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研究成果の刊行物・別刷り

The War against a Regional Disease in Japan A History of the Eradication of *Schistosomiasis japonica*

Noriaki Kajihara^{1,2*} and Kenji Hirayama³

INTRODUCTION



Figure 1. Monument commemorating the complete eradication of "regional disease"

Unveiled on December 26, 2002 at Oshikoshi, Showacho, Nakakoma-gun, Yamanashi, Japan. Calligraphy by Mr. Ken Amano, Governor of Yamanashi Prefecture.

Description

Regional disease (schistosomiasis) was endemic for more than 400 years in an area spanning some 20,000 ha along three rivers, Kamanashi River, Arakawa, and Fuefuki River. The people living there suffered from this fatal disease characterized by swollen abdomen and abdominal ascites.

Our regional eradication program was initiated when the regional leader of a village, Kasugai, Higashi-Yamanashi gun, submitted demand for the control of this disease to Governor Shiro Fujimura. The people struggled with this disease for 115 years until we finally declared its eradication on February 19, 1996.

We erected this monument to express our sincere apprecia-

tion to all the persons who contributed to this historical achievement and to commemorate it forever.

December, 2002

Yamanashi Prefecture Government, Kofu, Yamanashi, Nirasaki, Kasugai, Isawa, Misaka, Ichinomiya, Yatsushiro, Nakamichi, Sakaigawa, Toyotomi, Mitama, Masuho, Nakatomi, Ryuoh, Shikishima, Tamaho, Showa, Tatomi, Hatta, Shirane, Wakakusa, Kushigata, Kousai, Futaba, Association for the Eradication of schistosomiasis (Regional Disease) in Yamanashi Prefecture

Preface

Kimio Saitoh

President

Association for the Eradication of Schistosomiasis

(Regional Disease)

in Yamanashi Prefecture



The history of our eradication program began at the time the pathogen was found in 1904. The program was enhanced by the finding that *Oncomelania* snail was the intermediate host in 1913. Regional community-based control programs were conducted aggressively for more than 100 years, and finally our governor declared the end of this disease in Yamanashi Prefecture in February 1996.

Schistosomiasis *japonica* had been endemic in several regions in Japan, such as Hiroshima, Okayama, Fukuoka, Saga and Yamanashi. Our association was established in 1950 and worked as a organization for the control collaborating with other prefectures' associations. When we established this association, the national and the prefectural financial situation was very difficult due to Japan's defeat in World War II. However, our association strongly urged the Japanese government to make a time-limited law to support

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our eradication program mainly entailing snail control. I thank the people in the endemic areas for their voluntary efforts, which was essential and critical for this final success. Of course the great advancement of medical and pharmaceutical treatments contributed to this achievement.

In 1947, the life expectancy was 46.06 and 49.6 years for males and females respectively, but now it is 77.10 for males and 83.99 years for females in Japan. I am confident that our efforts against schistosomiasis contributed to the improvement of our prefectural health condition. On this historical occasion of the declaration of the eradication of schistosomiasis, we decided to publish this booklet entitled "The War Against a Regional Disease" to preserve all the precious records that should be kept as our common heritage. I hope it will be a first level historical record in the future.

I would like to express my sincere gratitude to all the persons who have supported our association and also contributed to this publication by donating manuscripts and other materials.

Notification

Association for the Eradication of Schistosomiasis (Regional Disease) in Yamanashi Prefecture
March, 2003

For a long period, the farmers living in the Kofu Basin area suffered from the regional disease *Schistosomiasis japonica*. Therefore, the eradication of this disease was a dream for them over generations and generations.

Our eradication project started after the discovery of the pathogen in 1904 and the intermediate host, *oncomelania* snail, in 1913. The inhabitants, and many doctors and researchers who were pursuing new methods for prevention and treatment, were conducting projects under the strong support of regional and prefectural offices. Those activities with additional public health improvements gradually decreased the morbidity and mortality, but until 1955, there were still many active patients in the region. After that there were sporadic cases until 1985. Finally the governor declared the eradication of the disease in February 1996.

Our association was established in 1950 and has been working as a organization for the control of schistosomiasis collaborating with other prefectures' associations. We have already published a series of books that describe the disease situation and history: "The War Against the Regional Disease, 1977", "The War Against the Regional Disease,

Memories of Soldiers, 1979", and "The War Against the Regional Disease, Medical Aspects, 1981". Since 1992, we have been collecting materials related to the eradication program to prepare this final memorial booklet which we hope will be informative for all the persons who are still suffering from *Schistosomiasis* in southeast Asia.

The contents of this volume are as follows:

The first chapter, "History of the Control Program Prefectural Government Control Program" briefly outlines the disease and the history of the control program and presents tables that summarize the complicated activities year by year. The second chapter, "The Collected Materials Tell the Story" provides pictures and the records that will help readers understand the situation more vividly. The third chapter, "Records During the War" describes each regional history by city, town, and village using records, newspaper articles, and books. Our association's history is also presented here as "Footprints of the Association for the Eradication of the Regional Disease." The fourth chapter, "Renewed Materials" includes two historical booklets, "I am a Doctor of Regional Disease!" published in 1917, and "Manuals for the Diagnosis of schistosomiasis" published in 1996 by the Society of Researchers of the Regional Disease. The fifth chapter, "Statistics Regarding the Regional Disease," shows the epidemiological records since the Meiji Era based on official reports, public health statistics and the materials stored in the Yamanashi Prefectural Institute of Health.

Even now we all have memories of the "100 years war" against the regional disease deep in mind. I hope this booklet will inform our children about the glorious history of the eradication of a disease that had caused suffering since pre-historic times.

HISTORY OF THE PREFECTURAL GOVERNMENT CONTROL PROGRAM

Outline of the control program in Yamanashi Prefecture

- The 1st stage: Suffering from unknown regional disease before the discovery of the parasite in 1903
- The 2nd stage: Identification of the pathogen and its life cycle. Initiation of education for prevention. 1904-1916.
- The 3rd stage: Initiation of the control program, 1917-1940.
- The 4th stage: Development of the control program 1941-1952
- The 5th stage: Establishment of the control program, 1953-1971



Figure 2. Surveillance of snails by villagers in Nakamichi in the spring of 1975.



Figure 3. Grass cutting before the spray of molluscicides in Kofu City around 1975.

The 6th stage: Completion of the control program, 1972-1985.

The 7th stage: Surveillance system and the declaration of eradication, 1986-2000

The history of the control program in Yamanashi is divided into seven stages. Each stage is described in a year by year style to grasp the outline of the history. The details will be described in later chapters, such as the chronology of the control program (no English translation), and the related statistics (partially translated).

The 1st Stage: Suffering from Unknown Regional Disease before the Discovery of the Parasite in 1903

The people of Yamanashi (formerly called Kai-no-kuni) had been suffering for many years from a disease of unknown origin that was characterized by abdominal ascites. After the Meiji Revolution in the 1860's, people looked to modern medicine to clarify the disease, and many pioneering researchers and doctors made efforts to understand the patho-

genesis.

In old archives, there are several stories about the disease. One is that the famous lord of Kai (old name of Yamanashi), Takeda Shingen (1521-1573) died of this disease. Another is a statement in "Kou-you Gun-Kan, the military book of Yamanashi" (1602) that one of the knights of Kai, Obata Bingo-no-kami, suffered symptoms similar to schistosomiasis. There remain records that a variety of traditional medicines were used for the treatment ascites, a characteristic of post-schistosomal liver cirrhosis, since 300 years ago in Ryuoh town in Yamanashi. An advertisement for the traditional medicine "Tsu-you-san, for the ascites fluid", is presented in a later chapter.

At least as early as in the 1600's, the Kofu basin area in Yamanashi was already endemic for schistosomiasis. There is no confirmative evidence, but it is almost certain that the Kofu basin was endemic for schistosomiasis in the Edo-era (1600-1867). The first available description of schistosomiasis in Yamanashi is a statement regarding "many patients with ascites that is difficult to cure" in the book *Honyaku Dan-doku-ron* ("Translation to Abolish the Toxin") published by the local medical doctor Hashimoto Hakuju in 1811. The record that the village "Shimotakasuna" in Yamanashi asked the governor to examine the quality of drinking water in the fountain "Nouzou-ike" in 1874, as well as the record that the people of another village "Miyazawa" asked the governor to permit them to move to another place where they could get clean water (free from disease) in 1874 and in 1878, are also related to schistosomiasis. In 1881, Kasugai villagers submitted a document entitled *Go-shiki-negai* ("Request for instructions for control") to the prefectural government. The village continued to report the situation of schistosomiasis between 1881 and 1887. These documents are useful to know how much the villagers suffered and how the government reacted to it. In 1884, the prefectural government initiated a study on the disease with clinical exams and drinking water examination in Kasugai village. Dr. Ohashi Shin, director of the prefectural hospital, compiled the first record on the clinical examinations entitled *Byojou Ryakki* or ("Brief description of the clinical findings"), but his conclusion was that the disease was caused by over-work and some unknown malfunction of digestion.

Two years later in 1886, a military doctor named Ishii Ryoisai reported to the prefecture that there was a problem in the drinking water that influenced the result of the physical test of the younger inhabitants for military service. After that, Kasugai village asked the government to repeat the examination of the water. The answer from the government was that there was no significant problem in the water.

Then, again, the village sent a request for governmental initiatives to clarify the pathogenesis of the disease in 1887. In response, the government sent Dr. Nagamachi Kohei, director of the prefectural hospital in to the village to conduct clinical study again. Dr. Nagamachi did a fecal examination, found the eggs of “duodenal worm” or “hook worm” and suggested that the ascites was caused by this worm. Dr. Nagamachi’s conclusion was wrong but his idea that some parasitic disease might cause the disease was significant. After his suggestion, several reports on unknown parasite’s egg in the tissue of the patients were made by the pathologists Mashima Eitoku (1888), Yamagiwa Katsusaburo (1890), and Kurimoto Tomei (1893).

Around the same time, doctors in the endemic area, Dr. Sugiura Kenzo and Dr. Ozawa Shikajuro, expressed their opinion that the disease showing the hepatosplenomegaly and the ascites frequently seen in Nakakoma County could be a *Chihou-byou* (“regional disease”). At that time, the term “regional or geographic disease” was not new and included malaria, leprosy, Vit.E, and B deficiency. In 1897, Dr. Ozawa Shikajuro in Tano-oka village summarized the clinical symptoms and epidemiological findings of over 90 patients with the disease and published a paper entitled “On the regional ascitic disease” in the regional journal of the Japan Private Society of Hygiene Yamanashi Branch. In the paper, he respected that patients were aggregated in Kita-Koma to Naka-Koma counties and were very difficult to cure and suggested that there must be some geographic pathogen present which was not known at the time.

In the same year 1897, the first autopsy was performed on a patient named Sugiyama Naka, a female farmer in Kiyota village of Nishi-Yamanashi county (Mukou-machi, present-day Kofu city) who died of this disease. The autopsy was officially performed at Seigan-ji Temple. Many medical and public health workers attended in the venue, especially the principal researchers, Drs. Yoshioka Junsaku, Ozawa Shikajuro, Sugiura Kenzo and others. The autopsy itself was performed by the pathologist Dr. Shimodaira Yosai, director of the prefectural hospital and his assistant Dr. Murakami Shota. They found not worms but a large number of eggs deposited in the tissue. Later Dr. Kanamori Tatsujiro (1898) confirmed that the egg was a new species that was similar to the species reported by Mashima Eitoku, Yamagiwa Katsusaburo, and Kurimoto Tomei, in 1880-1890. Dr. Katsurada Fujiro (1904) agreed with this finding.

In the same year, Dr. Ishii Ryosai reported that there were many patients with a unique hepatosplenomegaly among the physically mal-qualified examinees for military service and that they showed dwarfism. In 1900, Dr. Saburo Mikami in Ohkamata village reported in the

Yamanashi Medical Journal that the geographical disease was caused by a new species of parasite because many patients with this disease showed a new species of eggs in the fecal specimen that was different from hook worm. And in the next year, 1901, he proposed his new hypothesis that this disease is caused by a new parasite through the invasion of the infective form “cercaria.”

In 1902, a large meeting entitled “On the Cause of the Geographical Hepatosplenomegaly in Yamanashi” was convened at the prefectural hospital in the presence of many researchers from around country. Although nobody had definitive evidence, the conclusion of the meeting was that the disease was closely related to a new species of parasite. Since then, the name “hepatosplenomegaly syndrome” was used for this disease.

The period from 1850 to 1900 saw the discovery of pathogens of various infectious diseases. One was *Schistosoma heamatobium* found by Theodor Bilharz in 1851, and many more followed. Charles L.A. Laveran discovered malaria protozoa in 1880. Kitazato Shibasaburo found tetanus bacteria in 1886, and plague in 1894. Kiyoshi Shiga found shigealla bacteria in 1898. In Japan, the liver fluke was first identified in 1877 by Dr. Ishizaka Kenso. And in 1878, Erwin Baelz and Heirich B. Soheube found paragonimus eggs and hook worm eggs respectively. The researchers searching for the cause of regional disease were all influenced by findings of those newly identified pathogens in the world.

The 2nd Stage; Identification of the Pathogen and its Life Cycle and Initiation of Education for Prevention, 1904-1916

The period between the discovery of schistosoma japonicum and its intermediate host, Oncomelania nosophora miyairii was the time when the people began to understand the life-cycle and the need for prevention.

Dr. Katsurada Fujiro of Okayama Medical School, who studied the liver fluke disease in Okayama, was interested in the hepatosplenomegaly syndrome in Yamanashi because in the symptoms were similar to those of liver fluke. He attended the meeting in 1902 in Yamanashi. In 1904, he stayed in Dr. Mikami Saburo’s house in Ohkamata village and examined the patients. He also performed autopsies dogs and cats and finally on May 26, 1904 isolated a fragment of a worm from the liver of a cat. At almost the same time, Dr. Fujinami Akira of Kyoto Imperial University found the same species of worm during the autopsy of a murdered farmer in Katayama district of Hiroshima prefecture. After discovery, the researcher’s interest was focused

on how the pathogen infects humans. Again two competing doctors, Katsurada and Fujinami, made great efforts to clarify the route of infection. In 1909, both independently found that the infection was caused by the skin penetration of an infective form of the worm using dogs (Katsurada in Okayama) and cattle (Fujinami in Katayama).

Traditionally, people in Yamanashi had suspected drinking water as a source of the disease. This is confirmed by traditional songs and by the fact that the villagers asked the government to examine the drinking water as a cause of the disease. So that even after the identification of the parasite, the local doctors still looked at drinking water as the cause. In 1909, the Yamanashi Medical Association established a department of regional disease research to promote systematic research and elected Dr. Asada, director of the prefectural hospital, as the first chairman. In 1910, the department invited an expert technician Tsuchiya Iwaho and started a series of studies on clinical symptoms, pathology, pathogenesis, route of infection and migration in the body, life expectancy of the worm, seasonal changes of infection, intermediate host, prevention, and treatment.

The department confirmed the following significant facts: 1. The route of infection was skin penetration; 2. The transmission season was between June and October; 3. Protection of the lower legs with cotton cloth was effective for prevention; 4. Human feces should be stored for at least 2 wks before spreading into the rice field as fertilizer; 5. Quicklime powder was ovocidal in the storage of feces in the field; 6. Quicklime or carbon dioxide nitrite was effective for prevention after spreading in the rice field; and 7. Quinine sulfate was effective for treatment.

In 1911, the department conducted a survey on the hepatosplenomegaly syndrome patients. The preparations for this survey had already started two years before. Each district had a responsible medical doctor, and a total of 45 towns and villages were included in the survey. A total of 69,131 persons were examined, among whom 7,893 (11.4%) showed hepatomegaly, splenomegaly and/or ascites. This result was published in the proceedings on the exhibition of hygiene organized by the Japan Private Society of Hygiene Yamanashi Branch 1914.

After the morphological analysis of the adult worms and eggs, the researchers expected the presence of an intermediate host as the source of the infective form of parasite called "cercaria." Therefore, the identification of the intermediate host was the next target. Miyairi Keinosuke and Suzuki Minoru of Kyushu Imperial University collected a species of snail in Miyaki county, Saga Prefecture in August 1913. They kept the snails in the laboratory and let them make contact with a mouse for a few hours, then sacrificed the mouse one month after the contact. They found worms

in the mouse, which clearly showed that the snail was a natural intermediate host of *Schistosoma japonicum*. This snail is called "Miyairi snail" by The medical researchers in honor of the finder. The Japanese name is "Katayama snail" after the old endemic area "Katayama district."

In 1913, Tsuchiya Iwaho collected the same snail in Kokubo village (Present-day Kofu city) and reproduced the Miyairi experiment. Miyairi visited Yamanashi during that period, so he must have advised Tsuchiya as to how reproduce his experiment. At the same time Miyairi himself confirmed the cercaria migration from snails collected in Saijo Village in Yamanashi in collaboration with Sugiura Kenzo.

During the period (1904-1916), scientists established the the fundamental strategy to control schistosomiasis that basically persisted until the eradication in 1996. From this period to the beginning of the next stage, the greatest efforts were poured into conveying the idea of prevention and eradication and promoting educational activities in the community.

In July 1910, Tsuchiya Iwaho gave a lecture on the regional disease and its prevention at a symposium on disease prevention held by the Japan Private Society of Hygiene Yamanashi Branch. He also gave a lecture on the discovery of the intermediate host, life cycle, mode of infection and prevention at the hygiene exhibition held in 1913. Miyajima Mikinosuke of the Kitazato Institute gave a lecture on regional disease at a conference on tuberculosis prevention in 1915. Miyairi Keinosuke gave a lecture at a special conference held by the Education Committee of Yamanashi Prefecture and Japan Private Society of Hygiene Yamanashi Branch at Kofu Middle School. More than 100 people attended the lecture, and it was reported by the local newspaper. In 1917, the department of regional disease research published a textbook with colored pictures entitled "I am a Doctor of Regional Disease" for the education of primary school students and distributed it to interested parties.

In 1917, the first mass examination of feces was carried out at Hatta Primary School in Tomi village, and after that, the department engaged in continuous and active education and promotion activities including school-based health examinations. In 1916, Miyairi conducted a health survey in Nishi Yamanashi County as a committee member of the public health program. Around the same time, a Japanese species of firefly called "genji botaru" gathered attention as the snail's predator. A booklet entitled "The Firefly and its Relation to Schistosomiasis" by Miyajima Mikinosuke was published and distributed in the prefecture, and awareness regarding the protective activity of fireflies was promoted among adolescent society in the region.

The 3rd Stage: Initiation of the Control Program, 1917-1940

Snail control was adopted as the central strategy in the eradication program. Practical programs were created and implemented during this period. The major compound for the snail control used in this period was quicklime.

In the previous stage, the life cycle was clearly identified. The principle of the control program is expressed by Fujinami's description, "Prevention of invasion of pathogen, eradication of pathogen, and inhibition of the growth of pathogen" (Akira Fujinami, 1910). More practically, prevention of infection, treatment of patients and infected animals, and elimination of eggs and snails from the environment are the three major strategies that continue unchanged to this day. Our prefectural control program was initiated on the basis of a document entitled "Proposal to perform the control program against regional disease" made by the prefectural medical association organized by Governor Wakabayashi in 1914. The document contained six major methods, 1) Killing of eggs in feces, 2) Snail control, 3) Killing or inhibition of cercaria growth, 4) Prevention of skin penetration, 5) Toilet modification, 6) Cleaning of the field feces. It took three years for this program to be initiated due to the frequently changed governors. In 1917, the first snail control program was realized by picking snails. In 1918, Governor Yamawaki declared that the urgent task was to make a policy for prevention and eradication of the regional disease degrading peoples' health and reducing productivity. After this declaration, the control program was accelerated at the governmental level. The declaration of the governor and the snail control program by picking exerted a great impact on the people in the endemic area by making them realize the importance of the eradication program. There is an episode that indicates the attention paid to the program. A person living outside the endemic area was interested in snail control and sent a letter with an idea to eliminate them, which he said he got from God in 1919, but we do not know what the idea was now.

The snail picking campaign was performed by recruiting adolescents and health volunteers in the region. The government paid the volunteers 50 sen (0.5 yen) for picking 180 ml volume of snails, adding 10 sen per 180 ml more. The first year's harvest totaled 324 liters from one city and 44 towns, then from 1917 to 1924, a total of 900 liters of snails was collected per year. However, the effect was negligible even after seven years. Yamanashi prefectural government sent the head of the public health office, Tanaka Tomihei, to Hiroshima to study the molluscicide program conducted in Hiroshima prefecture in 1918-1920.

Snail control

In 1924, the new governor, Honma Toshio, had experienced the snail control program using molluscicide before moving from Hiroshima. He published a booklet entitled "On the prevention and eradication of regional disease" that introduced the Hiroshima snail control program. He invited Dr. Akira Fujinami to give a lecture on the prevention of schistosomiasis in the endemic villages. Land owners with more than two hectares of field were invited to the lecture.

Since it was necessary to determine the snail habitation, Dr. Nakamoto Momosuke was invited to perform the first large-scale surveillance of snails. This surveillance revealed 7,800 hectares of land belonging to one city, seven counties, two towns and 62 villages was snail polluted and needed to be controlled by the program. Then in February 1925, the prefecture organized the Cooperation Agency to Lead the Prevention and Eradication of Regional Disease (CALPERD) and held a grand ceremony to open the office in the presence of national governmental delegates. CALPERD consisted of the governor as president, Mr. Kawashima, chief of police office as chairman, and Mr. Tanaka, head of the public health as vice chairman. The total term of the enterprise was ten years and the budget was 400,000 yen (150,000 yen from donations, 200,000 yen from the endemic town, and 50,000 yen from the prefecture). For the first year, 33,000 yen was used for the control program, but this was not enough to eradicate the snails. The prefectural budget had a limit. So the congress of the prefecture decided to send a letter to the central government to ask for governmental support in 1927, and Governor Suzuki Shintaro submitted an application for national support to the Minister of National Affairs in June 1928. The same year, the prefecture congress sent another letter to the Minister of Financial Affairs and 51 representatives from endemic areas wrote to the ministers of national and financial affairs and the chairman of the financial support for the control program. Finally, the central government announced its intention to support the program by allotting 40,000 yen as a special national budget in 1929. But the worldwide economic crisis of 1929 made the control program more difficult than before. Kato Tatsuo summarized the overall snail control program using quicklime for 14 years since 1925, saying that "Although we have tried hard to accomplish eradication, the budget was not enough to deliver molluscicide to all the endemic areas during these 14 years. Even in the controlled area, more than 10 years after the delivery of molluscicides, the snail population has already recovered. It is apparently necessary to repeat the control program at appropriate intervals, which is also very disappointing. However, we still have to continue our work relentlessly, because we know that these efforts will surely make a dif-

ference.”

There were many trials of methods other than quicklime, such as boiling water, hot vapor, and drying mud in the bottom of the water irrigation, but none were successful. Only one method was adopted to complement the quicklime, i.e. burning the snails, using a burner with acetylene gas invented by Mitsui Hiroji of the prefectural public health office in 1931. Around 1935, the price of the molluscicides increased so much that the continuation of the program was more and more difficult. In 1938, the prefecture confirmed the effectiveness of a new compound, nitrogenous quicklime, as a molluscicide. After the resolution of the CALPERD in 1940, the prefecture urged the endemic towns to use this new compound, but the towns did not react. There is no clear record of events between 1940 and 1943.

Treatment of the patients

The snail control was promoted as described above. At the same time, great advances were made in the treatment of patients. Until 1920, there was no significant progress in treatment aside from the knowledge that quinine sulfate and hydro-quinine were somehow effective. In 1921, Kawamura Rinya reported the effectiveness of emetine HCl and in 1922, Nishi and Miyagawa reported that sodium salt of antimony tartarate was effective and had little adverse effect. They asked the Banyu Pharmaceutical Co. to make a product called “Stibnal” commercially available. In 1923, Dr. Mikami Saburo conducted a clinical trial of Stibnal under the suggestion of Miyagawa Yoneji and proved the drug was effective and applicable to the patients, though he noticed some adverse events. In 1924, a larger scale clinical trial of combination therapy with Stibnal and Emetin HCl using 60 volunteer patients of Ohkamata village was performed by the prefecture in response to the strong demands of the local community. This trial reproduced the effectiveness of Stibnal, but four persons died due to the adverse effect of Emetin HCl.

In 1931, the government enacted the Parasitic Disease Prevention Law that determined the following duties and financial support from the local government.

1. A doctor who diagnoses patients with schistosomiasis should report it to the director of the local health station.
2. The budget for fecal examination will be fully covered by the local government.
3. Two thirds of the budget for the prevention and treatment will be covered by the local government and half will be supported by the national government. The local government can cover whole or part of the expense for the examination of feces, etc.

Yamanashi Prefecture formulated an operating procedure for the Parasitic Disease Prevention Law and issued an

operation manual to implement the law including financial support for the improvement of toilets with three sequential reservoirs guided by official design, for the fecal examination of human and animals, and for the reporting and strict maintenance of infected cattle and horses. Moreover, the operating procedure included precise and detailed addresses of the targeted endemic area including one city, two towns, and 69 villages spanning about 8,500 hectares. The trial construction of the modified toilet with three reservoirs was performed in Tamaho, Tomi, and Kokubo villages from around 1927, and in 1931, before the enactment of the prevention law, Yamanashi Prefecture urged the villagers to make the improved toilet with financial support. However, that kind of toilet did not become popular.

The 4th Stage: The Development Phase of the Control Program, 1941-1952

In 1943, the prefecture enacted the operating procedure for eradication of regional disease in Yamanashi and started the large-scale snail control program that continued until 1952, during which period great confusion was caused by World War II. After the war, a collaborative team formed by the United States 406 Medical General Laboratory (406 MGL) and the Yamanashi Prefectural Medical Institute conducted epidemiological, ecological and snail habitation surveillance and re-organized the operating system in the prefecture. In 1950, the construction of concrete irrigation canals started. This period is characterized by the replacement in 1953 of nitrogenous quicklime with Na PCP as the molluscicide.

After the resolution of CALPERD in June 1940, the prefecture recommended the use of nitrogenous quicklime as a molluscicide, but it is not clear whether this was carried out or not. In 1943, the prevalence was so high that a regional disease prevention committee was organized by 31 members (at the second meeting, 45 members gathered) including prefectural officers, experts from inside and outside of the prefecture and other consultants. The committee reported the operating procedure of the eradication program that recommended snail control by nitrogenous quicklime, fecal examination, treatment of the inhabitants and the control of domestic animals. As a result, the molluscicide operation by nitrogenous quicklime started in all the endemic areas. These procedures were conducted until 1951, especially the treatment of infected cattle.

In December 1940, the Governor Mr. Tago Saneo issued a statement that schistosomiasis was still threatening the health of 200,000 inhabitants in one city, 56 towns and villages and that the disease reduced rice productivity by

10,000 hectares of rice field. The statement also proposed a three-year project for snail control by nitrogenous quicklime and for a detection and treatment strategy. Because it was war-time, the governor insisted that the control program would strengthen national military power through increased production and the cultivation of healthy individuals.

Fragmental records of endemicity suggest that the prevalence was extremely high. In 1942-1943, the egg positive prevalence was 15.5% among inhabitants and 49.6% among cattle. In 1944, the prevalence among primary school students was 24.2 % and that among cattle was 35.0%. This may be due to the switching of labor animals from horses to cattle because the farmers had to donate their horses to the army.

In 1945, the government established Yamanashi Medical School and Yamanashi Regional Disease Institute using the old building of Kofu Business School, but the building burned down when the US bombed Kofu city in July 1945. The annual report ordered by the Occupation government (GHQ-SCAP) records the opening of the institute in January 1948 in the presence of the new director Dr. Ishii Shintaro from the National Institute of Health Japan, showing that research was not interrupted even after the fire in 1945. In 1946, the prefecture opened the regional disease clinic for treatment. During the war in the Philippines, many American soldiers were infected with *Schistosoma japonicum*, and after the occupation of Japan, schistosomiasis committee experts were sent to investigate the situation in the endemic areas in Japan. In Yamanashi, Mr. Ienaga, head of the office of prefectural public health, and Dr. Sugiura Saburo participated in an interview and gave information to the American experts. At the beginning, the Americans were mainly interested in information that would be beneficial for their own soldiers, but later on they made efforts to improve the public health of their occupied people. In December 1947, the US launched a plan called "Special Research Project on Parasitic Diseases" that was designed for US-Japan cooperative research on issues including schistosomiasis. This cooperative research project between the Japanese National Institute of Health and the US Army 406 Medical General Laboratory (406 MGL) adopted schistosomiasis as a priority subject and started field research in the endemic areas in Yamanashi. In 1947, 406 MGL opened a tentative laboratory inside the Yamanashi Prefecture Office, but there is no available record as to the purpose.

In October 1947, Emperor Hirohito visited Tamahata Village, received information regarding the epidemiological situation and the present research from Dr. Sugiura Saburo and observed the microscopic examination of schistosomal eggs and the snail habitation. This visit was the second visit

by the Emperor. Crown prince had made a visit in 1912, at which time Dr. Tsuchiya Iwaho attended and explained the serious situation in Yamanashi. The people expected the Emperor to help their eradication program.

In December 1947, a train equipped for field research on schistosomiasis, called the "Parasite Train", arrived in Kofu station at Yamanashi. The train was composed of four cars, one of which was designed for laboratory work on fecal specimens. The cooperative study was fruitful and included achievements in epidemiology, snail control using molluscicides, preventive methods using skin ointment, application of skin test for diagnosis, etc. Many doctors and prefectural officers were actively involved in the cooperation effort.

The new governor Yoshie Katsuyasu conceived a grand design consisting of ten major political issues including a three-year schistosomiasis eradication program in 1947, and in 1948 he reorganized the previous regional disease eradication union established in 1944 as the Association of Regional Disease Eradication Unions. The program mainly adopted snail control using nitrogenous quicklime and continued until 1952, but the distributed nitrogenous quicklime was not always used properly, sometimes being used as a fertilizer due to the difficult situation after the war.

The regional disease institute was renovated as the Yamanashi Medical Institute consisting of three departments (diagnostic, regional disease research, and laboratory medicine) with a new director Dr. Tamiya Takeo in 1949. The Department of Regional Disease led by Dr. Sugiura Saburo started work on research and development for prevention, eradication and treatment and on the patient management. In collaboration with 406 MGL, they promoted research on new molluscicides, preventive ointments, and diagnostic skin tests, etc.

In 1950, the eradication program was transferred from the prefecture to the city and town level. The heads of cities and towns organized a society for the regional disease eradication and elected Dr. Ono Toru as president. This society continues to function as a center of the program today. The most significant contribution of the society was the construction of concrete irrigation canals. After the war, the high fecal egg prevalence persisted, being recorded as 44.2% during the 1947-49 period.

The 5th Stage: Comprehensive Control Strategy Decreased the Prevalence, 1953-1971

This period is defined as the Na PCP molluscicide snail control period. The extensive snail control project using Na PCP and concrete irrigation canals was performed. In 1957, the national government supported the building of a

concrete irrigation system for the control of schistosomiasis that led to great environmental improvements. Then in 1960, the first disease-free declaration was made in one of the previously endemic areas, 56 years after Katsurada's finding in 1904.

The US-Japan cooperative research on molluscicides confirmed the effectiveness of Na PCP, DN-1 and dowcide by repeated field trials in the prefecture. In the spring of 1953, US-made santbrite consisting of Na PCP was distributed to the endemic areas including 18 cities and towns to replace nitrogenous quicklime. In the spring of 1954, santbrite and later domestic Na PCP and DN-1 were applied for snail control. Na PCP showed the best efficacy of molluscicidal activity and was adopted for the control program in 1955. Na PCP was so effective in the endemic areas that the inhabitants became convinced that snail control was possible. On the other hand, there were many reports that fish died after the spreading of Na PCP. The local governmental offices took this seriously and urged citizens to perform the Na PCP snail control properly. The reports of environmental destruction subsequently decreased.

In 1953, the governor set up the Prefectural Regional Disease Eradication Promotion Committee as a think tank for making policy for disease control. The committee, which consisted of diet members, mayors and village leaders, scholars and experts, made suggestions for the operation. Their report called for the following:

1. Snail control with Na PCP but without environmental destruction.
2. The priority in constructing concrete irrigation canals should be determined by seven principles: 1) Upstream first, 2) Dense snail habitation, 3) High infection rate, 4) Other methods are difficult, 5) The construction should benefit the community, 6) The width of the irrigation canal less than 1m. 7) No future plan to change the land use.
3. Financial support to use preventive ointments.
4. Extensive treatment of patients.
5. Systematic implementation of snail surveillance and fecal examinations.

The committee functions as a policy making center in the prefecture to this day. In 1955, the Japanese gross national product (GNP) recovered to a pre-war level and showed a constant development. The governor, Mr. Hisashi Amano, established the headquarter of the control and development office of agriculture in the endemic areas in 1958. The office proposed to change rice fields to vegetable fields and orchards for the prevention of water contact and conducted interviews to see if farmers were interested in the idea. The reaction was rather negative but the construction

of concrete irrigation canals and other environmental modifications gradually shifted the structure of agricultural management to vegetables and fruits. Although the farmers did not intensively change their rice fields to dry fields for disease control, this constructive change in agriculture contributed enormously to regional disease control in addition to the extensive use of Na PCP.

On the other hand, in 1954, schistosomiasis patients were found in the non-endemic. Hara village (present Nakatomi town). After this new finding, it was revealed that 121 persons (13.4%) in the village were positive for fecal eggs and that the average infection rate of snails in the village was 2.3%, the highest being 16.0% in a specific area. These data were similar to the original endemic areas. After this surprise, extensive surveillance of the snail habitation and infestation was performed in 1955 and revealed that the endemic area had actually expanded to 19,603 hectares or the largest in history. Around 1955, floods occurred in many districts and the 1959 typhoon caused another flood that buried the snail habitation with mud in Nakatomi town and Nirasaki city.

After 1955, the control program reached the final goal, disease-free declaration disease, in some restricted areas or villages in Yamanashi. In 1960, Nagasawa of Masuho town, Kuruwada of Kushigata town, Higashi Ochiai of Kosai town made disease-free declarations, and in the next year, Shimo Obina, and Hirase of Kofu city, Iino and Kuruwada-Shinden of Shirane town, Kagami of Wakakusa town, Fujinuta of Sakaigawa town and Hitotsuya of Nirasaki followed.

The Society for Regional Disease Eradication was established in 1950 as described. In 1961, to garner governmental support for the eradication program in different areas in Japan, a nationwide committee for the control of schistosomiasis was established and worked to obtain financial support from the government. The increase in the number of areas making disease-free declarations greatly enhanced the control activity including advertisement car, seasonal campaign, and educational programs for school children. The skin test was also useful for the detection of patients.

By 1971, a significant improvement had been observed in the endemic situation mainly due to two major changes. One was the constructive change in agriculture, as well as the modern technology of chemical fertilizer and machines that replaced the use of animal labors. The other is Na PCP. The overall number of active patients was less than 1,000 and the percentage of egg positivity was less than 1% in 1971. The infection rate of dogs, which was 25.5% in 1957, decreased to 5.0% in 1962 and finally reached 0% in 1971. The cattle infection stopped in 1964. The infection rate of