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▣ MINI-REVIEW

Fifty Years of the Korean Society for Parasitology

Seung-Yull Cho*

Professor Emeritus, Sungkyunkwan University, Seoul 110-745, Korea

Abstract: In 1959, the Korean Society for Parasitology was founded by clinical scientists, specialists of public health, and 5 core parasitologists with experience in American science and medicine. The Society this year celebrates its 50th anniversary. Due to public health importance at the time of foundation, medical parasitology was the main stream for next 3 decades. Domestic problems of niche parasitic diseases, unlisted in 6 tropical diseases of major importance, had been studied by own efforts. To cope with the demand of parasite control, evaluation system for control activity was built up. Control activity against soil-transmitted nematodes, conducted for almost 3 decades, was evaluated as a success. Evaluation of praziquantel efficacy for clonorchiasis, paragonimiasis, and neurocysticercosis, population dynamics of *Ascaris lumbricoides* infection in a situation of continuous reinfections, diagnostic modalities of antibody tests combined with brain imaging developed for helminthiasis of the central nervous system and researches on intestinal trematodes were achievements in the first 30 years. During the recent 2 decades, science researches, such as cell and molecular biology of parasites and immunology of parasitic infections have been studied especially on parasitic allergens and proteolytic and anti-oxidant enzymes. Experiences of international cooperation for world health have been accumulated and would be expanded in the future.

Key words: history, parasitology, parasite, helminth, protozoa, Korea

FOUNDING THE SOCIETY

The Republic of Korea (ROK) in 1959 and in 2009 was 2 totally different nations. The agriculture-based country had suffered for at least past 2 decades by a series of wars and by resulting destruction, migration, and displacement of almost 10 million people. The Korea in 1959 was one of the poorest in the world. In health aspects, seasonal undernutrition and infections of various kinds prevailed. Tuberculosis, tertian malaria, typhoid fever, hepatitis, ascariasis, clonorchiasis, paragonimiasis, amebiasis, scabies, and others raged among dangerously overpopulated people.

Retrospectively, however, the ROK Government, founded in 1948, adopted some policies of pivotal importance for future of the nation; capitalism and anti-communism policy, land reformation, compulsory elementary school education, etc. All tenants turned to farm land owners in 1949. All school-aged children were able to enroll elementary schools starting in 1950, and literacy rate soared. Korea defended herself from communist invasion under the helps of the United Nations Forces (1950-1953) and has kept national security since 1954 by defense treaty alliance with the USA.

Old generation Koreans have long memories of clothes, powdered milk, breads, stationery, and everything else given by American philanthropic societies. Although the ROK Government depended heavily on the U.S. Congress budget allocation at the time, it prepared national reconstruction and industrialization plans of its own. Training of higher education staffs was an item in these plans. In the latter half of the 1950s, both governmental and civilian organizations of the U.S. provided scholarships for postgraduate training in the fields of medicine, agriculture, and engineering. The International Cooperation Agency of the U.S. Government and China Medical Board, Inc. of Rockefeller Foundation were the main benefactors. Of the hundreds of scholarship recipients who were staffs of universities or national institutes, 5 had attended the department of parasitology or tropical medicine of University of Minnesota and Tulane University for 1 or 2 years each. Those scholars, who had a Japanese education background, experienced American medicine and science, and were to become leaders in Korean parasitology.

By implicit and explicit policies of Chosen Colonial Government of the Empire of Japan, higher education in Korean peninsula was extremely limited until the end of the World War II in 1945, when about 40 eligible scientists were said to be available in the entire fields of science in Korea. There were no faculty members in the field of parasitology. In 1954, with a view

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* Corresponding author (seungyl@med.skku.ac.kr)

to the national importance of viable experts in parasitology, the dean of Seoul National University College of Medicine opened Department of Parasitology, the first such department in Korea, and appointed Dr. B.S. Seo as faculty. Yonsei University College of Medicine also established the department by recruiting Dr. C.T. Soh to the faculty staff. Thereafter, medical colleges in Korea opened one by one. The faculty members of the parasitology departments were active in research, and in 1959 they agreed to found an independent academic society. The Korean Society for Parasitology could only be inaugurated with the help of clinical scientists, and specialists of public health who recognized parasitic diseases as problems of major public health importance. Some relevant history on the foundation of the Society was described on the occasion of the 20th and the 30th anniversaries of the Society [1,2]. Since its foundation, the Society has been the first and only voluntary professional civilian organization in Korea devoting to the exchange research information on parasites and parasitic diseases.

ACTIVITIES IN THE 1960s: CONSTRUCTING BACKBONE

Academic Meetings

The first activity of the Society was the academic meeting held on 21 November 1959 at the Lecture Room "A" of Seoul National University Hospital [3]. A total of 30 research results were presented there. The first presentation was "A case of *Isospora belli* infection." Other presentations at the first meeting included histochemical studies on *Ascaris suum* and *Ascaris lumbricoides*, morphological studies on subgenus *Spirometra* tapeworms, excystation of *Clonorchis sinensis* metacercariae, epidemiological studies of human paragonimiasis in Cheju Island, trials of dithiazanine iodide on *C. sinensis*, anthelmintic evaluation of bephenium hydroxynaphthoate, a case of spinal paragonimiasis, a case of intestinal myiasis by *Sarcophaga* species, etc. The academic meeting was held once annually until 1966. In 1967, the Society began to have another periodic meeting in spring. Since 1963, the number of presentations at the Society meetings increased to 60-70 annually. As of 2009, the annual meeting and general assembly have been held yearly without interruption.

Literature

Another product of the Society activities was a literature database on Korean parasites and parasitic diseases published in 1961 [4]. A total of 777 articles, including those written before 1945 by Japanese scholars, such as Professor H. Kobayashi and his colleagues and those published around the Korean War by scientists and medical doctors of the U.S. Army Medical Corps, as well as by some Korean authors, were listed with their bibliographic data. In 1963, the *Korean Journal of Parasitology* was inaugurated. The journal was regarded by Korean medical scientists as one of the best medical journals published in Korea [5-6]. Bibliometric analysis of the journal articles appeared in a separate article in this supplement.

Organization and activity of parasite control

Members of the Society participated in founding the Korea Association for Parasite Eradication (KAPE), a business partner of the Society, in 1964 [7]. After the foundation of KAPE, there was a policy debate on how to promote the control activities against soil-transmitted helminthiasis. One was an enlightenment movement of people to combat parasitic diseases together with propagation of a new toilet tank device separating urine from feces in farm houses. Another was a parasite control program already undergone by the Japanese Association of Parasite Prevention, a business model of school-based selective mass chemotherapy undertaken twice a year. After the debate, it was decided to adopt the business model of mass chemotherapy. One difference from Japanese model was a legal base for its activity. The Japanese model of the business was purely civilian in which people voluntarily participated in a parasite control movement. To be successful in Korea, however, legal support was considered necessary. The Law of Parasitic Diseases Prevention was thus drafted, was agreed upon in the National Assembly, and was promulgated by the ROK Government in 1966. The Society members also participated in recruiting Japanese assistance for initiating KAPE's activity. Vehicles, drugs, instruments for microscopy and laboratory works, and training program of business and technical personnel were kindly provided by the Overseas Technical Cooperation Agency (OTCA, now JICA) of Japan for 6 years from 1968. Parasite control activity by KAPE actually began in 1969 and continued for 27 years until 1995. Domestically and internationally, the parasite control activity in Korea has been regarded as a success [8].

The progress of activity of the Malaria Eradication Team of the Ministry of Health and Social Affairs, collaborated with the World Health Organization (WHO), was scientifically analyzed and the results were read in academic meetings of the Society. Unstable vivax malaria in many previously endemic areas in Korea was found already regressive in the early 1960s, resulting

in "*anophelism sine paludism*." The Team reported the usefulness of passive case detection in the malaria control program and mapped regressing and persisting endemic foci in Korea. The Team stopped its activity in 1968 [9].

Introducing science and technology

Advanced science and technology of parasitology, new to Korea, were introduced from the USA, Europe, and Japan in order to solve domestic issues. Anti-parasitic drugs and diagnostics were welcomed with particular enthusiasm. Piperazine for ascariasis/enterobiasis and metronidazole for amebiasis were introduced. In the case of bithionol, its clinical efficacy was evaluated soon after its discovery in Japan for treating human paragonimiasis [10,11]. Hetol was once tried for clonorchiasis in 1965 and finally given up because of its nephrotoxicity.

Intradermal test for clonorchiasis and paragonimiasis using veronal-buffered antigen [12] and complement fixation test for paragonimiasis [13] were also introduced [14]. Based on the complement fixation tests of cerebrospinal fluid, patients of cerebral paragonimiasis could be diagnosed [15] and then treated with bithionol [16].

Many different stool examination techniques had been also evaluated. Of them, sensitivity of cellophane thick smear technique (Kato-Katz) was compared with that of the formalin-ether concentration technique [17]. Soon, cellophane thick smear was adopted as KAPE's main method of mass stool examination. Throughout the selective mass chemotherapy program that was undertaken for decades, infected students could be screened out using this simple and inexpensive technique that made mass stool examination possible. Application of Stoll's egg counting technique was extended to *C. sinensis* and *A. lumbricoides* in order to estimate burden of the infections. Egg counting was also used in evaluation of the efficacy of anthelmintics.

Importance of epidemiology of parasitic infections

Malaria, trypanosomiasis, leishmaniasis, schistosomiasis, filariasis, and leprosy were recognized by WHO as 6 major tropical diseases that needed worldwide research efforts. In Korea, except for regressing malaria and lymphatic filariasis, parasitic infections of domestic importance, such as soil-transmitted nematode infections, clonorchiasis, paragonimiasis, cysticercosis, etc., were not listed. Therefore, in order to combat domestic parasites, research on these infections had to be done locally without foreign supports. In such a context, concepts of epidemiology and social medicine were emerged as a reasonable approach. Fortunately, in the 1960s, many local surveys were undertaken in different villages, institutions or specific groups of people. Athletes and players who participated in the Olympic Games, for example, were examined for parasitic infections. Local endemic areas of filariasis, clonorchiasis, and paragonimiasis were mapped one by another. In comparing the survey results with those reported long before by Japanese, American or Korean researchers, differences in prevalence were recognized. However, it was difficult to tell whether the situations were improving or worsening, because the degree of infections varied greatly by area. There was therefore a need for comprehensive and realistic evaluation of the nationwide situation.

Korea in the latter half of 1960s began to industrialize; national wealth also began to accumulate. In 1970, for the first time, the ROK Government was able to draft national budget plan based solely on national tax revenue. In accordance with economic improvement, public health issues became more of a widespread concern, and modern medicine found an appreciative welcome. The ROK Government's Ministry of Health and Social Affairs supported civilian organizations acting against tuberculosis, leprosy and parasitic diseases which were assembled by medical professionals and business officers. The first issue that these organizations had met was to arrive at a reasonable estimate the national burden of the diseases. In 1965, the Korean Institute of Tuberculosis reported results of the first national survey of tuberculosis prevalence collected from a national random sample. The members of the Korean Society for Parasitology were impressed by the report and decided to follow the good example.

THE 1970s: SURVEYS, DRUG EVALUATION, AND MASS CHEMOTHERAPY

Surveys

After completing its second-year activity, KAPE reported in 1970 [18] that 10,871,280 fecal samples from elementary, middle and high school students nationwide were examined microscopically. The egg positive rates in the year were; *Ascaris lumbricoides* 55.2%, hookworm 1.0%, *Trichuris trichiura* 46.8%, *Trichostrongylus orientalis* 0.7%, *Clonorchis sinensis* 0.5%, *Paragonimus westermani* 0.01%, and *Taenia* species 0.6%, respectively.

These data showed the weight of social burden of parasitic infections. However, these data, together with those obtained in successive years, were criticized in 2 aspects. One criticism was that these data could not represent a general prevalence,

because only students were examined. Prevalence rates of the hookworm, *C. sinensis* and *Taenia* species were known to be much higher in adults than those in students. Another criticism was that sensitivity of mass fecal examination was a little lower than those obtained in the research laboratory. The problem of low sensitivity should be excused because the difference was not major, and the KAPE examination was done as a business and most importantly, heavy infection cases, which most needed anthelmintic treatment, did not escape detection. Though excused, in terms of its assessment of national prevalence, the data in KAPE reports were in any case defective. A national survey in random samples from whole Korean population was, therefore, necessary for proper evaluation of the progress of control activity. The Ministry of Health and Social Affairs agreed on the necessity, submitted budget plan for a survey to the National Assembly, and secured the budget. The National Statistical Office provided KAPE with a national random sample comprising of one sample from approximately one thousand people. KAPE staff collected fecal samples and examined them. Members of the Society reviewed survey plans including examination techniques and items of questionnaires, and prepared the reports. The surveys of prevalence of intestinal parasitic infection were conducted in this way every 5 years 7 times, in 1971, 1976 [19], 1981, 1986, 1992, 1997, and 2004. The surveys were a good evaluation system for parasite control although their coverage was limited to intestinal helminths. In retrospect, the 1970s was the most critical period in the change of parasitic infections in Korea. After initiating the national survey, local surveys of small size undertaken by researchers became more specific, focusing on possible hidden endemic areas of clonorchiasis, paragonimiasis, metagonimiasis, and others.

Drug evaluation

Until the end of 1960s, only a few kinds of anthelmintics, such as piperazine, santonin, kainic acid, and bithionol, were available in Korean market. Hexylresorcinol and tetrachlorethylene were also used but rarely. Pyrvinium pamoate for enterobiasis was imported since the mid-1960s. Anthelmintics were one of the most favored medicines at that time; people could purchase them without physician's prescription. In remote villages, fake or true anthelmintic were sold by unlicensed merchants. With economic development, the size of anthelmintic market increased further. New anthelmintics such as pyrantel pamoate and mebendazole were found to be safe and effective for intestinal nematodes, and were introduced in the early 1970s. A copy mebendazole appeared in the market almost exactly after the original was introduced.

Until the late 1970s, no safe and effective drug for clonorchiasis existed. A drug screening system for *Clonorchis sinensis* was thus established in experimental rabbits, which were orally infected with 500 metacercariae; and candidate chemicals were tested in the model. Dehydroemetine late-releasing tablets, niclofolan, bisbendazole and others were tried both in the model and in infected patients [20]. However, these were found to have either low efficacy or narrow safety margins.

In 1972, praziquantel was found to have anthelmintic activities in Germany. Its efficacy and safety evaluation in human schistosomiasis and intestinal cestode infections had already been done. Bayer, its manufacturer, wanted to extend its spectrum of efficacy to other helminth parasites. The efficacy of praziquantel in treating human clonorchiasis, were examined in Korea and reported in 1981 [21]. This discovery was nationally welcomed. The clinical efficacy of praziquantel was also evaluated for infections of *Hymenolepis nana*, *Taenia solium*, *Paragonimus westermani* [22] and *T. solium* cysticercosis [23]. No chemotherapeutics had hitherto been available for *T. solium* cysticercosis. Praziquantel became the first drug which was proved to be effective for neurocysticercosis. The efficacy was examined clinically by using either brain computerized tomography (CT) or biopsy of degenerating worms in subcutaneous nodules. Praziquantel became the first drug to cure hymenolepiasis. Praziquantel was also practically the first drug that treated human paragonimiasis. Bithionol had been used; however, because of its side effects such as drug eruptions, severe diarrhea and other gastrointestinal symptoms, patients could not comply with the recommended dose schedule. In the praziquantel evaluation for paragonimiasis, objective evidences of a cure were very difficult to secure, but the difficulty was overcome by long-term follow-ups of chest radiography, and antibody tests in addition to clinical improvement and egg negative conversion. Praziquantel was effective, and have negligible side effects, and was welcomed by patients, clinicians and parasitologists.

Mass chemotherapeutic control

The first trial of mass chemotherapeutic control of parasitic infections in Korea began in 1964 for human paragonimiasis in Cheju Island [24]. The well designed trial was based on the fact that zoonotic *Paragonimus* infections on the island was almost nonexistent, because the population of wild carnivora, cats and dogs were reduced to a level of extinction due either to defor-

estation or to national rat control program using rodenticide in the early 1960s. In this context, it was hypothesized that treating most paragonimiasis patients using bithionol would eliminate infection sources to freshwater snails and crabs, thus would control the human disease. The program was well progressed until the early 1970s when a confounding factor intervened. Streams were polluted with pesticides, insecticides and household and industrial wastes. Intermediate hosts disappeared from endemic foci only to reappear again decades later.

Mass chemotherapeutic control programs of lymphatic filariasis were done in the early 1970s also in Cheju Island, using diethylcarbamazine [25]. After examining night blood smears, microfilaremic cases were treated with the drug. The program was undertaken for 5 years, and collaborated with Japanese workers. In addition to control studies, microfilarial morphology and confirmation of causative pathogen as *Brugia malayi*, circadian rhythm of microfilariae, vector efficiency of *Aedes togoi* mosquitos, and mathematical modeling of filarial epidemiology were studied. Korean workers tried to reduce the severity of adverse reactions by reducing the initial dose of diethylcarbamazine. Japanese workers focused on clinical studies and made a cat model of *Brugia malayi* infection. Mass chemotherapeutic control of lymphatic filariasis was also confounded by improved living standard of local people such as use of bed nets, building new houses and extensive spraying of insecticide in orange farms in the endemic villages. Since 1975, the project of lymphatic filariasis control was transferred to local health centers.

In the case of mass chemotherapeutic control of *Ascaris lumbricoides*, an experimental epidemiologic study was designed to confirm a theoretical model. The model, proposed by a Japanese parasitologist, Dr. Y. Komiya, theorized the effects of mass chemotherapy in a situation of continuous occurrence of reinfection [26]. In the Korean field study, undertaken for 5 years in Hwa-Seong County, reinfection patterns were evaluated not only by egg positive rates but also by counting worms expelled by quick acting and effective pyrantel pamoate. In the study, it was concluded that a year's interval mass treatment could not lower the infection rates in a population. This conclusion was explained on the basis of life span of adult *A. lumbricoides*, which was estimated to be 7-8 months in human hosts. Worm populations were replaced every 7-8 months in host population. Therefore, it was found that the shorter the mass chemotherapy intervals were, the lower the resulting infection rates in a population [27]. In the case of 2-months interval mass chemotherapy, *A. lumbricoides* could not discharge eggs because they were removed before maturation. Reinfection was ceased when 2-months interval mass chemotherapy were repeated for 3 years, probably by depleting already contaminated infective eggs in environment. In the worm burden study, reinfection burdens were found to go parallel with reinfection rates. Korean experiments showed that *Ascaris* infections can be controlled by mass chemotherapy if repeated in appropriate intervals for a certain period. The worm frequency was found to be distributed in negatively skewed pattern in host population, which was mathematically fitted to the equation of negative binomial distribution rather than Polya Eggenburger distribution [28]. Other factors analyzed included seasonal incidence in Korea, egg discharging pattern in low worm burden cases, familial aggregation pattern of the infection. This study of population dynamics of *A. lumbricoides* seemed to impress the WHO staffs of tropical medicine. A research team of Epidemiology of Infectious Diseases, Imperial College, London, undertook a similar study in the fishing villages of southern India.

Control of familial enterobiasis had been difficult even though effective chemotherapeutics were available. In a series of experiments and observations, it was concluded that, in chemotherapeutic control of familial enterobiasis, all members should be treated with mebendazole or other anthelmintics simultaneously for 4 times each in 20-day interval. This conclusion was based on new findings of research on the life span of longer than 40 days in female *E. vermicularis* [29], and the limitation of efficacy of anthelmintics on early developmental stages as obtained in randomized, double-blind study [30].

Experimental studies

In the early 1970s, hookworm infection rates were found to have lowered very quickly in Korea. In order to find factors involved, pesticides and insecticides were examined for their effects on the third stage larvae of hookworm [31]. These chemicals were used extensively when the green revolution began in the early 1970s. Their killing effects on the larvae were proved. It seemed that these chemicals were one of active players in lowering hookworm infection in Korea, together with improved defecation habits, wide use of chemical fertilizer instead of human manure, clothing and shoes worn by most people etc. In short, reinfection of hookworms was quickly reduced during the time when society changed.

Toxocariasis studies were focused on the mode of transmission. Transplacental transmission was reported in experimental animals [32]. Eating raw cattle liver was studied as a human

infection source [33], which belatedly attracted attention in the late 2000s.

Over 90% of *Entamoeba histolytica* infected cases are asymptomatic. To explain the enigmatic low incidence of clinical amebiasis among the infected, host factors such as host immunity, stress, nutrition etc. were studied extensively in the 1970s [34].

Researches on antibody tests for paragonimiasis and clonorchiasis were also undertaken applying succesively immunodiffusion, immunoelectrophoresis [35], counterimmunoelectrophoresis and indirect fluorescent antibody test [36]. As in the complement fixation test, these antibody tests were difficult to undertake. Antibody tests for paragonimiasis, however, were found always diagnostic anyway.

THE 1980s: TRANSITION TO SCIENCE AND CLINICAL STUDIES

In 1981, the third national survey results of intestinal helminthic infections were reported. Egg positive rates were: *Ascaris lumbricoides* 13.0%, *Trichuris trichiura* 23.4%, hookworm 0.47%, *Clonorchis sinensis* 2.6%, *Metagonimus yokogawai* 1.2%. *Paragonimus westermani* 0%, *Taenia* species 1.1% and *Enterobius vermicuaris* 12.0% (by 1 anal swab). Korea in the 1970s was in turmoil of industrialization, and urbanization. Everything began to change away from traditional agricultural culture, and prevalence of parasitic infections also began to change. In particular, the rates of soil-transmitted nematodes were significantly lowered. These data convinced Korean parasitologists that their research attitude toward parasites and parasitic diseases should be changed from epidemiology orientation to that of other research fields.

Researches on intestinal trematodes

One line of research was classical one on intestinal trematodes. In addition to pathological studies on experimental *Metagonimus yokogawai* infection, studies began on fauna of intestinal trematodes in Korea. Starting with new locality descriptions of *Echinostoma cinetorchis* and *Heterophyes nocens*, surveys on rat and dog intestinal trematodes were undertaken. During 2 decades from 1980 to the end of 1990s [38], human intestinal infections of *Echinostoma hortense, Echinochasmus japonicus, Acanthoparyphium tyosenense, Pygidiopsis summa, Stellantchasmus falcatus, Stictodora fuscata, Stictodora lari, Metagonimus takahashii, Metagonimus miyairi, Plagiorchis muris, Centrocestus armatus, Neodiplostomum seoulense, Gymnophalloides seoi* etc. were described. Korea was a new locality to most of them. Life cycle, modes of human infection and fine tegumental structure of each trematode were described.

Of them, 2 trematodes were of particular interest. One was *Neodiplostomum seoulense*, a diplostomatid trematode of rodent intestine, for which human was a new host; the index human infection case was a snake eater. The trematode's life cycle was elucidated [39]. Another trematode was *Gymnophalloides seoi*, which was intestinal trematode of a migratory bird, Paleartic oystercatcher [40]. Its metacercarial stage was found in oysters. The intestinal infections with this trematode were found to be limited in seaside villages of southwestern Korea. This series of intestinal trematode research made both Korean and food hygiene specialists worldwide understand how many different parasitic infections could be contracted by eating raw freshwater, brackish water zone fishes and mollusks.

Progress in praziquantel application

After applying praziquantel in treatment of clonorchiasis and other parasitic diseases, 2 researches and a project were done in the 1980s. One was developing a new manufacturing process of praziquantel which was undertaken by a Korean pharmacist. The new process produced the medicine with higher purity and with low incidence of side effects. And it made the drug affordable.

Another research was a study on action mechanism of praziquantel against trematodes. By transmission and scanning electron microscopy, the process of tegumental vacuolizations and damages was observed in *C. sinensis*, *M. yokogawai*, and *P. westermani* after exposure to praziquantel [41].

Clonorchis infected Korean patients purchased and administered praziquantel voluntarily nationwide. Until the 1970s, clonorchiasis was known as a fatal disease. Before praziquantel, treatment of choice was surgical liver massage and draining bile through a tube in order to let liver flukes crawl outside. After marketing, demands for praziquantel were immediate and enormous. From 1983, the ROK Government purchased praziquantel and distributed it to local health centers to treat infected cases in rural villages. The egg positive rate in Korean people, however, remained unchanged even after the use of praziquantel. In the successive national surveys undertaken in 1986, 1992, 1997 [42] and 2004, the estimated numbers of *C. sinensis* infection were between 5 hundred thousand and one million. In contrast, the data of worm burden estimation by Stoll's egg count showed remarkable reduction of the number of patients in the category of moderate and heavy infections. About 90% of the

infected were in category of light infections (EPG below 1,000). The prevalence of clinical clonorchiasis with cholangitis was reduced while asymptomatic light infections persisted.

Clinical studies on tissue invading helminthiases

Enzyme-linked immunosorbent assay (ELISA) was originally developed as a method of protein measurement. This technique was modified to antibody tests for parasitic infections in 1974. Since then, it revolutionized antibody tests worldwide. ELISA was introduced in Korea in 1980 and was applied in antibody test for clonorchiasis [43]. Next, ELISA antibody test for paragonimiasis was developed [44]. By ELISA, pulmonary paragonimiasis could be screened out with ease among treatment-resistant tuberculosis patients. Paragonimiasis was once forgotten disease among specialists of chest medicine in Korea, mainly because of difficulty in diagnosis. After applying ELISA antibody test, 20-200 pulmonary paragonimiasis patients were diagnosed every year during past 2 decades. Antibody test for cerebral paragonimiasis using cerebrospinal fluid was requested by neurologists in Korea and was developed using cerebrospinal fluid of patients as a test sample.

Korean neurologists and neurosurgeons then requested antibody tests for neurocysticercosis because brain CT findings of the disease were highly variable. For example, there was a considerable number of neurocysticercosis patients manifesting only hydrocephalus without multiple low density lesions in brian CT. The antibody test using serum and cerebrospinal fluid were developed, and diagnostic sensitivity and specificity were evaluated [45]. Since 1986, brain imaging combined with antibody tests became routine procedures in diagnosing neurocysticercosis in Korea. Comparative evaluation of 2 diagnostic modalities was reported in 1988 [46]. Because each of positive antibody test and brain images are regarded as major findings in neurocysticercosis, patients with positive findings in the 2 diagnostic modalities could be diagnosed. In Korea, more than 3,000 neurocysticercosis patients were diagnosed by this method during past 2 decades.

Epidemiologic characteristics, and histopathologic findings of human sparganosis [47,48] had been studied in Korea. The disease has showed relatively high incidence in East Asian countries. Because cases of spinal sparganosis had been reported in Korea, and sporadic cases of brain sparganosis were known in the early 1980s, the antibody test by ELISA for sparganosis was developed and evaluated [49]. It was incorporated in multi-antigen screening system together with *T. solium* metacestode cyst fluid antigen and crude *P. westermani* antigen in patients with space occupying lesion. Though infrequent, serum and cerebrospinal fluid of unexpected number of patients reacted positively only to sparganum antigen in the multi-antigen screenings. By collaboration with neuroradiologists, the brain CT findings of surgery-confirmed, antibody positive patients were described [50]. As in neurocysticercosis, rarely occurring neurosparganosis could be diagnosed preoperatively by combination of neuroimaging and antibody test. Since the latter half of 1980s, the multi-antigen screening system, composed of 4 antigens including crude *C. sinensis* antigen with above-listed 3, replaced invasive intradermal tests in Korea.

Biochemical and immunological studies

After the development of antibody tests for tissue invading helminthiasis, nature of diagnostic proteins from the parasites began to be studied. Basic biochemical technologies such as hybridoma and monoclonal antibody, SDS-polyacryamide gel electrophoresis, immunoblotting, and protein separation techniques such as gel filtration, chromatography, affinity chromatography and isoelectric focusing, were introduced in parasite research. Since the latter half of 1980s, proteolytic enzymes of many helminth parasites, especially cysteine proteinase, began to be characterized in Korea [51]. One cyst fluid proteins of *T. solium* metacestodes was purified and partly characterized. Proteins in crude extracts of *P. westermani*, and *Spirometra mansoni* plerocercoids were also analyzed for their antigenic subunit bands.

Since the early 1980s, Korean strains of free living amoeba such as *Naegleria* species and *Acanthamoeba* species were isolated and maintained in laboratory animal models. Using the model, immunological studies of various kinds together with pathological studies were undertaken [52]. Not only antibody responses but also cell mediated immunity was observed in this meticulously built models [53].

International and domestic recognition

In the 1980s, international circles of parasitology and tropical medicine began to pay attention to the research products of Korean parasitology. Abstract journals, such as *Tropical Diseases Bulletin* and *Helminthological Abstracts* indexed a part of articles published in the *Korean J Parasitology*. The WHO library in Geneva, Switzerland requested compliment copies of the journal. The textbook *Clinical Parasitology* (9th edition, 1984) of Beaver PC et al. listed more than 20 Korean articles in its reference, and listed *Korean J Parasitology* as one of periodicals in the field of

parasitology. Most importantly, the U.S. National Library of Medicine began to index contents of the journal in Medline database since 1989.

In 1986, KAPE changed its name to the Korea Association of Health (KAH. later changed again to the Korean Association of Health Promotion, KAHP). The change was decided in a milieu of congratulating a success in parasite control. National activity of parasite control was transferred from KAPE to KAH. Based on the data of the fourth national survey on prevalence of intestinal helminths in 1986, the Expert Committee for Parasite Control of KAH resolved a decision to reduce the size of mass stool examination gradually over 10 years, ending it in 1995, and the resolution was agreed by the Government.

ACTIVITIES IN THE 1990s: EVOLUTION TO SCIENCE AND INTERNATIONAL COOPERATION

In the fifth report (1992) on the prevalence of intestinal helminthes infection in Korea, the infection rates of each parasites were described as follows: *A. lumbricoides* 0.3%, hookworm 0.01%, *T. trichiura* 0.2%, *C. sinensis* 2.2%, *P. westermani* 0%, *M. yokogawai* 0.3%, *Taenia species* 0.06%, and *E. vermicularis* 0.9% (by 1 anal swab). These data confirmed that soil-transmitted nematode infections were no more major public health problems in Korea. *C. sinensis* and *E. vermicularis* infections, however, persisted.

Classical researches of parasitology

Classical studies of parasitology were continued in the 1990s in Korea. The enigma of *Taenia saginata* infections in pork eating population was elucidated in Taiwan by discovering its metacestodes in the liver of locally reared pigs. The habits of raw eating of pig liver were not limited to Taiwan but widely practiced in Asian population including Korea. At first the discoverer of the new mode of infection considered the tapeworm a strain and then changed to a subspecies name *Taenia saginata taiwanensis* and finally named it as *T. saginata asiatica*. In Korea, after a series of meticulous studies on life cycle and morphology, a species name of *Taenia asiatica* was proposed [54]. This proposal elicited debates worldwide. Molecular parasitologists preferred the subspecies name while classical parasitologists agreed that it should be a separate species. Studies on molecular evidences are ongoing as to the taxonomic position of the tapeworm.

Another classical research was done in the epidemic of reemerging vivax malaria. ROK was free from indigenous vivax malaria for 14 years from 1979 to 1993 when an index case was detected. Immediately, Korean parasitologists proposed a surveillance system. And they depicted the epidemic, and defined it as a border malaria in 1998 [55]. Studies on reemerging malaria were described in a separate article in this supplement.

An occurrence of human infections of trichinellosis was diagnosed in Korea at last [56]. Searches for this important zoonosis had failed to find any infection in Korea until 1997, either in domestic pigs or in human. Eating undercooked badger meat was found to be the infection source in the first human infection. First Korean infections of *Capillaria philippinensis* [57], *C. hepatica* [58], and *Dirofilaria immitis* [59] were reported in the 1990s.

Studies on *Pneumocystis carinii* were undertaken. Two rat strains of *P. carinii* were identified in Korea. Their molecular karyotypes were utilized in epidemiologic tracing of the strains. As a mode of transmission, air borne infection was proved to occur in an experimental setting. It was found that most Korean children acquired infections and naturally immunized before 2 years of age [60].

Antibody positive rates of *Toxoplasma gondii* were examined in different groups in Korea for more than 15 years. The average rate was 5%, which was much lower than those in west Europeans. Two incidents of human foodborne toxoplasmosis outbreaks were described in Korea [61].

Studies on the pathology on *C. sinensis* infections continued in the 1990s. Carcinogenic effects of the infection were observed in dimethylnitrosamine administered hamsters [62,63]. This study was important in a changed situation of *C. sinensis* infection. Due to lowered infection burdens, morbidity of cholangitis reduced. However, cases of cholangiocarcinoma continued to be detected and were found to be associated with infection of *C. sinensis*. High incidence of cholangiocarcinoma was observed in high endemic areas in southern Korea than in low endemic areas.

Pathological changes of biliary tract were studied after praziquantel treatment in *C. sinensis* infected experimental animals [64]. After parasitological cure, however, dilated intrahepatic biliary ducts did not shrink to normal and periductal fibrosis remained unchanged or minimally reduced. These findings were important clinically because pathologic imaging findings in ultrasound or CT in human patients may not represent the present infection.

Clinical and epidemiological studies on amebic keratitis have been done utilizing molecular markers of *Acanthamoeba* species

[65]. Studies on medically important vectors have been undertaken since the 1990s. Two species of trombiculid mites, *Leptotrombidium pallidum* and *L. scutellare* were identified as main vectors of scrub typhus in Korea. And their ecology was described. *In vitro* culture system of *Dermatophagoides farinae* and *D. pteronyssinus* was set up and large amount of the mites are supplied to specialists of allergic diseases.

Cell biology, immunology, and biochemical studies

Availability of cells and protozoa from ATTC and laboratory maintained protozoan parasite such as RH strain *Toxoplasma gondii*, *Trichomonas vaginalis*, and free living amoebas stimulated cell biological, immunological and biochemical studies in Korea. Host cell penetration mechanism of *T. gondii*, energy metabolism, and physiology of *T. vaginalis* and host cell response, roles of cytokines and chemokines in trichomoniasis model have been studied [66]. Interleukin-8 gene expression was examined in human colon epithelial cell line which was exposed to *Entamoeba histolytica* [67].

Proteolytic and anti-oxidant enzymes in helminth parasites were also studied. At least 7 serine-, and a cysteine proteases of *Spirometra mansoni* plerocercoid (sparganum) were purified and partially characterized. Of them, a cysteine protease, characterized as secretory cathepsin S, was found to degrade human immunoglobulin G in a papain-like fashion [68]. Two different cysteine proteases of *P. westermani* metacercariae were involved in their excystment process [69]. The study result added a role of cysteine proteases in trematode life cycle. Many different trematodes metacercariae and protozoan cysts were found to utilize cysteine proteases in their excystment. The purified enzymes of *P. westermani* have been utilized in a series of works on their role in mobilizing host eosinophils. Anti-oxidant enzymes, such as glutathione S-transferase were also studied in helminth parasites.

International communications and cooperations

In relation to international academic activity, 2 big changes happened in the latter half of 1980s and early half of 1990s in Korea. In 1989, Koreans were allowed to travel abroad. Before that year, to save foreign exchange, the ROK Government allowed foreign travel after reviewing applications. A few elite Korean parasitologists, who were invited by congress secretariat, could attend international meetings. In 1992, for the first time in the Society history, more than 30 Korean parasitologists attended the XIIIth meeting of International Congress of Tropical Medicine and Malaria (ICTMM) held in Pattaya, Thailand. Thereafter, scores of Korean parasitologists attend ICOPA, ICTMM and other international meetings and communicated with specialists of foreign countries.

Another big change was the declaration of Globalization policy of the ROK Government in 1994. And ROK was accepted as a member country of OECD in 1996. Activity of the Korea International Cooperation Agency (KOICA) was expanded thereafter. As an NGO activity of KOICA programs, KAH and members of the Society participated in the cooperation project with Institute of Parasitic Diseases in Shanghai, Chinese Academy of Preventive Medicine for 5 years. In 1995, the Society members organized a voluntary meeting with Japanese parasitologists under the name of "Forum Cheju" and have had annual meetings.

Since 1995, many Korean universities required their faculties a file of Science Citation Index (SCI) journal articles as a proof of achievements when applied a promotion or tenure. In the same year, grant giving organizations, such as the Korea Science and Engineering Foundation and the Korean Research Foundation, also asked a list SCI articles authored by applicant when an application was submitted. The changed policy stimulated international academic communications of Korean scientists including parasitologists.

ENVIRONMENT OF KOREAN PARASITOLOGY IN THE 2000s

In 2007, Molyneux [70] defined 5 terminologies used in the control of parasitic diseases; control, disease elimination, infection elimination, eradication, and extinction. Two prerequisites for applying these definitions are deliberate efforts paid to the control and evaluation system for the control activity. According to the definitions, the states of malaria, clonorchiasis, paragonimiasis, enterobiasis, and cysticercosis in Korea can be termed "Control." Ascariasis and hookworm disease can be safely defined as "Disease Elimination." Lymphatic filariasis in Korea was declared already as "Infection Elimination." These definitions are based on the control efforts of past 40 years and evaluation system in Korea. Amebiasis in Korea may be defined "Disease Elimination" or "Control." However, the definition for amebiasis is groundless because systemic evaluations have been insufficient during the past 30 years. One thing to mention is that over 90% of Korean population is supplied with safe water.

The environment for Korean parasitology seems to be ambiguous. Few medical graduates applied medical parasitology or tro-

pical medicine since the latter half of 1990s. Positions in many medical colleges reduced to one faculty for each parasitology department. Among lay people and medical professionals, more and more think that parasitic diseases are problems no more in Korea. As experienced in the U.S. and European countries, diagnosis of parasitic diseases were sometimes delayed long in Korea because of low diagnostic priority.

Two aspects of social changes are encouraging to Korean parasitology and tropical medicine. One is international cooperation. As a recipient of assistance from the U.S.A. and other countries in the past, Koreans had been benefited tremendously. They are keeping the mind of appreciation for the help given long ago. Most Koreans now think that it is Korea's turn to help others. This consensus of Koreans will be reflected in the gradual expansion of the budget of KOICA. The projects of KOICA had been concentrated in constructions of school or hospital buildings. KOICA, however, has an intention to expand projects in health sector. In 2000, an international cooperation program of parasite control in China was executed by KOICA. This was KOICA's the first big project, undertaken in health sector. The program was conducted jointly by Chinese Academy of Preventive Medicine, Institute of Parasitic Diseases, Shanghai and 3 Provincial CDC. Members of the Society and KAHP helped the program as advisers. After China program, KOICA operates similar one in Laos and Cambodia.

With the Korean Society of Infectious Diseases and the Korean Society for Microbiology the Society hosted the first big international event at the International Convention Center in Jeju, Korea, for a week from September 29 to October 3, 2008; the 17th International Congress of Tropical Medicine and Malaria (ICTM-17). A total of 1,094 professionals from 55 countries participated in the ICTM-17. The theme of the ICTM-17 was "Tropical Medicine and Welfare; from Bench to Field." The Congress was organized with 11 plenary lectures, 81 symposia and scientific sessions consisted of 240 invited lectures and 106 oral presentations, and 624 poster presentations. Three satellite meetings were also convened with ICTM-17.

Another encouraging aspect is a contribution to science of parasitology and tropical medicine. After the financial crisis in 1997, the ROK Government chose big research program policy during the past 10 years. And the programs of top-down research dominated, which have been worried by many researchers. The top-down research policy may damage creativity of basic researches. On top of that, in the field of biomedical research, extremely high priority was given to researches in molecular and cell biology during past 10 years. Researches on neglected tropical diseases have been largely neglected. In such environment, the Korean Center for Disease Control and Prevention supported researches on parasitic diseases. Many Korean parasitologists utilized this new research environment and were successful in setting up molecular biology laboratories by winning the game of grant competition. Graduate students of science and biology background have been invited to the Korean parasitology laboratory. Many expressed sequence tags, and recombinant proteins were produced. One thing to mention was that most recombinant proteins were examined as potential diagnostic antigens [71]. Few sequences or recombinant proteins were examined as potential vaccines, drug targets or other biological modifiers, which reflected a shallow tradition of Korean parasitology as a biological science. In the 2000s, good studies have been reported on retrotransposon of helminth parasites [72], penetration mechanisms of juvenile *Paragonimus* in host tissues [73], role of a hydrophobic ligand binding protein in lipid metabolism of *T. solium* metacestodes [74], an immune evasion mechanism of *Entamoeba histolytica* at molecular level [75], and characterization of myrids of insect or mite proteins as allergens [76]. Prospects of scientific parasitology seem not grave.

LOOKING BACK

In the past 50 years, ROK achieved economic development. Few Koreans fifty years ago could imagine or predict the present prosperity and democracy. For thirty years after founding the Korean Society for Parasitology, efforts were made in solving domestic issues of endemic parasitic diseases. Korean parasitology has contributed in establishing baseline data and progress evaluation in control activity. Spirits of "Can do" and "Do it quickly" were there behind the scene. Dr. Ken Mott, the deceased former WHO staff of parasitic diseases, commended in an unofficial meeting, "so small group of parasitologists achieved so beautiful things." During the recent 20 years, Korean parasitology has accumulated experiences in science and international cooperation. Shallow tradition and tubular vision in science research have delayed progress.

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