	-	38	0	0
Ui-do	Ui 1gu	79	0	0	-	-	-	38	0	0
	Ui 2gu	49	0	0	-	-	-	17	0	0
Seosoui-do	Ui 3gu (Seori)	37	0	0	-	-	-	29	0	0
Dongsoui-do	Ui 3gu (Seori)	-	-	-	-	-	-	10	0	0
Subtotal		**750**	**82**	**15.7**	**139**	**0**	**0**	**94**	**0**	**0**
Total		**2,027**	**198**	**9.8**	**466**	**6**	**1.3**	**1,251**	**2**	**0.2** (Treat with DEC)

(Lee et al., 1986, 1987, 1988, 1989; Yong et al., 1988;Kim, 1994; Chai et al., 2003; Lee et al., 1992, 2002)

Table 9. Microfilaria rate among inhabitants on the islands of Jindo-gun, Jeollanam-do in 2002

Island	Village	No. exam.			No. pos.			% pos.		
		Total	Male	Female	Total	Male	Female	Total	Male	Female
Seogeochado	Seogeochado-ri	50	25	25	0	0	0	0	0	0
Donggeochado	Dongyuk-ri	75	31	44	0	0	0	0	0	0
	Dongmak-ri	31	10	21	0	0	0	0	0	0
Maengkoldo	Maengkoldo-ri 1gu	20	9	11	0	0	0	0	0	0
Jukdo	Maengkoldo-ri 2gu	6	1	5	0	0	0	0	0	0
Dokgeodo	Dokgeo-ri 1gu	13	5	8	0	0	0	0	0	0
Seoldo	Dokgeo-ri 2gu	8	7	1	0	0	0	0	0	0
Jukhangdo	Jukhang-ri	33	17	16	0	0	0	0	0	0
Cheongdeungdo	Cheongdeung-ri	27	14	13	0	0	0	0	0	0
Gwanmaedo	Gwanmae-ri	80	32	48	0	0	0	0	0	0
	Gwanho-ri	101	38	63	0	0	0	0	0	0
Daemado	Daema-ri	41	11	30	0	0	0	0	0	0
	Daemak-ri	15	4	11	0	0	0	0	0	0
Somado	Soma-ri	38	12	26	0	0	0	0	0	0
Gwansado	Gwansa-ri	57	16	41	0	0	0	0	0	0
Naebyeongdo	Naebyeongdo-ri	13	6	7	0	0	0	0	0	0
Oebyeongdo	Oebyeongdo-ri	13	4	9	0	0	0	0	0	0
Jinmokdo	Jinmokdo-ri	10	4	6	0	0	0	0	0	0
Total		**631**	**246**	**385**	**0**	**0**	**0**	**0**	**0**	**0**

(Kim et al., 2002)

Table 10. Microfilaria rate among inhabitants on the islands of Wando-gun, Jeollanam-do in 2003

Area	Island	Village	No. exam.			No. pos.			% pos.		
			Total	Male	Female	Total	Male	Female	Total	Male	Female
Bogil-myeon	Bogildo	Seonchang-ir	64	33	31	0	0	0	0	0	0
		Jeongdong-ri	84	40	44	0	0	0	0	0	0
		Book-ri	49	23	26	0	0	0	0	0	0
		cheongbyeol-ri	67	30	37	0	0	0	0	0	0
		Baekdo-ri	60	25	35	0	0	0	0	0	0
		Yesong-ri	141	67	74	0	0	0	0	0	0
	Total		**465**	**218**	**247**	**0**	**0**	**0**	**0**	**0**	**0**
Nohwa-up	Nohwado	Bukgo-ri	71	35	36	0	0	0	0	0	0
	Subtotal		71	35	36	0	0	0	0	0	0
	Neopdo	Nae-ri	174	76	98	0	0	0	0	0	0
		Bangchuk-ri	152	79	73	0	0	0	0	0	0
	Subtotal		**326**	**155**	**171**	**0**	**0**	**0**	**0**	**0**	**0**
	Seoneopdo	Seo-ri	75	33	42	0	0	0	0	0	0
	Eoryongdo	Eoryong-ri	25	16	9	0	0	0	0	0	0
	Masakdo	Masak-ri	8	3	5	0	0	0	0	0	0
	Norokdo	Norok-ri	15	5	10	0	0	0	0	0	0
	Total		**520**	**247**	**273**	**0**	**0**	**0**	**0**	**0**	**0**
Soan-myeon	Soando	Maengseon-ri	106	43	63	0	0	0	0	0	0
		Mira-ri	187	84	103	0	0	0	0	0	0
		Bukam-ri	45	18	27	0	0	0	0	0	0
		sojin-ri	108	52	56	0	0	0	0	0	0
	Subtotal		**446**	**197**	**249**	**0**	**0**	**0**	**0**	**0**	**0**
	Dangsado	Dangsa-ri	38	17	21	0	0	0	0	0	0
	Hoenggando	Hoenggan-ri	93	43	50	0	0	0	0	0	0
	Gudo	Gudo-ri	30	12	18	0	0	0	0	0	0
	Total		**607**	**269**	**338**	**0**	**0**	**0**	**0**	**0**	**0**

(Kim et al., 2003)

Table 10. Microfilaria rate among inhabitants on the islands of Wando-gun, Jeollanam-do in 2003 (continued)

Area	Island	Village	No. exam.			No. pos.			% pos.		
			Total	Male	Female	Total	Male	Female	Total	Male	Female
Cheongsan-myeon	Cheongsan-do	Dorak-ri	89	39	50	0	0	0	0	0	0
		Gukhwa-ri	30	14	16	0	0	0	0	0	0
		Dongcheon-ri	59	22	37	0	0	0	0	0	0
		Gwondeok-ri	21	8	13	0	0	0	0	0	0
	Subtotal		199	83	116	0	0	0	0	0	0
	Daemo-do	Modong-ri	54	21	33	0	0	0	0	0	0
		Moseo-ri	89	37	52	0	0	0	0	0	0
	Subtotal		143	58	85	0	0	0	0	0	0
	Somo-do	Mobuk-ri	33	14	19	0	0	0	0	0	0
	Yeoseo-do	Yeoseo-ri	63	30	33	0	0	0	0	0	0
	Jang-do	Ji-ri	12	4	8	0	0	0	0	0	0
Total			450	189	261	0	0	0	0	0	0
Geumil-eup	Pyeongi-ldo	Iljeong-ri	91	40	51	0	0	0	0	0	0
		Yeonghang-ri	46	25	21	0	0	0	0	0	0
	Subtotal		137	65	72	0	0	0	0	0	0
	Darang-do	Darang-ri	19	12	7	0	0	0	0	0	0
	Sorang-do	Sorang-ri	75	39	36	0	0	0	0	0	0
	Sin-do	Sindo-ri	29	10	19	0	0	0	0	0	0
Total			260	126	134	0	0	0	0	0	0
Saengil-myeon	Saengil-do	Yuchon-ri	81	37	44	0	0	0	0	0	0
		Yongchul-ri	32	12	20	0	0	0	0	0	0
	Subtotal		113	49	64	0	0	0	0	0	0
	Deogu-do	Deogu-ri	60	31	29	0	0	0	0	0	0
Total			173	80	93	0	0	0	0	0	0
Grand total			2,475	1,129	1,346	0	0	0	0	0	0

(Kim et al., 2003)

Table 11. Microfilaria rate among inhabitants on the islands of Yeosu-si, Jeollanam-do in 2004

Area	Island	Village	No. exam.			No. pos.			% pos.		
			Total	Male	Female	Total	Male	Female	Total	Male	Female
Samsan-myeon	Seo-do	Seodo-ri	163	86	77	0	0	0	0	0	0
		Deokchon-ri	112	40	72	0	0	0	0	0	0
	Dong-do	Jukchon-ri	109	39	70	0	0	0	0	0	0
		Yuchon-ri	39	13	26	0	0	0	0	0	0
	Sonjuk-do	Sonjuk-ri	90	41	49	0	0	0	0	0	0
	Sogeomun-do	Sonjuk-ri	12	5	7	0	0	0	0	0	0
	Cho-do	Uiseong-ri	36	15	21	0	0	0	0	0	0
		Gyeongchon-ri	21	11	10	0	0	0	0	0	0
		Jinmak-ri	69	33	36	0	0	0	0	0	0
		Daedong-ri	72	29	43	0	0	0	0	0	0
Total			**723**	**312**	**411**	**0**	**0**	**0**	**0**	**0**	**0**

(Kim et al., 2004)

Table 12. Microfilaria rate among inhabitants on the islands of Tongyeong-si, Jeollanam-do in 2004

Area	Island	Village	No. exam.			No. pos.			% pos.		
			Total	Male	Female	Total	Male	Female	Total	Male	Female
Hansan-myeon	Maemul-do	Maejuk-ri (Danggeum)	46	16	30	0	0	0	0	0	0
		Maejuk-ri (Daehang)	22	8	14	0	0	0	0	0	0
	Somaemul-do	Maejuk-ri	5	2	3	0	0	0	0	0	0
	Subtotal		**73**	**26**	**47**	**0**	**0**	**0**	**0**	**0**	**0**
Yokji-myeon	Yokji-do	Seosan-ri (Dodong)	51	24	27	0	0	0	0	0	0
		Seosan-ri (Yudong)	26	13	13	0	0	0	0	0	0
		Donghang -ri(Jabu)	59	27	32	0	0	0	0	0	0
		Donghang-ri (Gwancheong)	33	12	21	0	0	0	0	0	0
		Donghang-ri (Mokgwa)	18	7	11	0	0	0	0	0	0
	Yeonhwa-do	Yeonhwa-ri	88	45	43	0	0	0	0	0	0
	U-do	Udo-ri	11	4	7	0	0	0	0	0	0
	Dumi-do	Dumi-ri (Namgu)	31	14	17	0	0	0	0	0	0
		Dumi-ri (bukgu)	41	23	18	0	0	0	0	0	0
	Sangnodae-do	Nodae-ri (Sangri)	71	35	36	0	0	0	0	0	0
		Nodae-ri (Sandeung)	33	13	20	0	0	0	0	0	0
		Nodae-ri (Tanhang)	37	15	22	0	0	0	0	0	0
	Hanodae-do	Nodae-ri (Hari)	22	12	10	0	0	0	0	0	0
	Subtotal		**521**	**244**	**277**	**0**	**0**	**0**	**0**	**0**	**0**
Total			**594**	**270**	**324**	**0**	**0**	**0**	**0**	**0**	**0**

(Kim et al., 2004)

Table 13. Microfilaria rate among inhabitants on the islands of Yeonggwang-gun, Jeollanam-do in 2004

Area	Island	Village	No. exam.			No. pos.			% pos.		
			Total	Male	Female	Total	Male	Female	Total	Male	Female
Nagwol-myeon	Sangnakwol-do	Sangnagwol-ri	73	38	35	0	0	0	0	0	0
	Hanakwol-do	Hanagwol-ri	33	13	20	0	0	0	0	0	0
	Songi-do	Songi-ri	55	21	34	0	0	0	0	0	0
	Anma-do	Wolchon-ri	86	47	39	0	0	0	0	0	0
		Singi-ri	19	8	11	0	0	0	0	0	0
Total			**266**	**127**	**139**	**0**	**0**	**0**	**0**	**0**	**0**

(Kim et al., 2004)

Table 14. Antibody to *Brugia malayi* in elementary school children in Jeollanam-do, Gyeongsangbuk-do and Jeju-do in 2006

Area			Age and gender												Total	Total pos.
			10			11			12			13				
			M.	F.	Pos.	M.	F.	Pos.	M.	F.	Pos.	M.	F.	Pos.		
Gyeongsang buk-do	Yeongju-si	Yeongju-si Hamang-dong	69	60	0	72	72	0	75	65	0	74	42	0	529	0
		Yeongju-si Hyucheon 1-dong	133	121	0	105	87	0	105	99	0	106	84	0	840	0
	Sub Total		202	181	0	177	159	0	180	164	0	180	126	0	1369	0
Jeju-do	Buk Jeju-do	Aewol-eup	25	14	0	19	14	0	18	11	0	30	20	0	151	0
		Gujwa-eup	17	13	0	15	16	0	22	20	0	19	21	0	143	0
		Chuja-myeon Daeseo-ri	11	6	0	12	12	0	7	9	0	11	6	0	74	0
		Chuja-myeon Sinyang-ri	2	5	0	5	4	0	3	3	0	4	2	0	28	0
	Nam Jeju-do	Namwon-eup Harei	9	16	0	7	6	0	14	8	0	8	8	0	76	0
		Namwon-eup Sinrei	9	4	0	16	13	0	14	9	0	12	7	0	84	0
		Namwon-eup Wimi	30	33	0	34	27	0	32	29	0	37	32	0	254	0
		Namwon-eup Namwon	44	27	0	31	35	0	31	38	0	32	36	0	274	0
		Namwon-eup Taehung	14	13	0	13	10	0	14	12	0	21	10	0	107	0
		Seongsan-eup Sinsan	11	14	0	20	7	0	13	15	0	10	11	0	101	0
		Pyoseon-myeon Tosan	10		0	3	6	0	5	5	0	6	2	0	37	0
	Sub Total		182	145	0	175	150	0	173	159	0	190	155	0	1329	0
Jeollanam-do	Wando-gun	Nohwado Nohwa-eup Ipo-ri	12	6	0	11	7	0	12	7	0	11	6	0	72	0
		Bogildo Buhwang-ri Bogil	7	11	0	8	7	0	10	12	0	14	5	0	74	0

Table 14. Antibody to *Brugia malayi* in elementary school children in Jeollanam-do, Gyeongsangbuk-do and Jeju-do in 2006 (continued)

Area			Age and gender												Total	Total pos.
			10			11			12			13				
			M.	F.	Pos.	M.	F.	Pos	M.	F.	Pos.	M.	F.	Pos.		
Jeollanam-do	Wando-gun	Bogildo Jungtong-ri Bogil	1	4	**0**	3	0	**0**	3	3	**0**	3	4	**0**	21	**0**
	Sinan-gun Heuksan-do	Jin-ri Heuksan	6	7	**0**	9	6	**0**	5	4	**0**	3	10	**0**	50	**0**
	Hong-do	Hongdo Heuksan	4	0	**0**	0	1	**0**	3	3	**0**	2	2	**0**	15	**0**
	Yeongsan-do	Heuksan-myeon Yeongsan-ri	0	0	**0**	0	0	**0**	0	0	**0**	0	0	**0**	0	**0**
	Damul-do	Heuksan-myeon Heuksanbuk	1	0	**0**	2	1	**0**	1	1	**0**	0	0	**0**	6	**0**
	Heuksan-do	Heuksan-myeon Heuksanseo	1	1	**0**	0	0	**0**	1	0	**0**	2	1	**0**	6	**0**
	Daedun-do	Heuksan-myeon Heuksandong	2	2	**0**	2	4	**0**	0	0	**0**	1	1	**0**	12	**0**
	Hatae-do	Heuksan-myeon Heuk sanhatae	1	0	**0**	0	0	**0**	1	0	**0**	0	0	**0**	2	**0**
	Gageo-do	Heuksan-myeon Gageo	2	1	**0**	3	1	**0**	2	2	**0**	1	1	**0**	13	**0**
	Jindo-gun	Gwanmaedo Jodo-myeon Gwanmae	0	1	**0**	2	0	**0**	1	3	**0**	2	1	**0**	10	**0**
		Donggeochado Jodo-myeon Donggeocha	4	1	**0**	1	2	**0**	1	0	**0**	0	1	**0**	10	**0**
		Seogeochado Jodo-myeon Seogeocha	0	0	**0**	0	0	**0**	0	0	**0**	0	0	**0**	0	**0**

Table 14. Antibody to *Brugia malayi* in elementary school children in Jeollanam-do, Gyeongsangbuk-do and Jeju-do in 2006 (continued)

Area			Age and gender												Total	Total pos.
			10			11			12			13				
			M.	F.	Pos.	M.	F.	Pos.	M.	F.	Pos.	M.	F.	Pos.		
Jeollanam-do	Jindo-gun	Geomun-do Geomun-ri Geomun	2	3	0	6	5	0	3	2	0	2	6	0	29	0
		Seo-do Samsan-myeon Seodo-ri Seodo	1	1	0	4	0	0	1	3	0	1	1	0	12	0
		Seo-do Samsan-myeon Deokcheon-ri	0	1	0	0	1	0	1	2	0	2	1	0	8	0
		Dong-do Samsan-myeon Geomun	2	0	0	2	2	0	0	0	0	3	2	0	11	0
Sub Total			46	39	0	53	37	0	45	42	0	47	42	0	351	0
Total			814	691	0	757	655	0	751	688	0	787	604	0	3,049	0

(Kim et al., 2006)

Table 15. Antibody to *Brugia malayi* in resident people in Jeollanam-do, Gyeongsangbuk-do and Jeju-do in 2006

Area		Total	M.	F.	Total Pos.
Gyeongsangbuk-do	Yongsang2-ri	52	17	35	0
	Yongsang1-ri	40	16	24	0
	Sinchon2-ri	54	17	37	0
	Manbang2-ri	32	14	18	0
	Jidong2-ri	37	18	19	0
Subtotal		**215**	**82**	**133**	**0**
Jeollanam-do	seodo-ri	41	9	32	0
	Gemun-ri	61	18	43	0
	Yuchon-ri	21	6	15	0
	Seonchang-ri	48	19	29	0
	Beakdo-ri	14	5	9	0
	Jeongdong-ri	37	23	14	0
	Yesong-ri	52	18	34	0
	Jukchon-ri	38	19	19	0
	Hongdo1-gu	66	25	41	0
	Hongdo2-gu	40	14	26	0
	Jinri2-gu	28	13	15	0
	Mari	14	6	8	0
	Biri	29	12	17	0
	Gwanchon-ri	18	9	9	0
	Sipri	31	10	21	0
	Sari	56	20	36	0
	Chondung-do	28	13	15	0
	Seogecha-do	29	16	13	0
	Gwanmea-do	30	14	16	0
	Gageo-do	45	21	24	0
	Damul-do	31	11	20	0
	Deadun-do	33	6	27	0
	Yongsan-do	34	11	23	0
	Tea-do	41	12	29	0
Subtotal		**865**	**330**	**535**	**0**

Table 15. Antibody to *Brugia malayi* in resident people in Jeollanam-do, Gyeongsangbuk-do, and Jeju-do in 2006 (continued)

Area		Total	M.	F.	Total Pos.
Jeju-do	Wimi2-ri	56	28	28	**0**
	Gueom-ri	44	7	37	**0**
	Tosan2-ri	38	13	25	**0**
	Taehung1-ri	52	20	32	**0**
	Hare1-ri	40	25	15	**0**
	Gimnyong-ri	79	28	51	**0**
	Samdal2-ri	23	9	14	**0**
	Yecho-ri	47	10	37	**0**
	Sinyang2-ri	22	7	15	**0**
	Yonghung-ri	44	14	30	**0**
	Deaso-ri	1	1	0	**0**
Subtotal		**446**	**162**	**284**	**0**
Total		**1,526**	**574**	**952**	**0**

(Kim et al., 2006)

Table 16. Female mosquitoes collected by black light trap

Month		May	June	July	Aug	Sep	Oct	Total
Sinan-gun (2002)	*Aedes togoi*	-	-	134	202	65	31	432
	Anopheles sinensis	-	-	26	6	3	3	38
Wando-gun (2003)	*Aedes togoi*	93	163	217	134	62	53	722
	Anopheles sinensis	0	14	107	228	115	1	465
Yeosu-si (2004)	*Aedes togoi*	11	109	57	16	17	52	262
	Anopheles sinensis	0	0	0	0	0	0	0
Jeju-do (2005)	*Aedes togoi*	9	15	9	13	10	-	56
	Anopheles sinensis	0	0	1	0	0	-	1
Total	***Aedes togoi***	**113**	**287**	**417**	**365**	**154**	**136**	**1,472**
	Anopheles sinensis	**0**	**14**	**134**	**234**	**118**	**4**	**504**

(Kim et al., 2002, 2003, 2004, 2005)

Table 17. Seasonal variation of mosquitoes collected by black light trap in Sa-ri, Heuksan-do, Jeollanam-do in 2002

Month & week	*Aedes togoi*	*Anopheles sinensis*	*Culex pipiens*	*Culex tritaeniorhynchus*	*Armigeres subalbatus*	Total
Jul. 1st	-	-	-	-	-	-
Jul. 2nd	23 (1)	14 (1)	9 (7)	1	0	47 (9)
Jul. 3rd	1	1	3	0	0	5
Jul. 4th	4	0	4	1	0	9
Jul. 5th	17 (3)	2	4 (1)	1	0	24 (4)
Aug. 1st	25 (2)	0	19 (3.5)	4	0	48 (5.5)
Aug. 2nd	14 (2)	1	27 (5.5)	8	0	50 (7.5)
Aug. 3rd	8	1	2 (0.5)	0	1	12 (0.5)
Aug. 4th	26 (1)	0	4 (2)	1	1	32 (3)
Sep. 1st	7	0	13 (3)	2	0	22 (3)
Sep. 2nd	5	1	12 (1.5)	1	0 (1)	19 (2.5)
Sep. 3rd	4	0	20 (4)	1	0	25 (4)
Sep. 4th	3	1	14 (2.5)	0	0	18 (2.5)
Oct. 1st	2	1	12 (1)	0	0	15 (1)
Oct. 2nd	3	0	9 (1)	0	1	13 (1)
Oct. 3rd	1	0	7	0	0	8
Total	**143 (9)**	**22 (1)**	**159 (32.5)**	**20**	**3 (1)**	**347 (43.5)**
Average	**9.5 (0.6)**	**1.5 (0.1)**	**10.6 (2.2)**	**1.3**	**0.2 (0.1)**	**23.1 (2.9)**
Percent	**41.2 (20.7)**	**6.3 (2.3)**	**45.8 (74.7)**	**5.8**	**0.9 (2.3)**	**100 (100)**

*** ( ) : Male**

(Kim et al., 2002)

Table 18. Seasonal variation of mosquitoes collected by black light trap in Sim-ri, Heuksan-do, Jeollanam-do in 2002

Month & week	*Aedes togoi*	*Anopheles sinensis*	*Culex pipiens*	*Culex tritaeniorhynchus*	*Culex bitaenirorhynchus*	*Armigeres subalbatus*	*Tripteroides bambusa*	Total
Jul. 1st	-	-	-	-	-	-	-	-
Jul. 2nd	15	1	1 (2)	0	0	0	0	17 (2)
Jul. 3rd	18 (1)	2 (1)	11 (1)	2	0	0	0	33 (3)
Jul. 4th	2	0	3	0	0	0	0	5
Jul. 5th	12 (0.5)	1	4 (0.8)	1	0	0	0	18 (1.3)
Aug. 1st	20 (0.5)	0	29 (6)	7	0	0	0	56 (6.5)
Aug. 2nd	5	0	5 (3)	1	0	0	0	11 (3)
Aug. 3rd	9	1	6 (4)	2	0	1	0	19 (4)
Aug. 4th	2	0	4 (1)	1	0	0	0	7 (1)
Sep. 1st	6	0	17 (8)	2	0	0	0	25 (8)
Sep. 2nd	7	0	10 (16)	2	0	0	0	19 (16)
Sep. 3rd	6 (0.5)	0	26 (13.5)	3	0	1	1	37 (14)
Sep. 4th	2 (0.5)	0	35 (30.5)	5	0	1	0	43 (31)
Oct. 1st	3	1	21 (28)	3	1	1 (1)	0	30 (29)
Oct. 2nd	3 (0.3)	0	17 (26.7)	3	0	1	0	24 (27)
Oct. 3rd	2	0	13 (10)	0	0	0	0	15 (10)
Total	**112 (3.3)**	**6 (1)**	**202 (150.5)**	**32**	**1**	**5 (1)**	**1**	**359 (155.8)**
Average	**7.5 (0.2)**	**0.4 (0.1)**	**13.5 (10.0)**	**2.1**	**0.1**	**0.3 (0.1)**	**0.1**	**23.9 (10.4)**
Percent	**31.2 (2.1)**	**1.7 (0.6)**	**56.3 (96.6)**	**8.9**	**0.3**	**1.4 (0.6)**	**0.3**	**100 (100)**

(Kim et al., 2002)

Table 19. Seasonal variation of mosquito adults collected by light trap in Bogil-do, Wando-gun, Jeollanam-do in 2003.

Month & week	*Aedes togoi*	*Anopheles sinensis*	*Culex pipiens*	*Culex tritaenior-hynchus*	*Armigeres subalbatus*	*Aedes albopicthus*	*Aedes dorsalis*	*Culex bitaenior-hynchus*	Total
May 1st									
May 2nd	5	0	0						5
May 3rd	34.5	0	0						34.5
May 4rh	7	0	0.5						7.5
Jun. 1st	27.5	0	0.5				0.5		28.5
Jun. 2nd	10(3.0)	0.5	0						10.5(3.0)
Jun. 3rd	13.5(1.5)	0	0.5						14(1.5)
Jun. 4th	30.5(0.5)	6.5	0(0.5)		1				38(1.0)
Jul. 1st	31.5	6	1(0.5)						38.5(0.5)
Jul. 2nd	2(0.5)	2	0.5						4.5(0.5)
Jul. 3rd	38.5(0.5)	9(1)	5(0.5)	2.5	3(3.5)				58(5.5)
Jul. 4th	18.5(0.5)	12(0.5)	2.5(2.5)	1.5	2.5(1.5)				37(5.0)
Jul. 5th	18(0.5)	24.5(1.5)	10(2.0)	2	1.5(0.5)				56(4.5)
Aug. 1st	31(0.5)	63	30.5(2.5)		3(1.5)	0.5			128(4.5)
Aug. 2nd	3.5	13(0.5)	2(0.5)	9.5	0.5				28.5(1.0)
Aug. 3rd	25	24(1.5)	5.5	22.5	7.5(3.0)	0 (0.5)			84.5(5.0)
Aug. 4th	7.5	14	2.5	12	6.5(2.5)				42.5(2.5)
Sep. 1st	2.5	26(0.5)	0.5	19	10(2.0)				58(2.5)
Sep. 2nd	4(1.0)	8.5(0.5)	0	29.5	3(3.5)	0.5			45.5(5.0)
Sep. 3rd	7.5(0.5)	18.5(1.0)	1.5(0.5)	22.5	8(5.0)			0.5	58.5(7.0)
Sep. 4th	5	3	4(0.5)	9.5	9(3.5)		0.5		31(4.0)
Sep. 5th	12	1.5(1.0)	0.5(1.0)	8	4.5(1.5)				26.5(3.5)
Oct. 1st	13(0.5)	0.5		5.5(0.5)	3(2.0)				22(3.0)
Oct. 2nd	13.5(1.0)		0.5	1	3.5(1.0)		0.5		19(2.0)
Total	**361 (10.5)**	**232.5 (8.0)**	**68 (11.0)**	**145 (0.5)**	**66.5 (31.0)**	**1 (0.5)**	**1.5**	**0.5**	**876 (61.5)**
Average	**15.7 (0.5)**	**10.1 (0.3)**	**3.0 (0.5)**	**6.3 (0.02)**	**2.9 (1.3)**	**0.04 (0.02)**	**0.07**	**0.02**	**38.1 (2.7)**
Percent	**41.2 (17.1)**	**26.5 (13.0)**	**7.8 (17.9)**	**16.6 (0.8)**	**7.6 (50.4)**	**0.1 (0.8)**	**0.2**	**0.1**	**100 (100)**

(Kim et al., 2004)

Table 20. Seasonal variation of mosquitoes collected by black light trap in Geomun-do, Yeosu-si, Jeollanam-do in 2004

(per trap/night)

Month	Number of collection	*Aedes togoi*	*Culex pipiens pallens*	*Culex tritaenior-hychus*	*Armigeres subalbatus*	*Aedes albopictus*	Total
Mar.	1	0	0	0	0	0	0
Apr.	8	0.5 (0.4)	0	0	0	0	0.5 (0.4)
May	4	2.8	0.5	0	0	0	3.3
Jun.	7	15.6 (3.9)	0.1 (0.3)	0	0.3 (0.3)	0	16.0 (4.5)
Jul.	4	14.3 (0.5)	0	0	0.3 (0.5)	0	14.6 (1.0)
Aug.	4	4	0	0	0 (0.3)	0	4.0 (0.3)
Sep.	5	3.4 (0.6)	0.8	0	0	0	4.2 (0.6)
Oct.	7	7.4 (1.0)	4.0 (2.4)	1.1	1.0 (1.0)	0.1	13.6 (4.4)
Total		**48.0 (6.4)**	**5.4 (2.7)**	**1.1**	**1.6 (2.1)**	**0.1**	**56.2(11.2)**
Average		**6.0 (0.8)**	**0.7 (0.3)**	**0.1**	**0.2 (0.3)**	**0.01**	**7.0 (1.4)**
Percent		**85.4 (57.1)**	**9.6 (24.1)**	**2**	**2.8 (18.8)**	**0.2**	**100**

(Kim et al., 2004)

Table 21. Seasonal variation of mosquitoes collected by black light trap in Maemul-do, Tongyeong-si, Gyeongsangnam-do in 2004.

(per trap/night)

Month	Number of collection	*Aedes togoi*	*Culex pipiens pallens*	*Culex tritaeniorhy -chus*	*Armigeres subalbatus*	Total
Mar.	1	1	0	0	0	1
Apr.	8	3.8 (0.9)	0	0	0	3.8 (0.9)
May	7	17.9 (0.6)	0.3	0	0	18.2 (0.6)
Jun.	10	25.8 (2.6)	0	0	0.1	25.9 (2.6)
Jul.	7	21.1 (1.6)	0.3	0	0	21.4 (1.6)
Aug.	4	9.3 (1.0)	0	0	0	9.3 (1.0)
Sep.	6	2.7	0 (0.2)	0	0	2.7 (0.2)
Oct.	7	15.7	0.3 (1.0)	0.3	0.1	16.4 (1.0)
Total		**97.3 (6.7)**	**0.9 (1.2)**	**0.3**	**0.2**	**98.7 (7.9)**
Average		**12.2 (0.8)**	**0.1 (0.2)**	**0.04**	**0.03**	**12.3 (1.0)**
Percent		**98.6 (84.8)**	**0.9 (15.2)**	**0.3**	**0.2**	**100**

*** ( ) : Male**

(Kim et al., 2004)

Table 22. Larval density of *Aedes togoi* in rock pools by using meshed-sinking quadrat (100 cm^2) collection method in Geomun-do, Yeosu-si, Jeollanam-do in 2004

Month	Number of rock pools examined	No.of dips	1st-2nd		3rd		4th		pupa		Total	Salinity (%)	Water temperature (℃)
			No.	%	No.	%	No.	%	No.	%			
Mar.	7	31	10.4	15.9	32.4	49.6	22.4	34.3	0.1	0.2	65.3	0.2 (0-0.6)	5.8 (5.4-7.3)
Apr.	7	30	1.4	4.3	5.8	17.9	10.7	33	14.5	44.8	32.4	0.1 (0-0.2)	22.5 (16.6-25.3)
May	7	33	11.2	42.6	3.9	14.8	4.2	16	7	26.6	26.3	0.2 (0-0.8)	24.1 (21.2-25.4)
Jun.	7	34	34.1	36.5	52.5	56.1	5.8	6.2	1.1	1.2	93.5	0.8 (0-3.9	26.8 (23.1-29.1)
Jul.	7	35	13.2	33.8	13.4	34.3	6.3	16.1	6.2	15.9	39.1	2.6 (0.6-4.2)	32.8 (28.6-34.6)
Aug.	7	35	1.8	24.3	1.9	25.7	3.1	41.9	0.6	8.1	7.4	2.6 (0.8-3.8)	24.3 (23.8-25.1)
Sep.	7	33	6.2	27.8	9.7	43.5	4.3	19.3	2.1	9.4	22.3	0.6 (0-2.5)	24.7 (23.1-27.1)
Oct.	7	33	0.9	9.2	2.6	26.5	3.5	35.7	2.8	28.6	9.8	1.8(0.1-4.4)	18.8 (16.5-20.4)

(Kim et al., 2004)

Table 23. Larval density of *Aedes togoi* in rock pools by using meshed-sinking quadrat (100 cm^2) collection method in Maemul-do, Tongyeong-si, Gyeongsangnam-do in 2004

Month	Number of rock pools examined	No.of dips	1st-2nd		3rd		4th		pupa		Total	Salinity (%)	Water temperature (℃)
			No.	%	No.	%	No.	%	No.	%			
Mar.	7	23	2.1	8.4	19.1	76.7	3	12.1	0.7	2.8	24.9	0.6 (0.3-1.7)	16.1 (12.8-18.6)
Apr.	7	28	2.8	9.9	5.8	20.5	12.9	45.6	6.8	24	28.3	0.3 (0-0.7)	18.9 (16.3-21.8)
May	7	34	23.1	48.1	14.1	29.4	4.9	10.2	5.9	12.3	48	0.1 (0-0.2)	19.5 (18.9-20.3)
Jun.	7	32	46.2	63.4	10.3	14.1	10.1	13.9	6.3	8.6	72.9	0.1 (0-0.2)	20.2 (19.1-21.5)
Jul.	7	30	40.2	58.4	15.6	22.7	11.5	16.7	1.5	2.2	68.8	0.3 (0.1-0.8	29.7 (27.5-34.1)
Aug.	7	30	5	39.4	2.3	18.1	5.3	41.7	0.1	0.8	12.7	3.7 (0-5.1)	24.0 (23.4-24.5)
Sep.	7	33	3.5	76.1	0.6	13	0.3	6.5	0.2	4.4	4.6	4.1 (2.7-6.4)	21.2 (19.7-22.6)
Oct.	7	32	0.3	16.7	1.3	72.2	0.1	5.6	0.1	5.6	1.8	3.8 (0-6.6)	19.3 (16.4-22.9)

(Kim et al., 2004)

Table 24. Frequency distribution by salinity of *Aedes togoi* larvae and pupae in Geomun-do and Maemul-do, Jeollanam-do in 2004

Locality	Geomun-do			Maemul-do			Total	%
Salinity(%)	Number of rock pools	Number of larvae & pupae	%	Number of rock pools	Number of larvae & pupae	%		
0.0-0.4	27	1,373.9	68.6	13	1,126.50	78.1	2,500.40	72.5
0.5-0.9	6	257.5	12.8	5	182.2	12.6	439.7	12.8
1.0-1.9	3	93.2	4.7	2	11.2	0.8	104.4	3
2.0-2.9	8	200	10	3	7.6	0.5	207.6	6
3.0-3.9	5	79.4	4	2	16.4	1.1	95.8	2.8
4.0-4.9	0	0	0	9	89.1	6.2	89.1	2.6
5.0-5.9	0	0	0	2	0	0	0	0
6.0-6.9	0	0	0	2	10	0.7	10	0.3
Total	49	2,004	100	38	1,443	100	3,447	100

(Kim et al., 2004)

Table 25. Seasonal variation of mosquitoes collected by black light trap in Wimi-ri, Namjeju-gun, Jeju-do in 2005

Month	Week	*Aedes togoi*	*Anopheles sinensis*	*Culex pipiens*	*Culex tritaeniorhy-nchus*	Total
April	1	0.5	0	2	0	2.5
	2	0	0	0.5	0	0.5
	3	1	0	1.5	0	2.5
	4	0.5	0	0.5 (0.5)	0	1.0 (0.5)
May	1	1	0	1.5	0	2.5
	2	0.5	0	1	0	1.5
	3	0.5	0	1 (0.5)	0	1.5 (0.5)
	4	1	0	1 (1)	0	2 (1)
Jun.	1	1.5 (0.5)	0	2 (1.5)	0	3.5 (2)
	2	1	0	2 (0.5)	0	3 (0.5)
	3	1	0	1 (2.5)	0	2 (2.5)
	4	2.5	0	1 (1.5)	0	3.5 (1.5)
	5	2	0	2 (1)	0	4 (1)
July	1	0	0.5	3.5 (0.5)	0	4 (0.5)
	2	0.5	0	2.5	1	4
	3	1	0	1 (0.5)	0	2 (0.5)
	4	2.5	0	1.5	0	4
Aug.	1	1.5	0	2.5	0	4
	2	2	0	0	0.5	2.5
	3	2	0	2 (3)	0	4 (3)
	4	1.5	0	3.5 (2.5)	0.5	5.5 (2.5)
	5	2	0	1.5 (2.5)	0.5	4 (2.5)
Sep.	1	0.5	0	0.5 (1)	0	1 (1)
	2	1	0	1.5 (2)	0.5	3 (2)
	3	1.5	0	2 (0.5)	0.5	4 (0.5)
	4	1.5	0	2 (1)	0.5	4 (1)
Total		**30.5(0.5)**	**0.5**	**41.0 (27.0)**	**4**	**76**
Average		**1.2(0.02)**	**0.02**	**1.6 (1.0)**	**0.2**	**2.9**
Percent (%)		**40.1**	**0.7**	**53.9**	**5.3**	**100**

(Kim et al., 2005)

Table 26. Larval density of *Aedes togoi* in rock pools by using meshed-sinking quadrat (100 cm^2) collection method in Namwon-eup, Namjeju-gun, Jeju-do in 2005.

(No/dip)

Month	Number of rock pools examined	No. of dips	1st-2nd		3rd		4th		pupa		Total
			No.	%	No.	%	No.	%	No.	%	
Apr.	5	23	6.5	70.7	1	10.9	0.9	9.8	0.8	8.7	9.2
May	5	25	2.8	68.3	0.6	14.6	0.5	12.2	0.2	4.9	4.1
Jun.	3	15	14.6	99.3	0	0	0.1	0.7	0	0	14.7
Jul.	5	25	6	100	0	0	0	0	0	0	6

(Kim et al., 2005)

Appendix II

LIST OF FIGURES

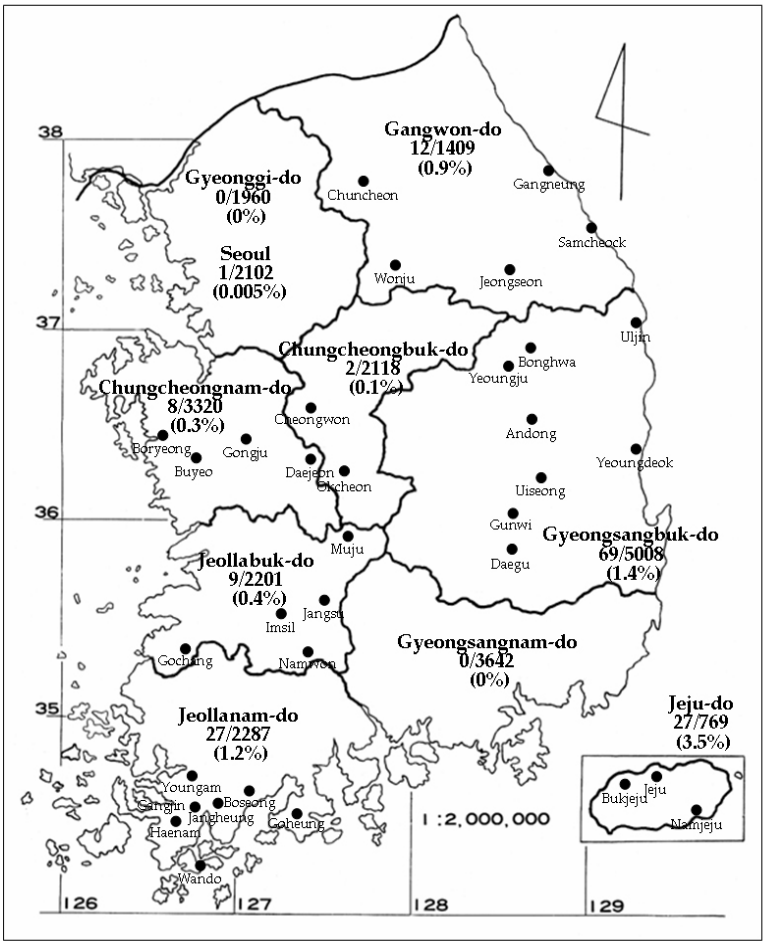


Figure 1. Microfilarial survey of night blood specimens collected from army recruitment camp in 1964 to 1967. (Seo BS, 1968)

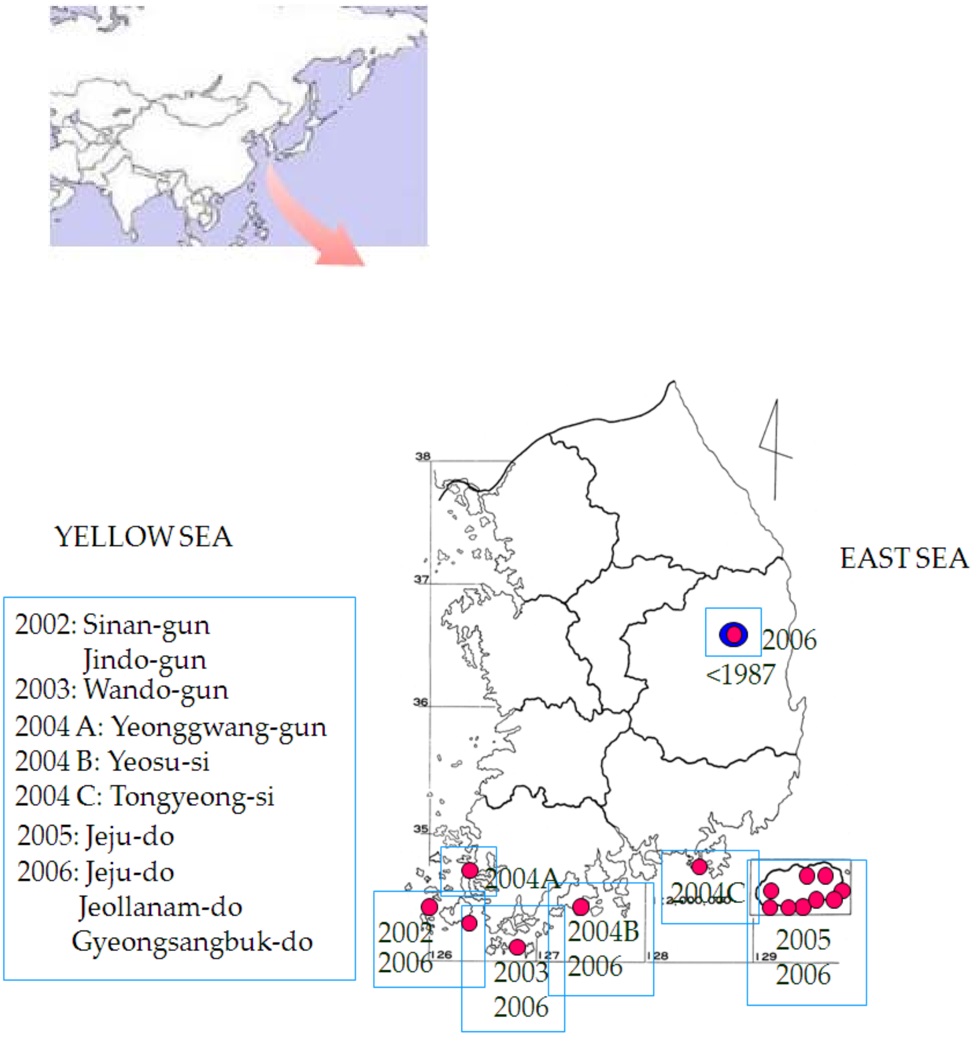


Figure 2. Areas surveyed for 5 years during 2002-2006.