

CONTROL OF CLONORCHIASIS IN KOREA

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I. INTRODUCTION

The liver fluke infections in man represent one of the major clinical and public health problems in widespread areas of the world. *Clonorchis sinensis* is an important human parasite and is widely distributed in Korea, China, Formosa, Japan and other parts of Asia. Stoll¹⁾ estimated the number of *Clonorchis* carriers at approximately 19 millions in 1947. In southern Korea alone more than 2 millions people are infected.

The traditional application of night-soil to vegetable gardens results in a most widespread condition of parasitism, with a variety of helminths found in Korea. In addition to the above fact, the peculiar habit of the consumption of raw vegetables, fish, crustaceans and mammals provides a mean of lifestations of helminths.

Extensive studies of clonorchiasis during the last sixty years in Japan, Korea, China and other countries have emphasized the difficulties of treatment and prophylaxis. We can expect from their investigation on the life cycle and epidemiology of this parasite, which will lay the foundations for

its successful control. However, compared to many other infectious diseases, little overall progress has been achieved in the control of clonorchiasis. This lack of accomplishment may be attributed to a number of factors. Among them are lack of basic data on the occurrence and importance of the disease, lack of more efficient control procedures, failure to develop better chemotherapeutics, insignificant progress in providing sanitary facilities, inattention to proper water management in irrigated areas, insufficient funds and the dearth of adequately trained personnel.

Recently in Japan²⁾, the incidence of infection decreased markedly, it is thought to have responsible for this reduction by water pollution from factories, and by insecticides, and by land development with drainage of swamps as well as public health education. Therefore, it may now be possible to control this disease.

II. EPIDEMIOLOGY

1) Distribution and prevalence of clonorchiasis

The geographical distribution of clonor-

Table 1. The prevalence rates of clonorchiasis in Korea

Authors	Year	Method of Exam.	No. of. Exam.	No. of. Posit.	% of Posit.
Ministry of Health	1958	Stool examination	14,519	1,701	11.7%
Watten and Chyu	1959	Intradermal test	9,771	2,066	21.1%
Korea Red Cross	1965-1967	Intradermal test	152,487	19,820	13.0%
Ministry of Health	1966-1967	Intradermal test	84,982	9,469	11.1%
Seo et al	1967-1968	Stool examination	40,581	1,907	4.7%
Seo et al	1968	Stool examination	3,880	450	11.6%

Table 2. The prevalence rates of clonorchiasis in the main five rivers (by intradermal test)

Name of river	School children			School teachers		
	No. of exam.	No. of posit.	% of posit.	No. of exam.	No. of posit.	% of posit.
Han River	41,779	2,489	6.0%	1,372	296	21.6%
Kum River	16,252	912	5.6%	502	39	7.8%
Youngsan River	20,506	2,541	12.4%	640	331	51.7%
Mankyong River	27,482	1,605	5.8%	1,116	254	22.8%
Naktong River	41,792	10,792	25.8%	1,046	557	53.3%
Total	147,811	18,343	12.4%	4,676	1,477	31.6%

chiasis closely parallels the distribution of the intermediate host, particularly snail host, known as *Parafossarulus manchouricus*. *P. manchouricus* is widely distributed but is confined in southern parts from Seoul.

During the last fifty years numerous reports were found on the prevalence of clonorchiasis among the Korean population in different parts of the country. Recently as part of an overall stool examination of 14,519 inhabitants, of which 1,701 (11.7%) were found to be infected. (Table 1) Other investigations by the intradermal test where performed the prevalence rate of clonorchiasis are shown 11.1 per cent to 21.1 per cent in the Koreans. However by Author's investigation³⁰, the positive rate out of 40,581 persons (mostly school children) examined the stool by the cellophane thick smear method revealed 4.7 per cent. On the other hand, out of 3,880 adults, 450 (11.6%) po-

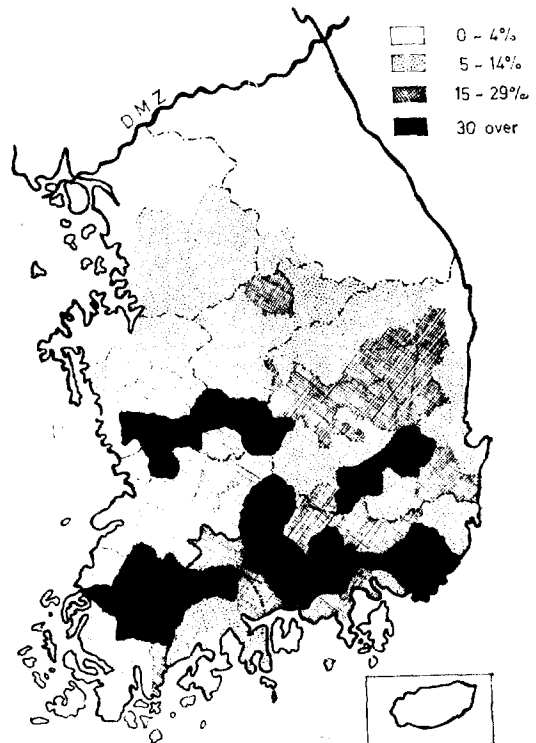
**Fig. 1.** Distribution of Clonorchiasis in Korea (by intradermal test).

Table 3. Mean EPG of *C. sinensis* infection by age and sex at Kim-Hae Gun.
(by Stoll egg counting method)

Age group	Male		Female		Total	
	No. of person	Mean EPG	No. of person	Mean EPG	No. of person	Mean EPG
0-9	22	3,377	13	3,692	35	3,494
10-19	40	8,682	37	11,184	77	9,884
20-29	19	7,247	22	6,923	41	7,074
30-39	22	15,866	25	11,200	47	14,235
40-49	18	17,450	24	11,217	42	13,880
50-59	21	15,154	13	16,339	34	15,507
60-69	4	29,175	4	1,275	8	15,225
Total	146	11,352	138	10,006	284	10,698

sitive cases are found also by cellophane thick smear method. According to the surveys by Korean Red Cross (1965-1967), the intradermal tests were performed on the primary school children and school teachers inhabiting along the drainage areas of the main five rivers in southern Korea (Han, Naktong, Kum, Yeongsan and Mankyong Rivers). Out of 147,811 school children examined, 18,343 (12.4%) were found positive with range from 5.6 per cent (Kum River basin) to 25.8 per cent (Naktong River basin). On the other hand, out of 4,676 school teachers examined, 1,477 (31.6%) were found positive with range from 7.8 per cent to 53.3 per cent. (Table 2) Thus school teachers (adults) are far more frequently infected than school children. Another nationwide survey has also been conducted by the local health centers under the project of Ministry of Health, during the period between 1966 and 1967. According to the results of this survey, among 84,982 inhabitants of 102 different cities and counties examined, 9,469 (11.1%) were found positive with *Clonorchis* antigen. With this results overall distribution of clonorchiasis is shown in Fig. 1.

From the above surveys, it turned out that endemic areas of clonorchiasis are scattered all over the country and the most extensive and intensive endemic regions are found mainly along the Naktong River and lower reaches of other rivers. On the lower reaches and in the delta of the Naktong River near Busan the most southeastern part of Korea, the prevalence rate is 69.0 per cent²⁾. In the highly endemic area, there is no significant difference among the incidence of *Clonorchis* infection by sex and age. However, in the other endemic areas approximately two times more men are infected than the woman, and adults are far more frequently infected than children. The average number of eggs per gram of feces (EPG) was 10,698 among 284 cases of inhabitants at Kim-Hae where is the most heavy endemic areas in the delta of the Naktong River. The mean EPG count of *Clonorchis* infection in this area was found higher among the higher age group. (Table 3)

2) Modes of human infection

The *Clonorchis* infection into the human being is established by Saking orally the

mature metacercaria with raw fish. The mature metacercaria in fresh water fish excysts in the upper part of the small intestine of the host, migrates into the bile duct and gall bladder 15 to 24 hours after liberation and develops into the adult after 23 to 25 days⁵⁾.

Clonorchis infection is, however, influenced by the social factor. From the older times, Koreans have had peculiar habit eating raw fish which is mainly served at drinking parties with rice wine. This is the main source of human infection. Therefore in the endemic areas, more men are infected than the women. The incidence in childhood is slight, but from 15 years of age to older age the incidence increases in amount, being highest at the age of 30 to 50 years.

Approximately 30 species of fresh water fish were found to serve as intermediate hosts. They belong to the family CYPRI-
NIDAE. Among 13 species of fresh water fish collected in Naktong River, *Pseudorasbora parva*, *Acanthorhodeus asmusi*, *Gnathopogon majimai*, *Sarcocheilichthys wakiyae*, *Pseudorasbora parva* and *Puntungia herzi* are the most heavily infected groups. 53.9 per cent of the small fish, *P. parva*, collected at Young-Chun (Middle reaches of Naktong River) are found infected⁶⁾ however the same fish collected at Kim-Hae (the lower reaches of same river), which is a more highly endemic area than the above are infected 100 per cent⁷⁾. The large fish, *Cyprinus carpio*, which frequently is eaten by the inhabitants in endemic areas is really low in the rate of infestation. It is an epidemicologically significant that in endemic foci most cases are caused by accumulated light infestations due to fre-

quent exposures for several years.

Infection has also been reported in pigs, rats and various species of fish eating mammals, but none of these hosts have been incriminated as playing a major role in the epidemiology of the disease. Japanese workers²⁾ have also indicated whether man can be infected by drinking water from a stream contaminated by the infected flesh of dead fish. Perhaps infection may take place occasionally in that way, but it has not been proved to occur under field conditions. However, another possible mode of human infection is an accidental transfer of the encysted metacercariae to the mouth through the handling of fish while preparing them as food.

III. PATHOGENESIS AND CLINICAL MANIFESTATIONS

Clonorchis sinensis infests chiefly in the bile ducts of the liver and the pathological changes soon appear when a large number of worms infest, and they may very gradually or may not appear when a small number of worms infest. The changes are progressive and their total effect on the function of the liver depends on the number of worms present from a single infection or from continuous reinfection over a period of years, as well as the length of the infection⁸⁾.

Clinical manifestation in human infections seemed to increase in severity progressively as the infection become older and as the flukes were gradually acquired. The earliest indications of illness were usually general malaise, abdominal discomfort and occasional diarrhea. These were sometimes followed by pain at the site of

the liver, transient urticaria and jaundice. Jaundice frequently appear in severe cases. The jaundice in clonorchiasis was caused by obstruction of intrahepatic biliary trees by worms or inflammatory changes and stated that it was necessary for the stagnation of bile to have a big number of parasite and mechanical disturbances of the intrahepatic biliary trees were chiefly attributable for genesis of jaundice, though the common bile duct and the head of pancreas might be somewhat responsible⁹⁾.

As the complications of clonorchiasis, the occurrence of gall-stone is caused by bile stagnation due to the mechanical obstruction and pressure of worms and ova to be nuclei for gall-stone. And cholangitis and cholecystitis are caused by bacillary infection during the obstructive disturbances of bile ducts. Liver cirrhosis and carcinoma of the bile ducts were often observed. It has been regarded that tumor may be induced not only from the chemical stimulation due to toxic secretes or toxic metabolic products from parasites, but from the physical stimulation due to mechanical injuries⁹⁾.

IV. CONTROL

1) Relation of *Clonorchis* life cycle to the prevention of clonorchiasis in man

Reduction of transmission should be the objective of a clonorchiasis control programme. There are four definitive places in the life cycle of *Clonorchis* where preventive measures may be instituted. They are the eggs, the snail, the fish and the chemotherapy of human phase of the infection.

a) Sterilization of feces

In order to secure efficient results in sterilizing the feces for *Clonorchis* ova in the endemic areas a modification of the present method of night-soil disposal would have to be effected. Some technique of feces disposal or utilization are effective in controlling the parasites. The disposal of night-soil is a real big problem for the control of clonorchiasis as well as soil-transmitted helminthic infections. In this connection, it has been recommended that night-soil before being used should be treated in compost pits, particularly in areas where night-soil is used as fertilizer for vegetable crops. However, there are many practical difficulties to be efficient.

The solution may rest in contribution of privies in such manner as to obviate dissemination of ova through overflow, drainage, or similar circumstances and in adequate treatment or storage of night-soil before use as fertilizer. There are generally three methods of night-soil disposal which are direct disposal, conservation and sewerage methods. Obviously the choice must be made in accordance with local custom, level of education and local economy.

On the other hand, the effect of chemicals on night-soil is complicated by the fact that this material is undergoing active decomposition, and complex mixture of organic substances present may reduce the effectiveness of the chemicals applied. Human urine will kill eggs when its urea concentration is more than 1 gram per 100 cu. cm. When protein is added to a mixture of feces and urine, decomposition of the eggs is hastened. Mixing ammonium nitrate with feces without urine, at a con-

centration of 1kg per cubic meter of feces, killed all the eggs in three days. Sodium nitrate¹⁰⁾ has a marked ovicidal effect within 24 hours at 28°C when mixed with nightsoil at a concentration of 1 : 2,000.

b) Available methods of snail control

The destruction of snail is regarded to be one of the best measures for the control of trematode diseases. *P. manchouricus* is commonly found in the muck at the shores of ponds and stagnant irrigation channels. The snails are markedly more abundant in waters containing a rich growth of suitable species of water plants; but such vegetation is not an essential feature of the habitat. Effective reduction or elimination of this snail population depends upon alternation of conditions in the habitat in such a way as to render it inimical to the molluscs, either by changing the original environment or by introducing molluscicides.

Some knowledge of the ecological requirements of snail is needed to achieve the habitat modifications necessary to render a locality unacceptable to them. In natural habitats the most effective measure against snail is drainage, where this is not possible, alternative measures such as weed clearance, straightening of banks, deepening of marginal areas and prevention of sewage pollution all contribute to the reductions of snail from its habitats.

In artificial habitats water management is a valuable asset, for rapid fluctuations in water level and flow rate have a disturbing influence on snails¹¹⁾. Irrigation systems and reservoirs should be designed so that such operations can be performed without difficulty and the control of aquatic weeds can be easily accomplished. Thus

several environmental control measures applicable to snails may have a profound influence on the control of mosquitoes. Moreover, such measures frequently coincide with those needed for modern agricultural practice. Water conservation and disposal, land reclamation and the proper management of fields and farms require, in many respects, the same kind of treatment of flowing and standing water and waterlogged soil as does snail control when carried out by radical measures. However it is only after careful study of all factors concerned that a rational decision can be made.

On the other hand, copper sulfate and pentachlorophenate have been effectively used as molluscicides. The selection of the most suitable method depends on a number of factors, including the nature of the snail habitat the type and accessibility of the body of water, the amount of labor available and cost considerations.

c) Sterilization of the fish by heat

Most of all fresh-water fish in Korea are to be regarded as possible carriers of the metacercaria of *Clonorchis*. The danger of human infection arises from the consumption of raw fish or insufficiently cooked fish. Most of the cases of human clonorchiasis in Korea result from the ingestion of the raw flesh-water fish. A practical solution of the problem of clonorchiasis in Korea might be brought about by preventing the use of infected fish. The destruction of fresh-water fish in highly endemic areas by engineering or biological control and the prohibiting of fishing in these areas cannot be recommended, since fresh-water fish represents the main source

of animal protein and is of great health and economic value. It seems, therefore, that the only effective measures should be directed toward the prevention of eating raw fish. This should be accomplished by a combination of legislative measures and health education.

d) Chemotherapy

Therapeutic prophylaxis in cases of clonorchiasis is still of doubtful value. Many earlier investigators have studied the treatment of clonorchiasis with antimony preparations, gentian violet, emetine hydrochloride, chloroquine diphosphate, bithionol and dithiazanine iodide etc. However, clinical improvement and negative or reduced egg counts were temporarily noted but the permanent results were questionable.

In recent years, however, much work has been done in Japan, Korea and China in the search for more satisfactory remedies for the treatment of clonorchiasis. Japanese worker (Yokogawa et al, 1965)^{12, 13} have shown that 1,4-bis-trichloromethylbenzol ("Hetol" Hoechst AG) has exhibited an excellent therapeutic effect in the animals experimentally infected with *Clonorchis sinensis* and in the cases of human clonorchiasis.

Since 1965 extensive investigations of Hetol on human clonorchiasis and opisthorchiasis have been strongly suggested that the drug is highly promising as the therapeutic agent. However, Hoechst A.G., the maker of Hetol, stopped its production because in chronic toxicity test using even 60 mg/kg for 30 consecutive days on dogs, it caused remarkable hypochromic anemia by the end of the study.

Recently by the Author^{14, 15, 16}, three drugs which are Hetol, Dehydroemetine late re-

lease tablet (Ro-1-9334/20) and Bilevon (Bayer 9015, niclofolan) have been used in the treatment of clonorchiasis. The therapeutic effect of Hetol in various dosages and duration of medication was observed in the 52 clinical cases with different degree of infection. In the result, a dosage of 50mg per kg daily for 5 to 12 medication days depend on the severity of infection appears to be safe and appropriate for the treatment of clonorchiasis. About 40 clonorchiasis patients were treated with Dehydroemetine late release tablet. High effectiveness was showing at the dose of 2.5 mg/kg every other day for 25 to 30 days. On the other hand, 35 adult patients were treated with Bilevon. In the result, the drug administered orally at the dose 1.0 to 2.0 mg/kg body weight for two or three days was highly effective for clonorchiasis.

During after treatment, most patients showed marked improvement usually with disappearance of upper abdominal pain, fatigue and recovery of appetite. Also in the cases previously affected liver, much improvement of their liver function test showed after treatment with Bilevon. Therefore, the possibility that human clonorchiasis could be successfully treated with two doses of Bilevon can be presumed from this study. Bilevon is a very promising drug for mass treatment against *Clonorchis sinensis* infection. However much further work is needed before mass treatment of this disease over large areas can be advocated.

2) Health education

A practical solution of the problem of the prevention of *Clonorchis* infection might be brought about careful educational propaganda whereby the enlightened element

of the population would be made aware of the cause of the infection and urged to put into practice the simple rule that needs be observed to prevent human infection, namely, sterilization of the fish by heat.

It was agreed that health education on clonorchiasis should not be treated as a separate subject but should be included with the general programme of health education¹⁷.

There are four aims of health education:

(a) It supplies a person with enough general knowledge about a disease to make the preventive measures.

(b) It makes a person feel sufficiently about the importance of his own health to make him alter his behavior and adopt these preventive measure.

(c) It makes him to be concerned for the health others.

(d) It tries to make him feel so strongly about the first three that he supports and even initiates preventive action by the community.

Health education is a many sided endeavour of such importance that it must be furthered by every possible means such as school, newspapers, radio and televisions. Governmental control is usually difficult to enforce since the people are jealous of their personal liberties and regard with suspicion and distrust persons outside their immediate community.

The consumption of raw fish in the homes could not be regulated by law, but if the leaders of the rural population, such as village leader, church pastors, school teachers and government employees or health workers, were instructed as to the dangers of consuming raw fish, a sympa-

thetic reaction in the general population could be expected. A careful educational program among the better educated members of the community to acquaint the people with the dangers of *Clonorchis* infection from eating raw fish should contribute a great deal toward the solution of the problem.

Educational efforts should be directed primarily toward school children because it is during the early years that most persons become infected, and also because children are less entrenched in their food habits, so that the educational process should be involved at various levels in successive changes of knowledge, attitude, behaviour, habit and custom of their lives.

V. DISCUSSION

The control of *Clonorchis* infection described above is theoretically very simple, as the infection can only invade the human body by way of encysted metacercaria which are taken into the body when eating passive intermediate host (fish). By contrast, it is far more difficult to take prophylactic measures in the case of other worms infections, in which the infective larvae enter the body either by way of active intermediate hosts (e. g. mosquito... filariasis) or by way of larvae which bore into the skin (e. g. cercaria in schistosomiasis or invading larvae in hookworm disease).

Although prophylactic measures in the case of the infection dealt with above merely consist in cooking or submerging the fish in hot water before eating them, it is exceedingly difficult to carry out such simple measures in face of century old tra-

ditions, to which the relatively primitive population clings with great tenacity.

The measures to prevent stools containing viable eggs from reaching bodies of water containing the snail intermediate hosts would apply only to the human population since water pollution by cat and dogs could not be controlled. Such a method alone would not be sufficient to bring about tangible benefits as a method of controlling clonorchiasis. The extermination of the snail by engineering or chemical measures could be much too expensive to be practical, because the snail is spread over a very large area in Korea. Although medicinal therapeutics leave much to be desired from a medical point of view, treatment of clonorchiasis is still in the experimental stage and the treatment itself is a complicated and difficult procedure. The mass treatment as a control measure is not at present a practical procedure.

There is not one universally applicable method of control. The choice of methods must be dictated by the nature of the environment, the habit and custom of the people, the pattern of transmission and the resources of the country.

Clonorchiasis control is fundamentally an enterprise directed at the reducing or eliminating transmission of the disease, so that no more new infections, reinfections or superinfections occur. There must exist a well organized public health infrastructure. Since a clonorchiasis control programme is of necessity on a long-term basis and continuity in its implementation is essential. The clonorchiasis control service should be established as a permanent agency of the health department.

From the biological standpoint, further

search for the intermediate hosts and their biology is necessary to determine whether a time and place exist at which they could be attacked most successfully. The present lack of cheap and effective antihelmintics, and the existence of animal host reservoirs prevent the applicability of control measures directed against the adult parasites.

In conclusion, the control of clonorchiasis in Korea is not an impossible task. A combination of efforts with major emphasis placed on the consumption of infected raw fish, by educational propaganda coupled with governmental aid in enforcing legislative public health measures could reduce the disease.

VI. CONCLUSION

Clonorchiasis is the most important endemic diseases in Korea, and this disease has been known to be of public health concern in many areas of southern part of Korea.

In view of the fact that, to succeed, a lasting control programme could need to involve as little expense as possible with no greater changes in the habits of the population than necessary, it seems that the only effective measures should be directed towards the prevention of eating raw fish. This could be accomplished by a combining of legislative measures and health education. The success of such a program would thus rest upon the cooperation of the people with the health officials and the government.

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