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Picture of the monument

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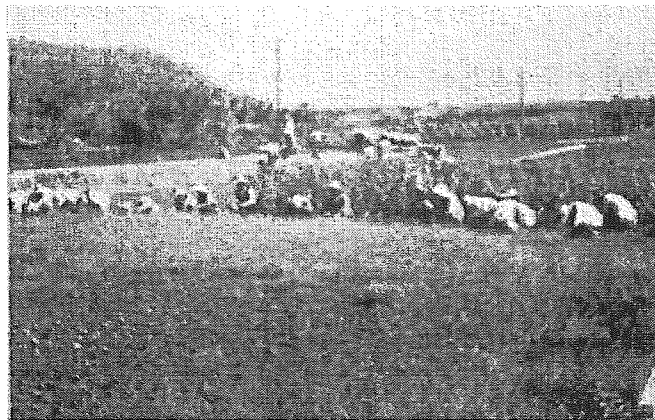
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## Chapter 1. History of the disease control in Yamanashi Prefecture

### 2. Outline of the control program in Yamanashi Prefecture



Upper: Surveillance of the snails by the villagers in Nakamichi in the spring of 1975

Lower: Grass cutting before the spray of molluscicides in Kofu City around 1975.

- The 1<sup>st</sup> stage: Suffering from unknown regional disease before the discovery of the parasite until 1903 (36 of Meiji Era)
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- The 4<sup>th</sup> stage: Development of the control program. 1941-1952
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The history of the control program in Yamanashi is divided into 7 stages. Each stage is described by the year by year style to grasp the outline of the history. The details will be described in the later chapters, such as the year book 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 until 1903 (The year 36 of Meiji Era)**

*The Yamanashi (formerly called Kai-no-kuni) people had been suffering from the unknown origin disease that was characteristic for abdominal ascites for many years and been accepting their destiny. After the Meiji revolution in 1860s, people hoped the modern medicine to clarify the disease and many pioneering researchers and doctors made an effort to understand the pathogenesis.*

It is not clear when the people realized the disease. In the old archives, there are several stories about the disease. One is that the famous load of Kai (Old name of Yamanashi), Shingen Takeda (-1573) died of this disease. The other is described in 'Kou-you Gun-Kan, the military book of Yamanashi'(1602) that one of the knights of Kai, Obata Bingo-no-kami, suffered the similar symptoms with schistosomiasis. There remained a record that a variety of traditional medicines were used for the ascites that is characteristic for post-schistosomal liver cirrhosis since 300 years ago in Ryuoh town in Yamanashi. The picture of the advertisement of the traditional medicine 'Tsu-you-san, for the ascites fluid' is included in the later chapter.

There is no evidence but at least in 1600s Kofu basin area in Yamanashi was already endemic for schistosomiasis japonica. There is no confirmative evidence but it would be almost certain that Kofu basin was already endemic for schistosomiasis at latest in Edo-era (1600 - 1860). The first description available to us now that there was schistosomiasis in Yamanashi is that "many patients with ascites that is difficult to care". In the book named "Honyaku Dan-doku-ron" or "Translation to abolish the toxin" published by a

local medical doctor Hakuju Hashimoto in 1811. The record that a village "Shimo-takasago" 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 another village "Miyazawa" asked the Governor to permit them to move to another place where they can get clean water (free from disease) in 1874 and in 1878 were also related to schistosomiasis. In 1881, Kasugai villagers processed a document named "Ask for the direction for the control" or "Go-shiki-negai" to the prefectural government. The Kasugai village continued to make a series of documents to report the situation of schistosomiasis at that period between 1881 and 1887. Those documents were informative to know how much the villagers suffered and how the government reacted to it. In 1884, the prefectural government initiated the study on the disease with clinical exam and the drinking water examination in Kasugai village. Dr. Tatsu Ohashi, director of the prefectural hospital made a first record of their clinical examination by the name "Byoyou Ryakki" or "Brief description of the clinical findings" but his conclusion was that the disease was caused by over-work and some malfunction of digestion which was not clear at all.

Two years later in 1886, a military doctor Ryosai Ishii reported to the prefecture that there was a problem in the drinking water that influence 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 the proposal for the governmental initiative to understand the pathogenesis of the disease in 1887. Responding to this proposal, the government sent Dr. Kohei Nagamachi, Director of the prefectural hospital in 1887, to the village to do the clinical study again. Dr. Nagamachi did a fecal examination, found the eggs of "duodenal worm" or "hook worm" and suggested that the ascites was derived from this worm. Dr. Nagamachi's conclusion was wrong but his idea that some parasitic disease might cause the disease was significant. After his suggestion, there were several reports on unknown parasite's egg in the tissue of

the patients made by the pathologists, named Eitoku Mashima (1893), Katsusaburo Yamagiwa (1890), Tomei Kurimoto (1893).

Around the same period, local doctors in the endemic area, Dr. Kenzo Sugiura and Dr. Shikajuro Ozawa showed their opinion that the disease showing the hepato-splenomegaly and the ascites frequently seen in Nakakoma County could be “regional disease” or “Chihou-byou”. At that time, the word, “regional or geographic disease” was not new and was including malaria, leprosy, Vit.E, B deficiency. In 1897, Dr Shikajuro Ozawa in Tano-oka village summarized the clinical symptoms and epidemiological findings of over 90 patients with the disease and reported a paper titled “On the regional ascitic disease” in the regional Journal of private society of hygiene in Japan, or “Dai-nihon shiritsu eisei kai Yamanashi Shikai kouhou.” In the paper, he described that the patients are aggregated in Kita-Koma to Naka-Koma counties and are very difficult to cure and that there must be some geographic pathogen present which was not known at that time.

In the same year 1897, the first autopsy of the patients named Naka Sugiyama who was a female farmer in Kiyota village of Nishi-Yamanashi county (Mukai-Machi, Kofu city in the present) and died with this disease was performed. The autopsy was officially performed; so many medical and public health workers were attending in the venue, Sei-gan-ji temple, especially the principal researchers, Drs. Junsaku Yoshioka, Shikajuro Ozawa, Kenzo Sugiura and others. The autopsy itself was performed by the pathologist Dr. Yosai Shimohira, Director of the Prefectural hospital and his assistant Dr. Shota Murakami. They could not find the worms but a lot of eggs deposited in the tissue. Later Dr. Tatsujiro Kanamori (1898) confirmed that the egg was a new species that was similar to the species reported by Eitoku Mashima, Katsusaburo Yamagiwa, and Tomei Kurimoto, in 1880-1890. Dr Fujiro Katsurada (1904) agreed with his finding.

In the same year in 1897, Dr. Ryosai Ishii reported that there were many patients with a unique hepatosplenomegaly in the physically mal-qualified examinee for the military service and they showed dwarfism. In 1890, local Doctor Saburo Mikami in Ohkamata village reported in

Yamanashi Medical Journal that the geographical disease was caused by a new species of parasite because many patients with this disease showed 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 the new parasite through the invasion of infective form “cercaria”.

In 1902, there was a big meeting entitled “On the cause of the geographical hepatosplenomegaly in Yamanashi” at the Prefectural hospital in the presence of many related researchers in the whole country. Although nobody got a definitive evidence, the conclusion of the meeting was that the disease was closely related to the new species of parasite. Since then, the name “hepatosplenomegaly syndrome” was used for this disease.

Around 1850-2000 is a periods of finding pathogens of varieties of infectious diseases. The most related finding was the *schistosoma heamatobium* by Theodor Bilharz in 1851 and many more followed. Charles L.A. Laveran found malaria protozoa in 1880. Shibasaburo Kitazato found tetanus bacteria in 1886, and Plague in 1894. Kiyoshi Shiga found Shigealla bacteria in 1898. In Japan, the liver fluke was firstly identified in 1877 by Dr. Kenso Ishizaka. And in 1878, Erwin Baelz and Heirich B. Soheube found Paragonimus eggs and hook worm eggs respectively. The researchers searching for the cause of the 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. Initiation of the education for the prevention, 1904 – 1916 (year 37 of Meiji Era - 5 of Taisho Era).**

*The period between the finding of schistosoma japonicum and that of its intermediate host, Oncomelania nosophora miyairii was the time when the people were educated and promoted to realize the lifecycle and its prevention.*

Dr. Fujiro Katsurada at Okayama Medical School who studied the liver fluke disease in Okayama was interested in the hepatosplenomegaly syndrome in Yamanashi that

is similar in symptoms to the liver fluke. He attended the meeting in 1902 in Yamanashi. In 1904, he stayed in Dr. Saburo Mikami's house in Ohkamata village in Yamanashi and examined the patients. He also did an autopsy of dogs and cats and finally on May 26, 1904, he isolated a fragment of the worm from the liver of a cat. Almost the same time at the end of May, Dr. Akira Fujinami at Kyoto Imperial University also found the same species of worm from the autopsy of a murdered farmer in Katayama district of Hiroshima prefecture. After the finding of the pathogen, the researcher's interest was focused on how they infect the humans. Again two competing doctors, Katsurada and Fujinami made a lot of effort to clarify the route of infection. In 1909, both independently found that the infection was occurred by skin penetration of the infective form of the worm by using dog (Katsurada in Okayama) and cattle (Fujinami in Katayama).

Traditionally, people in Yamanashi have been suspecting the drinking water as a source of the disease. This is confirmed by the facts that there are traditional songs related to this and that the villagers asked the government to examine the drinking water as a cause of the disease. So that ever after the identification of the parasite, the local doctors still believed the drinking water was the cause. In 1909, the Medical Association in Yamanashi establish the department of regional disease research to promote a systemic research and elected Dr. Asada, Director of prefectural hospital as the first chairman. In 1910, the department invited an expert technician Iwaho Tsuchiya and started a series of studies including clinical symptoms, pathology, pathogenesis, route of infection and its migration in the body, the life expectancy of the worm, seasonal change of infection, intermediate host, prevention, and treatment.

The department made a significant achievement as follows; 1. The route of infection was skin penetration. 2. The transmission season was between June and October. 3. The protection of the lower legs by cotton cloth was effective for prevention. 4. The feces should be kept stored for at least 2 wks before spreading into the rice field as a nutrition. 5. Quicklime powder is ovocidal in the storage of feces in the field. 6. Quicklime or

Carbon dioxide Nitrite was effective for prevention where they spread in the rice field. 7. Quinine Sulfate was effective for the treatment.

In 1912, the department did a surveillance of the hepatosplenomegaly syndrome patients. The preparation for this surveillance was already started 2 years before. Each district had a responsible medical doctor and totally 45 towns and villages were involved in this survey. 69,131 persons were examined and 7,893 persons (11.4%) showed hepatomegaly, splenomegaly and or ascites. This result was published in the proceedings of the exhibition of hygiene organized by private association of hygienist in Yamanashi Prefecture in 1915 (Year 3 of Taisho era).

After the morphological analysis of the adult worms and eggs, the researchers expected the presence of intermediate host as a source of infective form of parasite named cercaria. Therefore, the identification of the intermediate host was the next target. Keinosuke Miyairi and Minoru Suzuki at Kyushu University collected a kind of snail in Miyaki county, Saga prefecture in August 1914. They kept them in the laboratory and made them contact with mouse for a few hours and the mouse was sacrificed one month after the contact. They found the worms in the mouse, which clearly showed the snail was a natural intermediate host of *schistosoma japonicum*. This snail is called "Miyairi snail" by the medical researchers for the respectable finder. As a Japanese name, we call it "Katayama snail" that is related to the old endemic area "Katayama district".

In 1914, Iwaho Tsuchiya collected the same snail in Kokubo village (Kofu city in the present) and reproduced the Miyairi's experiment. Miyairi visited Yamanashi during that period, so he must have advised Tsuchiya to reproduce his experiment. At the same time Miyairi himself confirmed the cercaria migration from the snail collected in Saijo Village in Yamanashi in collaboration with Kenzo Sugiura.

This period (1904 - 1916) established the idea of the fundamental strategy to control schistosomiasis that basically persisted until the eradication completed in 1996. From this period to the beginning of the next stage, the most effort was spent to educate the people with the idea of

prevention and eradication and was to promote their activity as a community.

In July 1910, Iwaho Tsuchiya made a lecture on the regional disease and its prevention at the symposium of disease prevention held by Private society of hygienists in Yamanashi. He also made a lecture on the discovery of intermediate host, life cycle, mode of infection and prevention at the hygiene exhibition held in 1914. Mikinosuke Miyajima of Kitazato Institute made a lecture on regional disease at the conference on tuberculosis prevention in 1916. Keinosuke Miyairi gave a lecture at special conference held by Education Committee of Yamanashi prefecture and Society of hygienists in Yamanashi at Kofu junior high school. More than 100 audience attended the lecture and was actively reported by the local newspaper. In 1917, Department of regional disease research published a textbook with colored pictures titled "I am a doctor of regional disease" for the education of primary school students and distributed them to the related places.

In 1918, the first mass examination of feces was carried out at Hatta primary school in Tomi village. Since then, the department had been engaged in a continuous and active education and promotion activities including school based health examination. In 1917, Miyairi did a health survey in Nishi Yamanashi County as a committee member of Public Health program. At the same period, Japanese species of firefly named "Genji Botaru" was taken attention as the snail's predator. The booklet named "Beneficial firefly's life - related to schistosomiasis" by Mikinosuke Miyajima was published and distributed in the prefecture. The protective activity for firefly was promoted on the basis of regional adolescent society.

### **The 3rd stage: Initiation of the control program, 1917-1940 (Year 6 of Taisho Era - 15 of Showa Era)**

*Snail control was determined to be adopted as the central strategy in the eradication program. Practical programs were produced 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 was made by the 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 the patients and the infected animals, elimination of the eggs and the snails from the environment were the 3 major strategies that have been never changed until now. Our prefectural control program was initiated by the document named "Proposal to perform the control program against regional disease" made by the prefectural Medical association that was organized by the Governor Mr. Wakabayashi in 1915. The document contained 6 major methods, 1) Killing of eggs in the faces, 2) Snail control, 3) Killing or inhibition of cercaria growth, 4) Prevention of the skin penetration, 5) Toilet modification, 6) Cleaning of the field feces. It took 3 years after this document until the initiation of the program due to the frequently changed Governors. In 1918, the first program was realized as a snail control by picking them. In the next 1919, the Governor Mr. Yamawaki declared that the urgent task was to make a policy for prevention and eradication of the regional disease that abolish the peoples' health and decrease the productivity. After this declaration, the control program was potentially accelerated by the governmental level. The declaration of the Governor and the snail control program by picking gave a great impact on the people in the endemic area to realize the importance of the eradication program. There is an episode that indicated the heating up of the program. One person who was not living in the endemic area was interested in the snail control and gave an idea to eliminate them by sending a note describing his idea which he said he got from God in 1920 but we do not know what was the idea now.

The picking snails campaign was performed by recruiting the regional adolescence society and the health volunteers. The government provided the volunteers with the facilitating award money of 50 sen (0.5 Japanese yen) for 180 ml volume of snails, adding 10 sen per 180 ml more. The first year's

harvest was totally 324 litters from one city and 44 towns, then from 1918 to 1924, totally 900 litters of snails was collected per year. However, the effect was almost nothing after 7 years' program. Yamanashi prefectural government sent the head of the public health office, Tomihei Tanaka to Hiroshima to learn the molluscicide program performed in Hiroshima prefecture in 1918-1920.

#### *Snail control*

In 1923, the new Governor Mr. Toshio Honma moved from Hiroshima who had an experience of snail control program using molluscicide. He published booklet "On the prevention and eradication program against regional disease" that introduced the Hiroshima's snail control program. He invited Dr. Akira Fujinami to give the lecture on the prevention of schistosomiasis in the endemic villages. The land lords who had more than 2 Cho-bu (Hectare) of field were invited to the lecture.

For the snail control, it was necessary to know the snail habitation so that Dr. Momosuke Nakamoto was invited to perform the large scale surveillance of snails for the first time. This surveillance revealed that 7,800 Cho-bu (Hectare) of the land that belongs to one city, seven counties, two towns and 62 villages were snail polluted area to be controlled by the program. Then in February 1924, the prefecture organized the cooperation agency to lead the prevention and eradication of regional disease (CALPERD) and made a big ceremony of opening the office in the presence of national governmental delegates. CALPERD was consisted of the Governor, as president, Mr. Kawashima, head of police office as chairman, and Mr. Tanaka, head of the public health office as vice chairman. The total term of the enterprise was ten years and its budget was 400,000 JPY (150,000JPY from donation, 200,000JPY from the responsible endemic town, 50,000JPY from the prefecture). For the first year, 33,000 JPY was used for the control program. The budget was not enough to eradicate the snail. The Prefectural budget had a limit. So the congress of the prefecture decided to send a letter to the central government to ask for the governmental support in 1926, and the Governor Shintaro Suzuki processed the application to get a national support to Minister

of National affairs in July 1927. In the same year, the congress of prefecture sent a letter again to Minister of Financial affairs and 51 members of representation from endemic areas sent Ministers of national and financial affairs and the chairman of the lower house of congress the application to get the financial support to the control program by the central government. Finally, the central government realized the situation, and supported the program by making 40,000 JPY as a special national budget in 1928. But the world wide economical crisis occurred in 1929 that made the control program more difficult than before. Tatsuo Kato summarized the overall snail control program after 15 years of Quicklimes program since 1924, saying that "Although we are trying to make an accomplishment of eradication so hard, the budget was not enough to cover all the endemic area to deliver the Molluscicide during these 14 years. Even in the controlled area, more than 10 years after molluscicide, the snails population have already recovered. It looks necessary to repeat the control in an appropriate interval which is also disappointing us so much. However, we still have to continue our work constantly because we know that such an effect will surely make a difference."

There were many trials other than Quicklime such as boiling water, hot vapor, dry the mud in the bottom of the water irrigation but they were not successful. The only one method for burning the snail using the burner with Acetylene gas invented by Hiroji Mitsui of Prefectural public health office in 1931 was adopted to complement the Quicklime. Around 1935, the price of the Molluscicides raised so that the continuation of the program was getting more and more difficult. In 1938, the Prefecture confirmed the effectiveness of the new compound, Nitrogenous quicklime as a new molluscicide. And, after the resolution of the CALPERD in 1940, the prefecture recommended the endemic towns to use this new compound but the towns were not so much reactive. There is no clear record between 1940 and 1943.

#### *Treatment of the patients*

The snail control had been processed as described above. At the same period, the great advance was obtained in the treatment of the patients. Until 1920, there was no significant



progress for the treatment except for the knowledge that Quinine sulfate and hydro-quinine were somehow effective. In 1921, Rinya Kawamura reported the effectiveness of Emetine HCl and sequentially in 1922, Nishi and Miyagawa reported that Sodium salt of Antimony tartarate was effective to the disease and had a little adverse effect. They asked the Pharmaceutical company "Banyu Pharmaceutical" to make the commercially available products named "Stibnal". In 1923, Dr. Saburo Mikami performed the clinical trial of Stinabul under the suggestion of Yoneji Miyagawa and he proved the drug was effective and applicable to the patients though he noticed some adverse events. In 1924, A larger scale clinical trial of the combination therapy with Stibnal and Emetin HCl using 60 volunteer patients of Ohkamata village was performed by the prefecture in response to the strong requirement of the local community. This trial reproduced the effectiveness of Stibnal, however, 4 persons died due to the adverse effect of Emetin HCl.

In 1931, the Government enacted the Parasitic disease prevention law that determined the following duty and financial supports from the local government.

1. The doctor who diagnosed the patients as Schistosomiasis should report it to director of the local health station.
2. The budget for the fecal examination will be fully covered by the local government.
3. Two third of the budget for the prevention and treatment will be covered by the local government and its half will be supported by the national government. The local government can cover the whole or the part of the expense for the process of the feces and other things. Based on this law, Yamanashi Prefecture enacted the operating procedure of the parasitic diseases prevention law and the operation manual to perform the parasitic diseases prevention law including this financial support for the improvement of the toilet with 3 sequential reservoirs guided by the official design, for the fecal examination of human and animals, and the duty to reported and restrict keeping the infected cattle and horses. Moreover, in the operating procedure, the precise and detailed addresses of the targeted endemic area including one city, two towns, and 69 villages spanning

about 8,500 cho-bu (hectare). The trial construction of the modified toilet with three reservoirs had been performed in Tamaho, Tomi, and Kokubo villages since around 1927, and in 1931 before the prevention law, Yamanashi prefecture had already recommended 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 (Year 16-27 of Showa Era).**

*In 1943, the prefecture enacted the operating procedure for the eradication of the regional disease in Yamanashi and started the large-scale snail control program that continued until 1952 during the period there was a big confusion provoked by the World War II. After the war, the collaborative team consisted of the United States 406 Medical General Laboratory (406MGL) and the Yamanashi Prefectural medical institute performed the epidemiological, ecological and snail habitation surveillance and re-organized the operating system in the prefecture. In 1950, the construction of the concrete irrigation started. This period was specifically characterized by the use of Nitrogenous quicklime as the molluscicide that was replaced by Na PCP in 1953.*

After the resolution of the regional disease eradication oriented Union in June 1940, the prefecture recommended the use of Nitrogenous quicklime as a replacement of the precious molluscicide, but it is not clear whether actual performance was done or not. In 1943, the prevalence got so high that the regional disease prevention committee was organized by 31 members (At the second meeting, 45 members were collected) 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 the snail control by Nitrogenous quicklime, fecal examination, treatment of the inhabitants and the control of the domestic animals. Under the suggestion, the molluscicide operation

by Nitrogenous quicklime started in all the endemic area. The procedures were kept performed until 1951 especially the treatment of the infected cattle were intensively performed.

In December 1940, the Governor Mr. Minoru Tago gave a statement that schistosomiasis was still threatening the health of 200,000 inhabitants in one city, 56 towns and villages and the disease decreased the productivity of the rice from 100,000 cho-bu (hectare) of rice field. The statement also proposed the 3 year's project for the snail control by Nitrogenous quicklime and for the detection and treatment strategy. Because it was war-time, he put the words with the proposals that the control program will contribute to strengthen our national military power through the increase of the production, and making healthy individuals.

We could not find enough number of records of endemicity but the fragmental records suggested that the prevalence was extremely high. In 1942 - 1943, the prevalence of egg positive was 15.5% in the inhabitants and 49.6% in the cattle. In 1944, the prevalence of the primary school students was 24.2 % and that of cattle was 35.0%. This may be due to the switching the labor animals from horse to cattle because the farmers should have donated their horses to the imperial 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 out when the US bombed Kofu city in July, 1945. The residual paper (GHQ ordered annual report of the institute) recorded the opening of the institute in January 1948 in the presence of new director Dr. Shintaro Ishii from National Institute of Health Japan, so that the research team was not interrupted even after the fire in 1945. In 1946, the prefecture opened the regional disease clinic for the treatment. During the war-time in Philippines, many US soldiers got infection with *Schistosoma japonicum* and after the occupation of Japan, they sent the experts from Schistosomiasis committee to investigate the situation in the endemic area in Japan. In Yamanashi, Mr. Ienago, head of the office of prefectural public health, and Dr. Saburo Sugiura got an interview and gave the information to the US experts. At the beginning, the US side was only interested in the disease information that

would be beneficial for their own soldiers, but later on they were planning to improve public health of their occupied people. In December 1947, the US made a plan named special research project on parasitic diseases that is designed for the US-Japan cooperative research including schistosomiasis. This cooperative research project between National Institute of Health Japan and US army 406 medical general Laboratory (406 MGL) adopted schistosomiasis as priority subject and started the field research in the endemic area in Yamanashi. In 1947, 406 MGL opened a tentative laboratory inside the government house of Yamanashi prefecture, but there is no available record describing the purpose in our hand.

In October 1947, Showa Emperor Hirohito visited Tamahata Village, heard the story regarding the epidemiological situation and the present research from Dr. Saburo Sugiura and observed the microscopic examination of Schistosomal eggs and the snail habitation. This visit was the second visit for the Emperor. The last time was made by Meiji Emperor in 1912 when Dr. Iwaho Tsuchiya attended and explained the serious situation in Yamanashi. The people expected the Emperor to help their eradication program.

In December 1947, the train that was equipped for the field research on Schistosomiasis called "Parasite Train" arrived in Kofu station in Yamanashi. The train was composed of four cars, one of which was designed for the Laboratory work for fecal examination. The cooperative study was fruitful with many achievements including epidemiology, snail control using molluscicide, preventive methods using skin ointment, application of skin test as a diagnostic etc. Many doctors and prefectural officers were actively involved in the cooperation.

The new Governor Katsuyasu Yoshie made a grand design consisted of 10 major political issues including 3 years' schistosomiasis eradication program in 1947 and in 1948, he reorganized the previous regional disease eradication union established on 1944 to the association of the regional disease eradication unions and started implementation of this program. The program mainly adopted the snail control using Nitrogenous quicklime and continued until 1952, but the distributed Nitrogenous quicklime was not always

used properly and was used as a field nutrient due to difficult time after the war.

The regional disease institute was renovated to be the Yamanashi medical Institute consisted of three departments, diagnostic, regional disease research, and laboratory medicine with a new Director Dr. Takeo Tamiya in 1949. Department of regional disease research conducted by Dr. Saburo Sugiura started their work on the research and development of the prevention, eradication and treatment and on the patient's management. In collaboration with 406 MGL, they processed researches on new molluscicide, preventive ointments, and diagnostic skin test, etc.

In 1950, the eradication program was transferred from prefecture to city and town level. The heads of the city and towns organized the society for the regional disease eradication and elected Mr. Toru Ono as President. This society has been functioning as a center of their program until now. The most significant contribution of this society was the construction of concrete irrigation. After the war, the fecal egg prevalence persisted to be very high as recorded 44.2% during 1947 - 49 periods.

**The 5th stage: Comprehensive control strategy decreased the prevalence, 1953 – 1971 (Year 28-46 of Showa Era)**

*This period was defined as Na PCP molluscicide snail control period. The extensive snail control project using Na PCP and concrete irrigation was performed. In 1957, the National government started the support to build concrete irrigation system for the control of Schistosomiasis that greatly enhance the environmental modification. Then in 1960, the first declaration of a disease free area by one of the previous endemic areas. It was 56 years later 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 consisted of Na PCP was distributed to the endemic area including 18 cities and towns for the replacement of Nitrogenous quicklime In the

spring of 1954, at the beginning, Santbrite and later domestic Na PCP and DN-1 were applied for the snail control operation. Within those, Na PCP showed the best efficacy of molluscicidal activity and was adopted to the control program in 1955. Na PCP showed so effective in the endemic area that the inhabitants got convinced that snail control was possible. On the contrary, there were many reports that fish died after spreading Na PCP. The local governmental offices took this serious and gave warning to perform the Na PCP snail control properly. The reports of environmental destruction decreased after such activity.

In 1953, the Governor set up the prefectural regional disease eradicated promotion committee as a think tank for making a policy for the disease control by the Governor. The committee was consisted of parliament members, Mayors and village leaders, scholars and experts and made a suggestion for the operation. The report mentioned the following things.

1. Snail control with Na PCP but without environmental destruction.
2. The priority to construct concrete irrigation should be determined by 7 principles (1. upstream first. 2. Dense snail habitation. 3. Infection rate is high. 4. Other method is difficult. 5. The construction should benefit the local. 6. The width of the irrigation less than 1m. 7. No future plan to change the land use.)
3. The financial support to use the preventive ointment.
4. Extensive treatment of patients.
5. Systematic performance of the snail surveillance and fecal examinations.

The committee has been functioning as policy making center in the prefecture until now. In 1955, Japanese gross national production(GNP) recovered to the level of pre-war-time, and was getting a constant development. The Governor Mr. Hisashi Amano established the headquarter of the control and development office of agriculture in the endemic area in 1958. The office proposed to change the rice field to vegetable field and orchard for the prevention of water contact and performed the interview if the farmers are interested in the idea. The reaction was rather negative but the construction of concrete irrigation or other

environmental changes gradually changed the structure of their agriculture management preferable to vegetables and fruits. Although the farmers did not intensively change their rice field to dry field for the disease control, this constructive change in the agriculture contributed enormously to the regional disease control in addition to the extensive use of Na PCP.

On the other hand, in 1954, the Schistosomiasis patients were found in the non endemic area, Hara village (present Nakatomi town). After this new finding, it was revealed that 121 persons (13.4%) in the village showed positive fecal eggs and the average infection rate of the snails in the village was 2.3% including the highest 16.0% in some specific area. Those data were almost similar to the original endemic areas. After this surprise, extensive surveillance of the snail habitation and infestation was performed in 1955 and revealed the endemic area had actually expanded to 19,603 hectare that was the largest in the history. Around 1955, there occurred flood in many districts and the 1959 typhoon made another flood to bury the snail habitation with mud in Nakatomi town and in Nirasaki City.

After 1955, the control program reached the final goal, declaration of disease free area, in some restricted areas or villages in Yamanashi. In 1960, Nagasawa of Masuho town, Magariwada of Kushigata town, Higashi Ochiai of Kozai town declared the disease free area and in the next year, Shimo obino, and Hirase of Kofu city, Iino and Magariwada-Shinden of Shirane town, Kagami of Wakakusa town, Fujishiro of Sakaigawa town and Hitotsutani of Nirasaki followed.

The Society for the regional disease eradication was established in 1950 as described. In 1961, to facilitate the governmental support for the eradication program in different areas in Japan, nation wide committee for the control of schistosomiasis was established. This national committee for the control actively worked for getting financial support from the government. The increase of the number of areas where declaration of disease free finished greatly enhanced the control activity including advertisement car, seasonal campaign, and educational program for school children. The skin test was also useful for the detection of the patients.

Until 1971, significant improvement was observed in the endemic situation mainly due to two major changes. One is the constructive change in the agriculture and the modern technology of chemical nutrition and machines that replace the use of organic nutrition and animal labors. The other is Na PCP. Overall number of the active patients showed less than 1,000 and the percentage of the egg positive showed less than 1% in 1971. The infection rate of the dogs was 25.5% in 1957, decreased to 5.0% in 1962, and finally reached to 0% in 1971. The cattle infection stopped in 1964. The infection rate of the snails also decreased and the habitation got restricted.

#### **The 6<sup>th</sup> stage: Accomplishment of the control program, 1972-1985 (Year 47-60 of Showa Era).**

*The disease entered into the resolution stage when all of the endemicity markers got negative. In 1984, the epidemiological surveillance was performed and reported that the risk of new infection was extremely low. In 1985, all the project for the construction of concrete irrigation finished.*

Yurimin was known to be effective as molluscicide that was originally reported by Dr. Toshihiko Iijima of Institute of health and was used as a supplement of Na PCP in some area since 1968. In 1972, Na PCP was banned to use because of its toxicity in the water, so that Yurimin was the only one for the practical usage. Yurimin was prepared by the granular powder form so it was relatively easily to deliver to the field by using simple machine compared with automated spraying machine for Na PCP. On the other hand, there was a deviated distribution of the chemicals in the field. Also there were several reports of fish and rice damage. In 1975, Dr. Tokuaki Kajiwara confirmed the efficacy of B-2 (2,5-dichloro-4 bromophenol) and its safety to human and animals by performing the field trials. B-2 was adapted to be the major molluscicide since 1977. At first B-2 preparation was powder type and in 1981, the preparation was changed to 25% solution that can be applied to spraying machine. B-2 had been used until the end of the snail control operation in 1995 but there was no report of water pollution. After

the stop of Na PCP, the inhabitants noticed the effect of the replaced chemicals were not so much dramatic as Na PCP. Even after the extensive education of the new concept of the snail control that consider the natural protection and the safety of foods and human health, people did not fully understood why such a non-effective chemicals should be used. Moreover, the number of patients drastically decreased at that time, so they were not so much interested in devoting themselves more than before. In 1970, in Usui-Marsh of Tatomo-cho, the inflected snails were detected and, the snail control was done immediately after the detection. In 1971, there was no snails. In 1972, the infected snails were detected again and they confirmed the snail habitation area was located. The snails were infected with schistosome through the year at the average of 4.3% and 31.9 % of the captured a wild mice mainly composed of Hata-nezumi were infected. The inhabitants in the town made a request to the prefecture that the Usui-Marsh needed to be dried up and buried by the modification of river for the eradication of schistosomiasis. Usui-Marsh was famous for the place where the birds of passage rested during their moving. There was a big discussion between the inhabitants and the wild birds society on the conflict of disease control versus protection of nature. The discussion symbolized by the question "Human life or wild birds' ?" developed in the prefectural Parliament because the Governor proposed a prefectural plan to locate a big project in Usui-marsh that included commercial and residential quarters, and park. Finally, the construction and modification plan that was requested by Tatomi town was approved by the parliament in 1976. Now we can not see the previous landscape anymore.

In 1981 Mr. Masaru Minai at Prefectural Institute of Hygiene visited Leyte island in Philippines and established the biological method to detect the contaminated water by immersing the mouse for two hours per day for 3 days. He applied this method to the endemic area in Yamanashi. In 1982, he found the positive test in Tatsuoka town of Nirasaki city but there were no new patients, no infected snails and no infected wild rats, detected in the follow up investigation. Those two examples of Usui marsh and Tatsuoka of Nirasaki City

strongly suggested that schistosome life cycle had been maintained in some part of the prefecture even after no new infection reported during the years. During the period between 1972 and 85, the percentage of positive skin test and egg positives were constantly decreasing to reach less than 10%. In 1982, three persons (0.03%) were reported fecal egg positive and those were the final patients with new infection in Yamanashi. In 1989, national surveillance for schistosomiasis was performed and there was no infected patient, snails and animals detected although there were many skin test and ELISA positives as shown in the Table.

The results of the national survey in 1989.

| Test              | Tested Samples | Positives | %    |
|-------------------|----------------|-----------|------|
| ELISA             | 814            | 182       | 22.4 |
| Fecal examination | 182            | 0         | 0    |
| Skin test         | 5,389          | 873       | 16.2 |
| Past history      | 5,389          | 1,888     | 35.0 |
| Snail             | 57,155         | 0         | 0    |
| Wild mouse        | 120            | 0         | 0    |
| Immerging test    | 531            | 0         | 0    |

The surveillance committee made a conclusion that there is no possible epidemic in future in the previous endemic area in Yamanashi, however, to maintain this situation and to eradicate the disease, the prefecture should maintain their efforts to completely eliminate the snails and to survey the infection. The construction of concrete irrigation that had been processed since 1950 completed all the program after the final project of maintenance of the damaged irrigation in 1985. After the national survey in 1989, the prefecture decided to maintain the activities for the surveillance even after there was no new active infection.

**The seventh stage: Surveillance and the declaration of disease free, 1986-2000 (Year 61 of Showa Era – 12 of Heisei Era).**

*We continued the control program especially focusing on the surveillance during this period even after all the epidemic markers showed negative. After the declaration of disease free in February 1996, the surveillance was maintained*

for more 5 years.

Because it was possible to remain some life cycles in the prefecture, the control project was maintained until 1995, 13 years after the final case report. Since 1981, the patient's detection was performed by 3 step examinations including Skin test, ELISA and fecal examination, and since 1984, skin test was eliminated. Table shows the summary of the results during this period.

| Examination     | 1986-90      | %    | 1991- 95  | %   |
|-----------------|--------------|------|-----------|-----|
| Fecal exam      | 0/1,544      | 0    | 0/135     | 0   |
| ELISA adults    | 2,616/19,739 | 13.3 | 254/6,232 | 4.1 |
| School child    | 0/1,702      | 0    | 0/5,170   | 0   |
| Infected snails | 0/283,412    | 0    | 0/154,152 | 0   |
| Immersion test  | 0/3,124      | 0    | 0/778     | 0   |
| Wild rats       | 0/90         | 0    | 0/30      | 0   |

|   | 1996 | 1997 | 1998 | 1999 | 2000 |
|---|------|------|------|------|------|
| ELISA   | 0 %  | 0    | 0    | 0    | 0    |
| snails  | 0 %  | 0    | 0    | 0    | 0    |
| immersion   | 0 %  | 0    | 0    | 0    | 0    |
| Density snails/<br>25cm <sup>2</sup> × 25 in<br>120 different place | 13.3 | 8.2  | 9.1  | 10.4 | 20.5 |

The seropositive persons were all above the age 41 years old and the test for school children in 1991 showed all negative indicating there was no new infection since 1982. In March 1995, the Governor asked to make a special committee named the regional diseases eradication promotion committee to give him suggestions for the direction of future policy of the control program after the result of 10 years' surveillance that there had been no new infection for ten years. The committee reviewed all the accumulated data for ten years and finally proposed the following suggestions.

1. The schistosomiasis has already been eradicated in Yamanashi prefecture.
2. The control program has already reached its final goal and is not necessary to continue.

3. Some new surveillance mechanisms are necessary for the safeguard against re-emergence of the disease due to the maintained snail habitation.

In February 1996, after getting the suggestions from the committee, the Governor Takeshi Amano officially declared that the regional disease (schistosomiasis Japonica) in Yamanashi prefecture was eradicated. The suggestions contained the necessity to keep the surveillance even after the declaration. The Governor made a new surveillance project for 5 years including the town meeting for the explanation of the present policy of control project and the continuation of surveillance. Snail surveillance was performed by two different methods, one is the classical examination of the snails that were collected and processed to the town and the prefectural institute of health by the farmers and the surveillance officers, the other was the sentinel surveillance system that 120 different places in the rice field area along the Kamanashi River were determined to monitor the snail habitation. The sentinel surveillance had been continued since 1996 to 2000. During the surveillance period, total number of the snails within 25x25cm square of two points in the sentinel rice field was counted (Table). The results of the surveillance were all negative as shown in the table. The density of the snail habitation in the sentinel surveillance increased after the termination of the snail control (Table). Along the snail surveillance, the social conceptional study, the tissue deposited eggs examination survey, and the chronic schistosomiasis survey were performed by the suggestion of the regional disease surveillance program committee (Chairman: Toshihiko Iijima, Professor of Kyorin University, Members; Yutaka Inaba, Professor of Juntendo University, Tsuyoshi Kurata, Vice Director of National Institute of Infectious Diseases, Moriyasu Tsuji, Professor of Kyorin University, Yasuo Nakajima, Professor of Yamanashi Medical University, Yukio Hosaka, Visiting Professor of Tokyo Medical and Dental University, Kiyoshi Makita, Associate Professor of Sangyo Medical college and Hiroshi Yokoyama, ex-President of Prefectural Central Hospital). The detailed study on the inhabitants concept on the disease was performed by the prefectural health promotion

office (Head: Masahiro Kaminota, Officers: Masahiro Okubo, Shigeo Watanabe) showed that 88% of the examinee expressed their emotional fear to the disease and 43% their anxiety to become endemic again even after the effective medicine (Prasiquantel) was available. Even now (2003), the inhabitants still remember the evil disease. Thirty three % of the examinee wanted to continue the snail surveillance, 43% agreed to reduce the size of the control, and 12% agreed to stop the surveillance (See the statistics section of this volume). Surveillance of the tissue deposited eggs showed 139 positive cases (0.56%) out of 24,950 examinations during 5 years. The detected eggs were all dead and only from older generation over 54 years old in 1996. Finally, 292 hospitals and clinics in Kuninaka district were surveyed for new patients and the result was negative.

On the 15<sup>th</sup> of February 1996, the regional disease surveillance program committee processed the report saying that,

1. It is not necessary to continue the surveillance activity by the medical stand point of view. However, since the inhabitants are still anxious about the possible epidemic, the public sector should consider the continuation of the examination of the possible origin of the re-emerging of the disease.
2. To solve the anxiety of the inhabitants,

educational programs on schistosomiasis should be continuously performed.

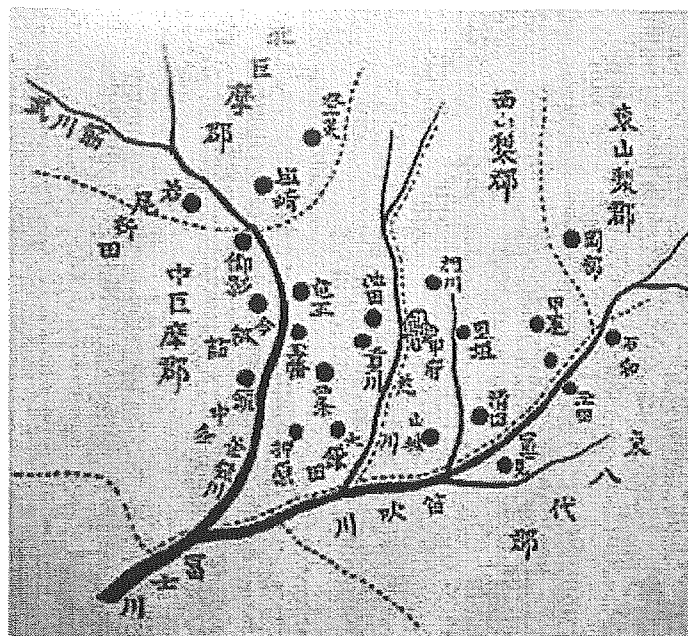
宣  
言

山梨県知事 大野 建

平成八年二月十九日

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## Chapter 2. The collected materials that tell the myth



The map of Kofu basin, endemic area of schistosomiasis around 1904 (I. Tsuchiya, K. Tohyama, Yokyo .Med. Ass. J. 9 (3), 1904

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| 1. Until the finding of pathogen          | 38 |
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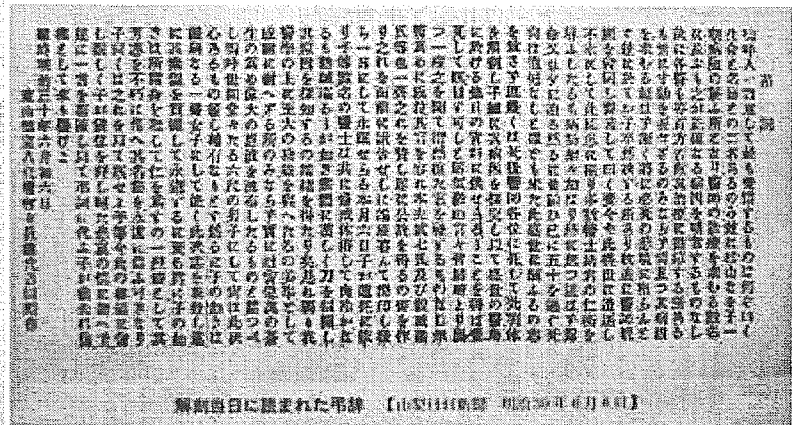
## 2. Contribution of Naka Sugiyama

Before the findings of schistosoma in 1904, a lady farmer, Naka Sugiyama, who died with schistosomiasis voluntarily donated her body for autopsy in 1897

Requirement for autopsy described by Naka Sugiyama on May 30, 1897



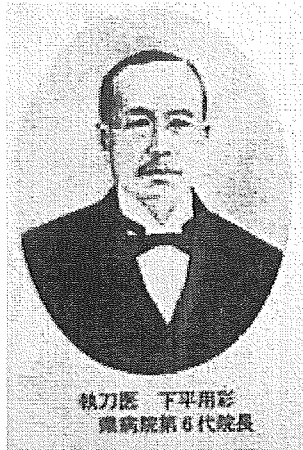
Junsaku Yoshioka (1868 - 1955) A physician who took care of Naka Sugiyama and was asked to perform autopsy by her. He helped to build the memorial monument of Naka for her good will.



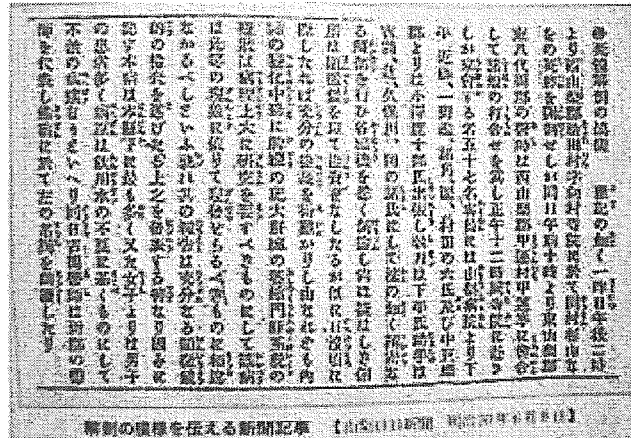
The statement dedicated for her qutopsy published in the local news paper. (Yamanashi Daily News, 1897)

## The contribution of Naka Sugiyama - 2 -

Naka's autopsy was performed on the next day of her death, in Seigan-ji temple related to sugiyama family.



Dr. Yosai Shimohira performed the autopsy.



The news report of autopsy.

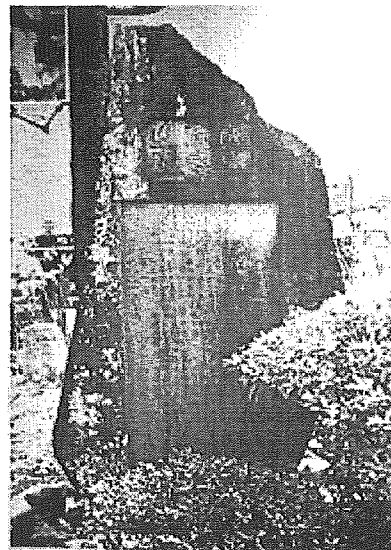


On the right side of the monument, Naka's daughters were standing at the opening ceremony.

The memorial monument established in 1911 in the yard of Seigan-ji Temple that was donated by Medical Association of Higashi-Yamashiro county, Yamanashi.



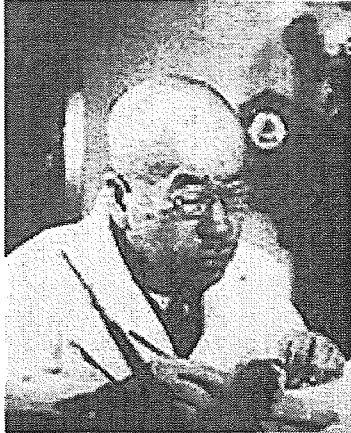
Grave stone of Mr and Mrs Naka Sugiyama.



The memorial monument for Naka Sugiyama was built in 1911, 15 years after the autopsy.

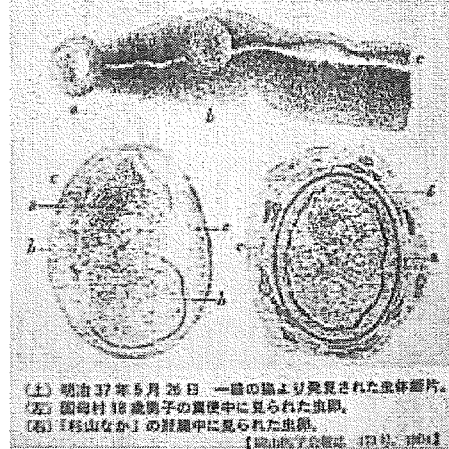
### 3. Finding of Schistosoma.

In 1904, Prof. Fujiro Katsurada found a novel helminth '*Shisotosoma japonicum*' from a cat liver with Dr. Saburo Mikami who was a general physician in Ohkamata Village (Kofu city at present).



Professor Fujiro Katsurada (1867 - 1946)

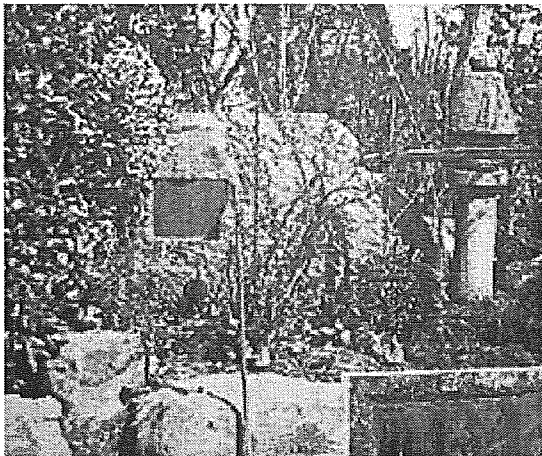
In 1904, He found *S. japonicum* and in 1911 he showed the skin penetration of cercaria using dogs.



Upper: the head of the worm.

Lower left: Eggs from the feces of 18 years old boy in Kokubo Village.

Lower right: The egg found in the liver of Naka Sugiyama.



The memorial monument for the finding of schistosome on July 30, 1904, in the garden of Mikami clinic in Kofu.



Dr. Saburo Mikami (1873 - 1958) He helped Prof. Kasturada. He showed that stibunal was effective by clinical trails in 1922.



The house where prof. Kasturada Stayed search for schistosome located inside Mikami clinic in Kofu, Yamanashi. (Taken kn 1972)