

**PROCEEDINGS
OF
THE PHILIPPINE - JAPAN JOINT CONFERENCE
ON
SCHISTOSOMIASIS RESEARCH AND CONTROL**

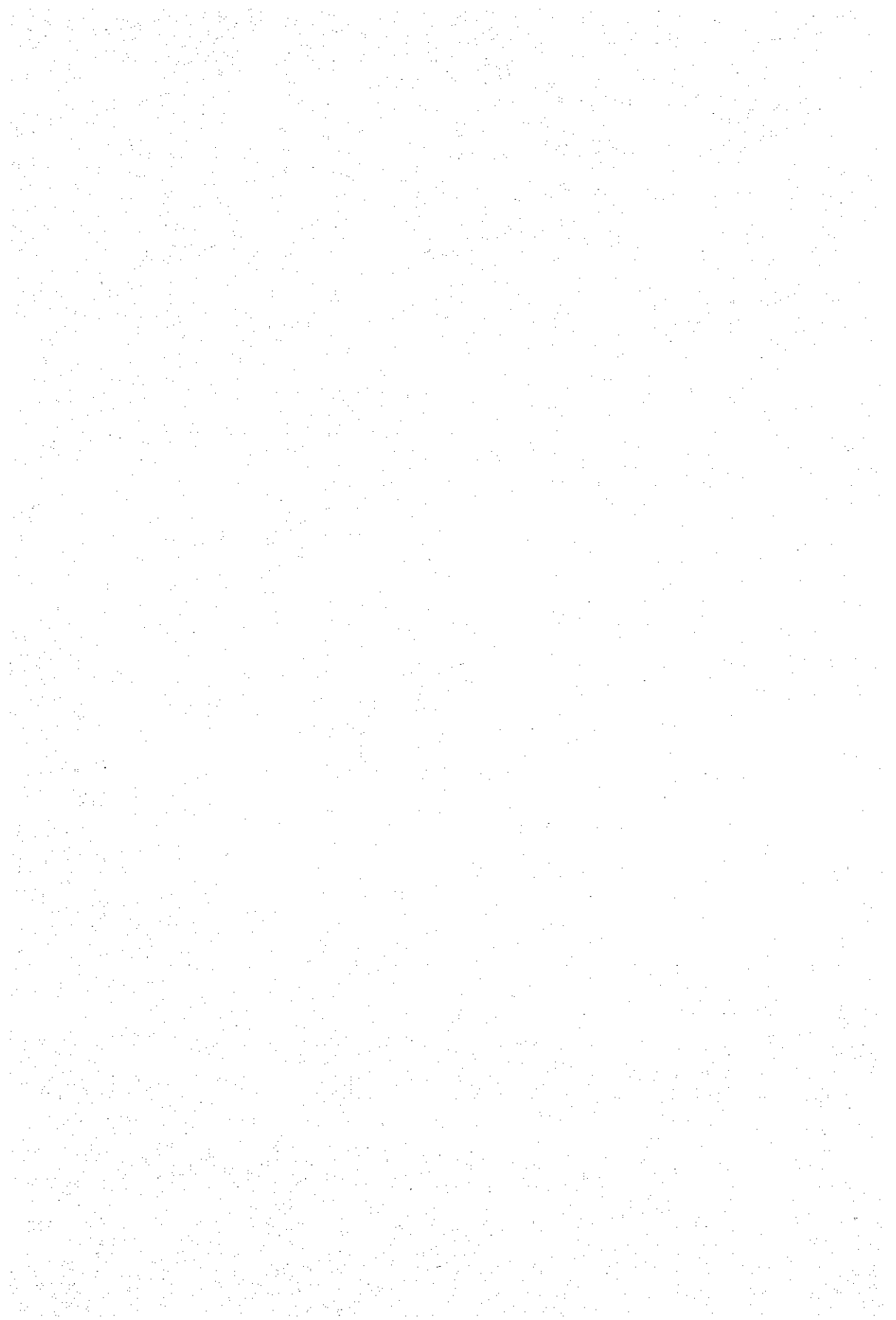
20th - 23rd November, 1979

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The Joint Organizing Committee of the Conference**

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SCHISTOSOMIASIS CONTROL AND RESEARCH SERVICE
MINISTRY OF HEALTH, REPUBLIC OF THE PHILIPPINES

San Lazaro Compound, Manila, Philippines

PREFACE

The Japan International Cooperation Agency (JICA) has been extending medical cooperation on the Schistosomiasis Research and Control Project to the Government of the Republic of the Philippines since 1972.

Prior to the termination of the medical cooperation on this Project, it was proposed that Philippine-Japan Joint Conference on Schistosomiasis Research and Control would be held in Manila, Philippines, from 20 to 23, November, 1979, in order to figure out a methodology applicable to the schistosomiasis control, as well as to promote the spread of the latest technology of the control.

The Conference was successfully completed, with the attendance of more than 100 researchers and health personnel.

As a result of the above Conference, this monograph has been compiled and published. I hope that this monograph would contribute to the advancement of the welfare of the people and to the promotion of friendly relations between our two countries.

February, 1980



Keisuke Arita

President

Japan International Cooperation Agency

FOREWORD

The Philippine-Japan Joint Conference on Schistosomiasis Research and Control was organized by the Schistosomiasis Control and Research Service, Ministry of Health, the Schistosomiasis Control Council, Republic of the Philippines and the Japan International Cooperation Agency and held on 20th to 23rd November, 1979 at the Leyte/Samar Conference Rooms, Philippine Plaza, Manila.

The conference was planned by the joint organizing committee to collect, summarize and review the recent results of researches on schistosomiasis including recently developed methodology for the implementation of the schistosomiasis control in the Philippines which were brought about not only by the Philippine-Japan Collaborative Research Program, but also by researches of other institutions and organizations in the Philippines and foreign countries and those of the World Health Organization.

Researchers and concerned officials in the Philippines and Japan as well as from other countries and international organizations were invited to this conference to discuss various aspects along the objectives mentioned above.

During the first two days of scientific sessions, 37 papers were presented and discussed and on the following two days, the participants were divided into four working groups, with each group assigned to one of four topics, i.e., diagnostic method, chemotherapy, snail ecology and molluscicide, and epidemiology and control, to summarize, discuss and prepare reports on the important subjects for the research and control of schistosomiasis which will serve as guideline for future planning of schistosomiasis control in the Philippines.

The conference was also intended to provide an opportunity for sharing the updated knowledge on the research and control of schistosomiasis with all participants.

In accordance with the purposes of the conference, the reports of the working group meetings are presented as the principal part of this monographic proceedings and the abstracts of individual scientific presentations are attached as annexes after the principal report, together with descriptions of discussions after each presentation.

The joint organizing committee hopes that whatever knowledge obtained from this conference may reach all those who are interested in schistosomiasis research and control.

February, 1980

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Dr. Alfredo T. Santos, Jr.
Dr. Ernesto J. Zerrudo
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PHILIPPINE-JAPAN JOINT CONFERENCE
ON SCHISTOSOMIASIS RESEARCH AND CONTROL

WELCOME ADDRESS

Dr. Alfredo T. Santos, Jr.

*Executive Director, Schistosomiasis Control and Research Service,
Ministry of Health, Philippines*

The Honorable, the Deputy Minister of Health, Dr. Jesus Azurin
Dr. Yoshio Hirose, representing His Excellency, the Japanese Ambassador to the Philippines
The Deputy Director, Medical Cooperation Department, JICA, Dr. Masaharu Ito
Guests and fellow participants in this Conference

In behalf of the Joint Organizing Committee, it is my great privilege and honor to welcome you to this Philippine-Japan Joint Conference on Schistosomiasis Research and Control.

Schistosomiasis is one of the major public health problems not only in the Philippines but also in other parts of the world where it is endemic. The problem is multifaceted in view of the complexity of the approach for its control requiring skills and resources of various disciplines, such as the engineer, agriculturist, social scientist, the public health physician, etc.

In recognition of this and the role of the schistosomiasis problem as a deterrent to agricultural development, His Excellency, the President, Ferdinand E. Marcos directed that expertise of scientists from Japan, one of the few countries that has successfully controlled schistosomiasis, be tapped in the research and control efforts of the country. Thus, this Philippine-Japan technical cooperation program came about in 1972.

The convening of this RP-Japan Joint Conference on Schistosomiasis at this stage offers us the opportunity to pause and assess the progress of our accomplishments during the past years. We are indeed honored by the presence of local and international experts whose contributions to the control and research efforts are undeniably significant. We are confident that this Conference will bring us not only the wealth of knowledge on what has been done but also serve as a spring board to enhance further advances that would lead to the control of schistosomiasis.

On this note of optimism and enthusiasm, let me reiterate our warm welcome to our distinguished guests and participants. I thank you.

OPENING ADDRESS

Dr. Jiro Yamamoto
Director, Medical Cooperation Department
Japan International Cooperation Agency

Excellencies, Ladies and Gentlemen

It is a great honour for me to make a congratulatory address on behalf of the Japan International Cooperation Agency, at this opening ceremony of the Philippine-Japan Joint Conference on Schistosomiasis Research and Control.

The Conference is intended to figure out a methodology applicable to the schistosomiasis control, by summarizing and evaluating the performance of the schistosomiasis research and control project which has been jointly carried out by the two countries since 1972.

It is expected that the knowledge and experience obtained through the implementation of the project will be brought to the attention of the participants of the Conference, and will be fully discussed from various angles, for the purpose of establishing an appropriate technology to be applied to its control.

The achievement of the Conference will also be supplied and made available to the countries confronted with the same problem, for their benefits.

I am confident that the result of the Conference will contribute greatly not only to the development of measures for control of this parasitic disease, but also to further improvement of health conditions of the community people.

As you may be aware of, the Japan International Cooperation Agency has been undertaking 30 health and medical cooperation projects in 22 developing countries aimed at the advancement of welfare in those countries.

Requests for our cooperation from the developing countries have been increasing in their number, and have been becoming larger in their scope. It is our Agency's intention to expand our health and medical cooperation programmes in both quantity and quality to meet these requests.

I am sure that through this Conference, our mutual understanding will be deepened, and our friendship will be promoted further.

I sincerely hope that the Conference will be a great success.

I would like to conclude my address by expressing heartfelt thanks to all those who have devoted so much for the preparation of the Conference.

Thank you

ADDRESS

His Excellency Kiyohisa Mikanagi
Japanese Ambassador to the Philippines

Honorable Dr. Jesus Azurin, Deputy Minister of Health,
Distinguished Guests, Friends and Participants

It is a great honor and pleasure for me to welcome you all to this Philippine-Japan Joint Conference on Schistosomiasis Research and Control. As I understand it, this conference has three important tasks to discharge in the coming four days.

Its first task is to summarize and evaluate the achievements of the schistosomiasis research and control work which has been jointly undertaken by the Republic of the Philippines and Japan together with other related institutions.

Then, you are asked to work out a future plan of the schistosomiasis control project in the Philippines and to promote the development of technology in this field.

Finally, the results of the Conference should be published for the benefit of all countries interested in the schistosomiasis public health project and to contribute to the advancement of the welfare of the people in those countries.

As I recall, schistosomiasis research and control project was first started in Palo, Leyte in 1953. After some discussions and preparations, Japan first extended its cooperation programme to the Department of Health in 1972 to control schistosomiasis. During these years, I have learned many things about this disease, such as that this schistosomiasis disease is caused by the parasite *Schistosoma japonicum* which is found in snails called *Oncomelania quadrasi*.

It is my great pleasure to learn that, today, a great deal of knowledge and experience has been accumulated. For instance, establishment of diagnostic methods, development of the molluscicides of plant origins, and improvement of diagnosis and treatment of the cerebral schistosomiasis are considered to be major accomplishments. To this, I would like to express my heartfelt respect to the researchers of this project.

In concluding my short remarks, let me emphasize that this achievement of research on schistosomiasis would not have been made possible without the joint efforts and sacrifices of the people concerned of our two countries. I hope that this joint project will continue not only to promote the health conditions in the Philippines but also to strengthen and enhance friendly relations between our two countries.

Let me hope for the success of this Conference, and thank you very much for your kind attention.

ADDRESS

Honorable Enrique M. Garcia,
Minister of Health

Excellency, the Japanese Ambassador to the Philippines, Kiyohisa Mikanagi
The Director of the Western Pacific Regional Office of the WHO, Dr. Hiroshi Nakajima
Distinguished Guests and fellow workers in health

It is an honor to have been invited to address this morning such a distinguished gathering of international and local experts on schistosomiasis on the occasion of the Philippine-Japan Joint Conference on Schistosomiasis Research and Control.

This conference, I am convinced, lends to the growing recognition of schistosomiasis as one of the leading public health problems.

Indeed, schistosomiasis is one of the most important public health problems in our country today. Considering its widespread distribution and the segment of population it affects - mostly farmers and their families, who in our agricultural-based economy, are considered our economic backbone - it becomes more imperative that its control be one of our deepest concern. Our statistics showed that approximately more than half million people, or about fifteen per cent (15%) of the four million population exposed in twenty-two (22) provinces, are affected by the disease.

Conservative estimates place known snail infestation at about 46,300 hectares of otherwise productive arable lands. The actual figure may well be more and reach to ten per cent (10%) of the total land area of the country. These places where schistosomiasis thrive are low-land areas that are most suitable to agriculture and as such, has placed the disease problem the primary sector of concern in our agricultural development efforts.

We have known to have lived with schistosomiasis in our country since its discovery in 1906 by Dr. Wooley. Serious efforts to know more about the disease, however, have been started not more than three decades ago now with the establishment of a pilot research project in Leyte in 1952. By sheer dedication and despite our limited facilities then, we have at least known a little more of this scourge and how to effectively control it. Our research is still going on at present with continuing collaboration of the government with other governments and international organizations.

This experience on control that we have acquired, limited as it were, had somehow to be launched from the laboratory table to actual field practice. We established our first regional schistosomiasis control teams in 1961. Further, recognizing the complexities of the nature of controlling the disease, which involved not only health but also infrastructure measures, the Schistosomiasis Control Council has been created to effectively coordinate a national control program participated in by various agencies of the government.

Although some efforts to contain this problem had been made during the past two decades, it was only during the advent of the New Society that greater strides in combating the disease problem are being undertaken. This was due to the improvement of the country's financial and economic situation under the stewardship of His Excellency, The President Ferdinand E. Marcos.

The Ministry of Health, also having recognized the importance of the disease problem, have lent unconditional support to the control program. This could be gleaned in the schistosomiasis budget which increased fourteen-folds in the past seven years from about ₦0.9 million in 1971 to ₦12.2 million in 1972.

Likewise, funds estimated at no less than ₦400 million have been provided both from local budgets and loan proceeds from various international banks/agencies to finance development projects which include schistosomiasis control components - most especially those tied-up with irrigation. These infrastructure investments, which primarily reflects cost for irrigation development and shall we say, incidentally, for schistosomiasis control, nevertheless underscores the importance the government has placed on the control of the disease. It is thus expected that whatever amount is allotted to these projects will produce great dividends not only in terms of agro-economic returns but also in the improvement of the health and living conditions of the population in the endemic areas.

In the past, our efforts to control this disease had been besieged with the prohibited cost of the combined health and infrastructure approach.

We still want to see an approach which could offer the same or more benefits of controlling the disease at the least possible cost. This it seems to be the promise fulfilled with the recent discovery of the new anti-schistosomicidal drug, praziquantel. And beyond this, from the public health's stand point, also the promise of more accurate diagnostic and evaluation techniques to which advances are now being made.

Judging from its objectives, we are optimistic that this conference - which is gird to assess and evaluate experience of all concerned in the field of schistosomiasis research and control and, on this basis, forge plans for future undertakings - we are confident that its outcome will have a far-reaching significance in our efforts to lick the schistosomiasis problem.

We are grateful, indeed, that busy as you were, you have allotted your precious time and effort to be with us to share your experiences and knowledge. It is our fervent hope that your collective efforts will bring this conference into a successful one.

Thank you and good day.

AGENDA

Nov. 20 (Tue.) 1979

OPENING CEREMONY

Welcome Address:	Executive Director, SCRS
Opening Address:	Director, Medical Cooperation Department, JICA
Address:	Japanese Ambassador to the Philippines
Address:	Minister of Health, Philippines

SCIENTIFIC SESSION

EPIDEMIOLOGY

Chairman:	B.D. Cabrera
Secretary:	P.F. Velasco
Rapporteurs for all sessions:	J.S. Noseñas, C. de los Reyes, V. de Veyra, and H. Tanaka
Chairman:	E. Garcia
Secretary:	B.L. Blas

BIOLOGY

Chairman:	M.G. Yogore
Secretary:	K. Yasuraoka

Nov. 21 (Wed.)

CHEMOTHERAPY AND CLINICAL STUDIES

Chairman:	E. Domingo
Secretary:	A.T. Santos

ECOLOGY OF *ONCOMELANIA*

Chairman:	R. Garcia
Secretary:	H. Tanaka

MOLLUSCICIDE

Chairman:	B.L. Blas
Secretary:	M.G. Santos

CONTROL PROGRAM

Chairman:	E.J. Zerrudo
Secretary:	L. Tormis

Nov. 22 (Thu.)

WORKING GROUP MEETING

To discuss, summarize and formulate reports on the important subjects in each group for the proceedings of the conference.

Group No.	1	2	3	4
Subject	Diagnostic Method	Chemotherapy and Clinical Studies	Snail Ecology and Molluscicide	Epidemiology and Control
Room	Panay	Samar	Negros	Leyte
Chairman	B.L. Blas	A.T. Santos	K. Yasuraoka	H. Tanaka
Rapporteur	V. de Veyra	G.P. Portillo	C. de los Reyes	J.S. Noseñas
Secretary	A. Daya-on	M. Hayashi	K. Makiya	P. Velasco

Nov. 23 (Fri.)

WORKING GROUP MEETING (Cont.)

Reports of groups are to be submitted to the secretariat by 10:00.

Film showing: Snail Fever and Development of the Philippines

PLENARY MEETING

Chairman: A. Reyes
 Secretary: K. Yasuraoka
 Rapporteurs: J.S. Noseñas, C. de los Reyes, V. de Veyra, and H. Tanaka

Discussion and adoption of the reports from the working groups.

CLOSING ADDRESS:

Executive Director, SCRS,
 Ministry of Health, Philippines
 Executive Director, Medical Cooperation Department,
 JICA

CLOSING ADDRESS

Dr. Alfredo T. Santos, Jr.
Executive Director, SCRS

Distinguished Guests and Fellow Participants

During the last few days, I have witnessed the enthusiasm and interest you have shown in this seminar-workshop. I am indeed happy and grateful for your active participation and your sincerity in sharing what you know and in giving constructive criticisms and comments which in whole contributed much to the success of this conference.

Our task, however, does not end here and I take it to myself, rather, as a starting point of future undertakings in our effort to control schistosomiasis. The recommendations that resulted in the discussions have been very enlightening and are very useful as guideposts to direct and redirect some policies relative to schistosomiasis research and control management. Likewise, these discussions, further, confirm our belief that indeed there are more in schistosomiasis that we need to know and discover to fully understand this problem - not only in the medical aspect, but also in such diverse agro-socio-economic fields.

I therefore, would like to reiterate my deepest appreciation to your participation and to your valuable contributions that have led to the success of this seminar-workshop.

I thank you.

CLOSING ADDRESS

Dr. Masaharu Ito

*Deputy Director, Medical Cooperation Division,
Japan International Cooperation Agency*

Distinguished Guests, Ladies and Gentlemen

It is a great pleasure that the Philippine-Japan Joint Conference on Schistosomiasis Research and Control has successfully been completed.

As a member of the Joint Organizing Committee of the Conference, I am very much satisfied with the outcome obtained in the course of discussions made by the participants from various fields and institutions, not only from those connected with the Philippine-Japan Joint Cooperation Project but also from those who in their own way want to assist and know more about the project.

From these results, I hope to get most of the major guidelines for the future schistosomiasis research and control activities.

Furthermore, I would be very much pleased if this conference will serve as a catalyst or instrument to hasten further collaborative works and ventures among different institutions and agencies to promote integrated effort against schistosomiasis.

Lastly, I would like to extend my heartfelt thanks to all those in one way or another, made this Conference a successful one. We hope that this will pave the way to a bigger and continuous cooperation among us to combat and control this dangerous disease.

Thank you very much and good day to all.

REPORT OF THE WORKING GROUP MEETING

1. **Diagnostic method**
2. **Chemotherapy and clinical studies**
3. **Snail ecology and molluscicide**
4. **Epidemiology and control**

REPORT OF THE WORKING GROUP MEETING

1. DIAGNOSTIC METHOD

1.1 Introduction

With all the schistosomiasis control activities being implemented by several independent agencies, standardized methods of diagnostic technique should be used in research and surveys. It is the task of the working group to review and evaluate the different diagnostic methods as a basis for standardization, taking into considerations the many identified constraints.

1.2 Methods

1.2.1 *Smear method*

It was decided by the group that emphasis should be on quantification in stool examinations, hence the direct fecal smear and the original cellophane thick smear by Kato were left out of the discussion.

1.2.2.1 *Quantitative thick smear (modified Kato-Katz)*

It was pointed out that since only about 40 milligrams of stool is examined, the method has a low sensitivity among patients with egg counts 20 and below, and in a survey of the general population, light cases maybe entirely missed. The placing of eosin over the wettable cellophane cover slip is to provide contrast to the fecal materials against the egg, so that the latter could easily be identified.

To increase the sensitivity of the technique, it was suggested to examine more aliquots.

It was decided to study further solutions used in the technique, such as Diafix which can apparently preserve the miracidium.

1.2.2 *Concentration methods*

1.2.2.1 *Merthiolate-Iodine-Formaldehyde Concentration (MIFC)*

It was mentioned that in this technique the iodine was already omitted since protozoan cyst is not intended to be included in the examination.

The sensitivity of the technique could be further improved by using a stainless steel mesh wire screen and a detergent, Tween 80 or Triton X.

1.2.2.2 *Formalin Ether*

This technique is considered to be less expensive than and has the same principle as the MIFC technique. The pH of the formalin to be used should be about neutral to increase egg recovery.

1.2.3 *Serological methods*

1.2.3.1 *Gel-diffusion including IEP*

The Ouchterlony test is simple to perform and has the advantage of being able to distinguish false positive. This method was deemed a good technique for the further evaluation of therapy. In human schistosomiasis, the counterimmuno-electrophoresis appears to be considerably more sensitive than the Ouchterlony test. However, further investigation will be necessary to distinguish the false positive of this test before being used for diagnostic purposes.

1.2.3.2 *Circumoval Precipitin Test (COPT)*

The filter paper and plasma COPT techniques were discussed. The use of plasma, since it is undiluted, is definitely much better than using a diluted serum in the case of the filter paper COPT. It was emphasized that generally, the results of the filter paper COPT can be comparable to that of MIFC and can still be useful in areas where the heparinized capillary tubes are not available.

When using the plasma COPT, the standardization of the antigen and the reading would be necessary. It was, likewise, emphasized that vacuolated reaction would mean a recently acquired infection.

It was recommended to standardize the preparation of egg antigen and preferably to come from one source. It was pointed out that properly stored and used lyophilized egg antigen may remain reactive for as long as 15 years. The storage and use should be properly designed to prevent moisture from affecting antigen quality.

1.2.3.3 *ELISA*

This technique has many advantages such as the number that can be examined in one day, its high sensitivity, and can be a quantitative procedure.

For treatment evaluation purposes, this technique can be used since ELISA reactions became weakened ten weeks after the initiation of treatment with amoscanate in an animal experiment.

It is felt that this technique has not been sufficiently studied. Field application is not recommended at this stage.

1.2.3.4 *Fluorescent Antibody Technique (IFA) using cercarial antigen adhered to the slide*

This method has high sensitivity, simple, and can be quantitated but will need a conjugated antisera and a fluorescence microscope.

It is felt that IFA technique needs further study.

1.2.3.5 *Radio-Immunoassay (RIA)*

This was mentioned since it maybe more specific than ELISA and will remove the factor of subjectivity in reading the results.

However, disadvantages such as high cost of equipment, maintenance of special facilities, and risk of spreading radioactive substance should be taken into considerations.

1.3 General Considerations

After the process of review and evaluation, it is the consensus of the group that these diagnostic methods have its problems and deficiencies - and, therefore, a need for further refinement is suggested.

It is further suggested that:

- a) a quantitative technique should be used for evaluation of treatment;
- b) procedures to be standardized;
- c) a common criteria adopted for reading and interpretation of results; and
- d) a sustained training program for laboratory and field technicians be conducted.

2. CHEMOTHERAPY AND CLINICAL STUDIES

Objectives of the report in this group are:

1. To review the characteristics of the clinical manifestation of schistosomiasis in the Philippines.
2. To evaluate the existing drugs used in the treatment of schistosomiasis.
3. To evaluate the present status of the development of new drugs.
4. To recommend or set up policies in the parasitological and clinical evaluation of new drugs for schistosomiasis.

2.1 Characteristics of Clinical Manifestations of Schistosomiasis in the Philippines

2.1.1 *Clinical study of cerebral and hepatosplenomegaly cases assisted with schistosomiasis in Leyte*

Since 1975, we have been studying the clinical symptoms of 75 patients with central nervous symptoms and 78 patients with hepatosplenomegaly and their electroencephalogram.

As for the clinical features of the cerebral schistosomiasis, 71 patients showed the paroxysmal disease. Of the 71 patients, 52 showed convulsion, 13 showed psychomotor seizure and one automatic seizure. 58 patients or 82% of the paroxysmal disease group showed the localize lesion of the brain. The late onset paroxysmal diseases were present in 49 or 69% of the group. There were 51 patients having attacks more than once a month and they represented 72% of this group. The results of EEG was normal in 24 or 32%, borderline in 13 or 17% and abnormal in 38 or 51% of this group. The characteristic abnormal findings of EEG was the random and paroxysmal slow waves with asymmetry in the background rhythm of diffuse alpha pattern.

In 78 patients with hepatosplenomegaly, the ratio of male to female was 75 to 3 and most of the males were below 20 years old. Abdominal enlargement occurred within 3 to 12 months after the appearance of bloody mucous stools. The clinical time span was less than 3 years in 86%, as the prognosis of this group is poor. Hepatomegaly was located in the center of

the epigastrium, being symmetrical in the tip of the ensiform process. All 30 patients who underwent blood examination revealed marked anemia, 5 had slight liver impairment. EEG findings were normal in 63 patients, borderline in 10 and abnormal in 5. There was no case with neurological manifestation. There were 12 family cases in these subjects, and the type of the abdominal enlargement was almost similar in the same family except one group.

2.1.2 Discussions

A. General Physical Condition

1) Heights and Weights

As reported by Lewert *et al.*, the heights and weights of infected individuals are less than those of the uninfected members of a population in San Antonio, Basey, Samar and are significantly less than average figure for Filipinos.

2) Sexual Development

Among young infected individuals, there is a delay of menarche, and amenorrhea and undeveloped secondary sexual characteristics. It was observed that after extracorporeal hemofiltration, some patients developed secondary sexual characteristics.

3) Hepatosplenomegaly

Discussions on which lobe of the liver undergoes initial enlargement, led to the observation that commonly, it is palpable below the xyphoid process, but later as it undergoes a decrease in size, it has a tendency to shift to the right side below the RMCL. Hepatosplenomegaly usually develop 2 - 3 years after infection (Hayashi *et al.*)

4) CNS Symptoms

In the diagnosis of cerebral schistosomiasis, history of exposure to endemic area, stool and immunologic examinations for *S. japonicum* are main considerations. A detailed family and clinical history should be taken to differentiate it from genuine epilepsy and brain tumor. The seizure pattern of cerebral schistosomiasis suggests a localized brain dysfunction and manifests as either a Jacksonian or psychomotor type, occasionally progressing to grand mal. Usually, there is late onset of neurologic symptoms, frequently after 20 years of age. In epilepsy, an early onset is observed. The typical EEG finding in cerebral schistosomiasis is a diffuse alpha pattern (not found in brain tumor) with slight asymmetric theta waves remarkable in posterior and temporal leads. Seizure discharges are characteristically absent, unlike in epilepsy where it is a common finding. Paragonimiasis can be ruled out by the absence of a history of respiratory symptoms and ova in the sputum and by sero-diagnostic tests. Lastly, a therapeutic response is often obtained after antischistosomal therapy.

In the absence of adequate and complex laboratory facilities, the EEG pattern should be correlated with the laboratory and clinical findings to confirm the diagnosis of cerebral schistosomiasis.

The worldwide distribution of epilepsy is 0.3 - 0.5% while in Palo, Leyte the prevalence rate of individuals with paroxysmal disease is 1.1%. This rate which is 2 to 3 times higher could be attributed to exogenous factors such as endemicity of *S. japonicum* in this area.

B. Mental Conditions

A thesis report on the poor learning habits of infected individuals was noted. However, further studies on mental status would be difficult as it will require a large sample because of

many variables. Besides, advice from professional group as psychiatrists, etc. would be needed if accurate observations are to be attained.

C. Alimentary Tract

Dysenteric symptoms are significantly more frequent in the infected than in the uninfected individuals and this frequent is related to egg output as reported by Lewert *et al.*

D. Lungs

In autopsy cases (Pardo de Tavera) schistosome eggs were actually recovered from lung tissues. Hence, there is a possibility that pulmonary schistosomiasis particularly when occurring concomitantly with PTB, is being misdiagnosed.

E. Kidneys

Urinalysis findings of infected cases are usually nonspecific.

Recommendations:

In conducting studies on cerebral schistosomiasis, there should be a control group in a non-endemic area in order to obtain more conclusive and accurate observations.

2.2 Evaluation of Existing Drugs

2.2.1 *Stibophen*

Parenteral drugs are all antimonials. Fuadin or stibophen has 78.2% cure rate. With 48.6% negative conversion rate and 96.2% egg count reduction six months after treatment but highly toxic at a dose of 1 cc per 10 kg body weight given at every other day with maximum 5 cc per infection.

2.2.2 *Astiban*

Astiban administered intramuscularly as a 10% solution at a dose of 10 mg/kg body weight every other day for 4 days shows 79% to 90% cure rate but with severe toxic reactions and one death after the 4th dose has been reported.

2.2.3 *Sodium Antimony Dimethylcysteine Tartrate*

Sodium antimony dimethylcysteine tartrate has 100% cure rate but reversible myocardial injury has been observed in 9 out of the 10 cases treated.

2.2.4 *Dehydroemetine tablets*

Oral preparation against *S. japonicum* are dehydroemetine given at 2.5 mg per kg body weight per day for 20 days is active in suppressing egg excretion.

2.2.5 *Hycanthone*

Hycanthone at 2.5 mg per kg body weight per day for 5 days is slightly active.

2.2.6 *Pararosaniline Pamoate*

Pararosaniline pamoate, a derivative from gentian violet has mild side effects and 87% cure rate during 1st 3 months after administration.

2.2.7 *Niridazole (Ambilhar)*

Initial studies on niridazole using 10 - 15 mg per kg body weight per day for 24 days resulted in 78.8% stool negative conversion rate 6 months after treatment. Another study using the same dosage for 10 days showed 28.6% stool negative after 1 month and none after 6 months. Further studies of the drug at the same dosage for 10 days repeated every 3 months for 9 months resulted in 31% stool negatives after 6 months. Because of the high incidence of side reactions and the long duration of treatment, there was a high drop-out rate in the various studies. The most common side reactions were headache, abdominal pains, dizziness, and body weakness. The most alarming was neurotoxic in nature i.e. hallucinations, insomnia, convulsion and psychotic behaviour.

2.2.8 *Discussion on Blas paper*

Deworming with the use of combantrin or pyrantel pamoate was done prior to Ambilhar treatment. Deworming was not actually for treatment of schistosomiasis, but to see whether the abdominal reactions such as nausea, vomiting and abdominal pain can be reduced. Half of the cases in one trial were dewormed and the other half were not dewormed. The results were then compared as to their reactions to niridazole treatment. Valium and phenobarbital were given for symptomatic relief of hallucinations and convulsive seizures. Patients were followed up for 6 months after treatment for effect on *S. japonicum* egg. The suppressive dose of niridazole was thought of in order to reduce its side effects. No determination was done for effect of suppressive dose on the transmission of the disease.

In praziquantel treatment, patients were divided into different groups based in their egg counts. No other stratification of patients was done before treatment. All patients were without hepato-splenomegaly.

2.2.9 *Chemotherapeutic studies on cerebral schistosomiasis*

In summary, 56 patients of 71 cases of suspected cerebral schistosomiasis with paroxysmal symptoms were treated in 1975 and followed-up 1½ years later.

In the 31 cases treated with Fuadin (28) niridazole (3); seizures disappeared in 20 or 64.5% and EEG improved in 16 or 51.6%. Eleven (11) patients who had continued seizures even after antischistosomal therapy and 10 patients without antischistosomal therapy received anticonvulsant drugs. Of these 21 patients seizures disappeared in 12 patients, improvement noted in 6, but no change in EEG findings was observed. Carbamazepine was apparently effec-

tive for the psychomotor type, while a combination of DPH and phenobarbital seemed to be effective for the Jacksonian type.

Antischistosomal therapy is apparently effective in early cerebral cases and apparently has a direct effect on the granuloma formed in the brain. In chronic cases, where EEG is exceedingly abnormal and seizures are uncontrolled, proper anticonvulsant therapy should be maintained. More cerebral cases are being treated with praziquantel and initial encouraging results were obtained.

Recommendations for Existing Drugs (2.2.9)

Existing drugs, especially Fuadin and niridazole although observed to have toxic effects and some deficiencies should not be totally phased out due to possibility of emergence of resistant strain of *S. japonicum* against the new drugs.

2.3 Present Status of Development of New Drugs in Their Evaluation

2.3.1 Amoscanate

2.3.1.1 Amoscanate in experimental animals

A new schistosomicidal compound, 4-isothiocyanate-4'-nitro diphenylamine was lethal to *Schistosoma japonicum* *in vitro* at a concentration of 0.015 mg/ml for 120 hours. In mice experimentally infected with a Philippine strain of *S. japonicum*, the drug administered as a single oral dose of 20 mg/kg, produced a complete parasitological cure. More than 95% reduction in adult worms was obtained when treated with a single oral dose as low as 5 mg/kg. Mice treated with a curative dose of the drug tended to gain weight after treatment, while untreated control mice lost weight. Although no schistosomicidal effect was seen against 1 week juvenile schistosomula, there was no apparent difference, in the susceptibility of the parasites to the drug when the age of infection varied between 3 and 5 weeks. The efficacy of the drug was likely to be slightly higher with a diluted form (0.8 mg of the active ingredient per ml of vehicle, 1% cremophor El and 25% glycerol) than with a concentrated form (40 mg of the active ingredient per ml of vehicle).

In rabbits, the drug caused a worm reduction of 93.2 - 100% when treated with a single oral dose of 20 mg/kg. No indication of a higher susceptibility of female worms than of males was observed in *S. japonicum* infected rabbits.

2.3.1.2 Amoscanate in light to moderate human infection

Amoscanate was tried in Palo, Leyte at doses of 20 mg/kg, 40 mg/kg and 60 mg/kg in 10, 20, and 20 patients respectively. Follow-up stool examinations 6 months after treatment gave egg reduction rates of 61, 90 and 89% and stool negative rates of 0, 33, and 35% for those given 20, 40 and 60 mg/kg respectively. Reactions were generally mild to moderate (97.5%) and severe (dizziness and vomiting and jaundice) in only 2.5% and only in those that received the higher dose of 60 mg/kg. Overall efficacy is fair.

2.3.2 *Praziquantel (Biltricide)*

2.3.2.1 *Praziquantel in light to moderate human infection*

Efficacy and toxicity of praziquantel was assessed in 86 patients at a single dose of 50 mg/kg and a dose of 60 mg/kg given in three doses at 4 hour intervals. Reactions were generally mild. Severe reactions consisting of abdominal pain and hyperpyrexia occurred only in those receiving the single dose. Efficacy was very good with egg reduction rates of 98.7 and 94% and stool negative rates of 75.8 and 53.8% for those that received the divided and single dose respectively.

2.3.2.2 *Praziquantel in hepato-splenic cases*

Thirty-eight (38) hepato-splenic cases of schistosomiasis were given a one day treatment course with praziquantel in Leyte. One group received a single dose schedule of 1 x 50 mg/kg body weight, the second group, a divided dose of 3 x 20 mg/kg body weight at 4 hour interval and the last group, received placebo.

No clinical or encephalographic evidence showed central nervous system irritation neither adverse effects referable to various organ systems were noted. Side reactions were generally mild and transient. The sixth month post-treatment stool follow-up showed parasitological cures of 83.3% and 72.0%, and egg reduction rates of 97.1% and 89.7%, respectively.

2.3.2.3 *Praziquantel in experimental mice*

Praziquantel at dose of 3.1 to 600 mg/kg with 6 weeks infection resulted in deaths of 17 out of 20 mice. Deaths occurred within 2 - 3 hours in 14 mice, after 7 days in 2 mice and after 8 days in one mouse.

Drug administered to mice with 25 - 35 days infection at a dose of 300 to 1,200 mg/kg in one day resulted in one death out of 17 mice within 50 minutes after treatment.

2.3.3 *Discussion*

The use of placebo in the initial trial with praziquantel was necessary to allow a more careful assessment, specially of drug related toxicity and to a lesser extent efficacy since egg-output normally fluctuates.

Disturbing observations of what appears to be reinfection among 6 apparently successfully treated patients who were stool negative and when hepatomegaly has subsided one year after treatment developed acute manifestations of dysentery and progressing to hepato-splenic disease with one death 2 years after treatment suggest the possibility of loss of premunity. If eventually substantiated by follow-up of the other treated patients, there may be a necessity to give sub-curative doses to maintain immunity.

The question of whether to give praziquantel to the population at risk or only to confirmed cases in communities when prevalence is high, as is being done in Brazil, was raised. While cost may be an overriding factor, there may be cultural and ethical consideration against treating total population at risk.

Recommendation

1. Study possible interaction of praziquantel with other commonly used drugs especially anti-tuberculosis drugs.
2. Follow-up of patients treated with praziquantel under Phase II for several years as to status of egg intensity, clinical manifestations, liver and/or spleen enlargement to answer questions related to premunition among previously stool negative patients and duration of significant egg reduction among those remaining positive after treatment.
3. Conduct survey of herbs used by herbolarios to treat schistosomiasis and/or tape-worm infection and screen in experimental animals for possible anti-schistosomal activity, in view of high cost of praziquantel.
4. Conduct further studies on praziquantel in mice with appropriate control.

2.4 Parasitological and Clinical Evaluation of New Drugs

Discussion and Recommendation

For the determination of the parasitological efficacy of a new drug, considerations should be started with the selection of subjects. Patients for drug studies should be with light to moderate infection and be in the pre-hepatosplenic stage in order to get a valid and comparable results with previous drugs. The parameters to be employed will be stool examination of two consecutive stool sample and for each stool sample a quantitative examination should be done on two aliquots using Kato/Katz techniques. Egg hatching technique using the Faust Meleny technique should be an added parameter to determine egg viability before and after treatment. Concentration technique (MFC) is to be performed if negative by Kato/Katz during follow-up.

In the clinical evaluation, proper documentation of findings should be emphasized. The clinical improvement of patients during the post-treatment examination should be compared to pre-treatment complaints.

For drugs found to possess high parasitological cures, longitudinal follow-up for several years on the effects on subsequent reinfections should be studied further since these people are living in highly endemic areas. The immune system of the patient may be affected when a complete parasitological cure is attained.

3. SNAIL ECOLOGY AND MOLLUSCICIDE

3.1 Ecology

3.1.1 *Migration and dispersal*

Dispersal is influenced by light, temperature, humidity, current and barriers. The replacement of individual snails in a habitat is due largely to migration which in turn is influenced by fluctuation in water level.

3.1.2 *Distribution and habitat*

Geographical distribution is related to topography and rainfall. Among the places inhabited by *O. quadrasi* are the following: (1) flood plain forest and swamps, (2) ricefields, (3) streams, (4) small swamps or pockets, (5) road ditches and borrow pits and (6) irrigation canals

Discussion and Recommendation

It was pointed out that dispersal and migration play an important role in the repopulation of snail areas where the density has been brought down by snail control measures.

The group recommends that studies be undertaken on the dispersal of young snails which are entirely aquatic and may be passively carried by the water current to outlying areas.

3.1.3 *Preference of sampling method*

There is no significant difference in efficiency between the filter paper method and the tube method of snail sampling. The former method can also be used in sampling deep water habitat while the latter cannot. However, the filter paper easily disintegrates when wet and maybe completely consumed by other species of aquatic snails.

The group recommends the use of either method depending on the type of habitat.

3.1.4 *Determination of sample size*

The method of determining sample size based on dispersion index provides the mathematical basis. For practical purposes, however, the group recommends the continued use of the SCRIP procedure of sampling every five meter interval and taking a minimum of 30 samples.

3.1.5 *Comparative study of snail densities*

For comparison of snail densities, use of the regular method for comparing two arithmetic means of snail densities by *t*-test would lead to a wrong conclusion since snails are distributed unevenly. Therefore, for the significance test like the *t*-test and the analysis of variance, snail count (*x*) per sample should be transformed into $y = \log(x + 0.01)$, thereafter transformed count (*y*) should be used to reach the correct result.

3.2 Molluscicide

3.2.1 *Evaluation of molluscicides of plant origin*

The molluscicidal activity of Gogo (*Entada phaseoloides*), Tuba (*Croton tiglium*) and Tubang-bakod (*Jatropha curcas*) were tested in the laboratory using the immersion method (Komiya *et al*, 1962) on the adult *O. quadrasi*.

The Gogo ethanol extract gave LC₅₀ values of 5.8 ppm and 3.6 ppm for the first and

second test, respectively. The potency of the extract was less affected by sunlight and water hardness than was NaPCP. However, it was found to be piscicidal.

The crude extract from Tuba (*Croton tiglium*) seeds gave an LC_{50} value of 0.87 ppm against adult *O. quadrasi*. In field trials, a satisfactory kill more than 90% mortality of snails was obtained with the dose of 4 - 8 g/m² of the crude seed, indicating that exposure to the sun played but a small part in the reduction of molluscicidal activity of the seed.

The crude extract from Tubang-bakod (*Jatropha curcas*) seeds gave LC_{50} and LC_{90} values of 25.5 ppm and 48.5 ppm, respectively, against adult *O. quadrasi*. In limited field tests, however, the crude extract was as effective as Tuba. Tests also showed that piscicidal concentration was much higher than that needed to kill the snails. Additional advantage to be considered is that Tubang-bakod is much more abundant than Tuba in the Philippines.

3.2.2 Discussion

The group sees the need to undertake more intensive studies on molluscicides of plant origin. These studies should take into consideration the biocidal properties as well as the other undesirable effects that any molluscicide may exert on the environment.

Recommendations

1. Study of the residual effect on survivor snails.
The observation should last for one month and must include residual effects on physiological processes of snails.
2. Continue large scale study on Tubang-bakod in the SCRIP, Palo using the crude extract. Further studies should be carried out to determine its active ingredient.
3. The group strongly suggests and recommends that snail control is still a vital part in the control of schistosomiasis in the Philippines inspite of the discovery of a new drug against the disease because of animal reservoir hosts. The foci of infection will still pose a problem to the population for one cannot prevent the people from getting reinfected.

4. EPIDEMIOLOGY AND CONTROL

4.1 Surveillance

The group adopted the definition of surveillance by the WHO Study Group on Surveillance of Tropical Disease, Atlanta 27 - 31, March 1978 as "the continuous scrutiny of the factors that determine the occurrence and distribution of disease and other conditions of ill health. Surveillance is essential for effective control and prevention and includes the collection, analysis, interpretation and distribution of relevant data for action." Thus, to carry out an effective surveillance for schistosomiasis under this concept, it is necessary to have the following: 1) systematic and well-organized methods of case finding using standard, simple and reliable diagnostic techniques; 2) an adequate knowledge of the transmission dynamics of the disease; 3) a good understanding of the habits, practices and social attitude of the inhabitants; and 4) full cooperation and participation of the community, particularly in the collection of speci-

men and other relevant epidemiological data.

To be able to cover sufficiently the target population, sampling must be undertaken at a time when most if not all of the household members are at home, and this means either early in the morning or late in the afternoon or on any pre-arranged day. This is particularly true and important in blood sampling. For stool collection, it is also equally important to see personally the head of the family or any responsible member who shall receive the instruction how to collect and place the specimen in the distributed boxes which shall be collected the following day(s). This procedure will avoid the possibility of sampling only those left in the house during daytime who are usually small children and househelpers and who are the least exposed sector of the population.

The group also recommended the training of the local personnel of the Rural Health Unit (RHU) in surveillance procedure so that they can easily take over the responsibility in the event that the Schistosomiasis Control Team (SCT) which is presently assigned to these surveillance activities, is transferred to other localities.

4.2 Methods of Case Finding

The present methods of case finding which include the examination of representative samples of the population to determine infection rate and the detection of cases for treatment either by a house to house survey or by routine laboratory diagnostic consultation among those who voluntarily come to the center for diagnostic purposes will have to be improved. First, it is essential that there should be standard and simple diagnostic techniques that can easily be mastered by the technicians in order to obtain comparable and reliable results. Secondly, there is a recognized need for a central monitoring unit to develop a registry for schistosomiasis cases so as to avoid over or under reporting. For this purpose, it is imperative that active coordination and cooperation among health agencies operating in the endemic locality be developed to insure a free flow of information regarding cases found which shall all be reported to the central monitoring unit which ideally should be the RHU. Moreover, a system of recording has to be devised such as the use of individual index card to be kept by the RHU. A consolidated list of all newly discovered cases in the municipality shall be submitted regularly by the RHU to the Provincial Health Office (PHO) which shall be the central monitoring unit for the province. The PHO in turn submits a consolidated list of cases found in the province to the Regional Health Office (RHO) which shall be the central monitoring unit for the region. On the national level, the Schistosomiasis Control and Research Service shall be the repository of all records for case finding from all endemic areas. The RHU, likewise, must make its record of all registered cases available at all times to the SCT for cross-checking. In this way, the old and new cases can be easily sorted out and a reliable registry of schistosomiasis cases can be obtained at anytime.

4.3 Transmission Dynamics: various factors influencing the danger of infections

4.3.1 *Man water contact*

Farmers and inland fishermen are the occupational groups who frequent bodies of water and because of the nature of their livelihoods, their contact with water cannot be avoided.

Consequently, among the various occupational groups studied; the highest infection rate is observed among the aforementioned occupational groups. However, for infected individuals who are neither farmers nor fishermen, studies should be made as to which bodies of water they frequented and why. In other words, more studies on water contact of people in the endemic areas should be undertaken to pinpoint sources of infection. Meanwhile, efforts should be directed to protect children, who are the vulnerable group, from acquiring the infection through a systematic and sustained health education by their teachers. A parallel health education program on schistosomiasis control and prevention for parents has also to be carried out.

4.3.2 *Defecation habits and sites of defecation*

Studies have likewise been suggested to find out the defecation pattern of the people, the sites they usually like to defecate and the reason(s) for this. Defecation habits may not be changed, but it can be modified.

4.3.3 *Sites of snail habitats in relation to distance to the population center*

Determining the snail infested areas and the extent of the area where the people will be at risk of the infection is necessary in order to formulate necessary safeguards for the people. The use of sentinel mice may be able to identify the danger zone and this must be demonstrated to the people so they will be convinced of the risk. Danger zones must be clearly identified and marked for all people to see.

4.3.4 *Reservoir hosts*

The fact that *S. japonicum* in the Philippines also affect animals which serve as reservoir hosts, an adequate information as to their role in transmission must be made available to all concerned so that everybody shall participate in preventing stray animals. It should be mentioned that as chemotherapy becomes available for all infected individuals, reservoir hosts will be playing a more important role in transmission than before.

4.4 *Choice of Control Measures*

4.4.1 *Snail control*

The present method of control by the agro-engineering methods such as drainage, clearing, ponding in areas that cannot be drained, filling if materials are available and scientific rice farming is very effective. However, due to the high cost of implementing these methods, it is necessary that their implementation be tied up with development projects such as the NISIP program. In this connection, it is worthwhile to conduct studies on the effect on snails of the velocity and variation of water levels in irrigation canals as well as the height and shape of the canal. There is also a need to continue the study of the molluscicidal activity of some local plants to discover cheaper sources.

Mollusciciding as a snail control measure has limited use since it is not effective in un-cleared areas. This, plus its high cost necessitates that it be used only as a terminal measure

following the institution of agro-engineering measures or in pockets that are difficult to drain.

4.4.2 *Chemotherapy*

The primary purpose of chemotherapy as a control measure is to reduce transmission by stopping or reducing egg production and secondarily to improve the clinical condition of the patient. The success of chemotherapy as a control measure however depends on the availability of a safe and effective drug that can be given orally for a short period and relatively cheap. An important consideration in chemotherapy is the choice of whether to treat every discovered infected case or to carry a selective mass treatment to include only a segment of the population that is responsible for transmission. Another consideration is the frequency of treatment necessary to obtain both beneficial public health and clinical effects.

It was mentioned that assessment of the impact of chemotherapy alone in the control of schistosomiasis is difficult to assess in the NISIP Project in Leyte since the four-pronged approaches of control are being implemented. Nevertheless, there is an opportunity to test the effect of chemotherapy alone as a control measure in selected areas in Samar since no other control measures are proposed there, except chemotherapy.

4.4.3 *Environmental sanitation*

Discussion was made on the different activities being undertaken in improving sanitation as preventive measures such as the construction and use of water-sealed toilets, prevention of stray animals, construction of footbridges and provision of safe water supply. The group felt that these measures are necessary and must be pursued whenever resources are available. It was emphasized, however, that the success of these measures will depend on the people's active involvement and participation so that a vigorous and sustained health education program must necessarily proceed and accompany the environmental sanitation program.

4.5 *Social Attitude*

Certain social attitudes of the people often times slow down public health projects because people place a low value on health as compared to other basic needs. For instance, it is commonly observed that a good number of households without toilets have radios or even televisions. While it was pointed out that people in certain instances who are only renting the lot may want to construct toilets, but the lot owners do not allow them to construct toilets. For some others, the reason for not constructing or using water-sealed toilets is either the lack of adequate water supply to flush the toilet after use or the inconvenience of fetching water, especially if the source is quite far. Many really do not see the relationship between toilet construction and utilization to the control of fecal borne diseases. Culture of the people has also to be considered in changing undesirable social attitudes since certain practices fulfill socialization needs like washing together in rivers.

4.6 *Community Participation*

Social preparation of the community is essential in order to develop an awareness and

understanding of the objectives, activities and benefits of the health projects to ensure active community participation and involvement. This necessarily involves the establishment of good understanding and relationship with community leaders who should first be informed of the objectives of any health program, their importance and the benefits to be derived by the people. This way they will be able to understand well the program and can help much in informing the general public and when rapport is established between the health personnel and the inhabitants, better community participation can be expected.

In generating community participation, educational, economic and social levels as well as beliefs, values, political structure and relationship of people should be constructed. To ensure community participation and sustained support, a multi-pronged approach using the different strategies like person-to-person health education in the clinics and health centers; group approach such as barangay meetings and assemblies, mass media like print, radio and folk media must be developed to complement and supplement the first two.

4.7 Health Education

The value of health education in public health programs is well recognized. Studies on Knowledge, Attitude, Practices (KAP) are available for planning a health education program. The most recent and relevant to schistosomiasis is the KAP study in Leyte by the Institute of Public Health, University of the Philippines. Implications can also be drawn from other studies conducted in the past. However, there is a need to make in-depth studies on water behavior and other psychosocio-cultural factors so as to improve health practices of people and to serve as a basis for planning an organized and systematic health education component for a schistosomiasis control program.

4.8 Future Prospect on Schistosomiasis Control

There exist a number of effective control measures which usually are used concomitantly. Which of these measures should be employed will depend on the local situation, in particular the economic factor. In areas where a development project is in operation, every effort should be exerted to insure that a schistosomiasis complement be included not only to prevent the spread of the disease, but also to improve the health of the people. Praziquantel appears to be a good chemotherapeutic agent and probably as costs improve and reactions minimized, it would be one of the main control measures to be used. Evaluation of all measures need to be undertaken in particular the use of incidence and prevalence figures, snail densities, snail infection rates, the use of sentinel mice and snails' etc.

The necessity of a built-in training and refresher programme not only for new but also for old health personnels in endemic areas is emphasized. Regular checking of laboratory proficiency, the preparation of training and other manuals on schistosomiasis should be done. Lastly, the involvement of the rural health infrastructure which after all will remain in the community long after the special programmes are terminated should be done from the very beginning. The need for promoting and strengthening the present interagency or ministerial collaboration should be continued. With the full development of the above-mentioned activities, the future prospects of schistosomiasis control in the Philippines seem to be bright and encouraging.

LIST OF PARTICIPANTS OF WORKING GROUPS**Group I – DIAGNOSTIC METHOD**

Room: PANAY

Participants: Dr. Bayani L. Blas, Chairman
Engr. Vicente I. de Veyra, Rapporteur
Ms. Anastacia B. Daya-on, Secretary
Dr. Hajime Matsuda
Dr. Mariano Yogore, Jr.
Dr. Kunioki Araki
Dr. Robert Lewert
Dr. Masanori Kawanaka
Dr. Benjamin Cabrera
Dr. John Cross
Dr. Amante Cruz
Dr. Roger Abear
Dr. Nelia Salazar
Dr. Felix Gillego
Dr. Raul Villarete
Mrs. Felicitas Sajona

Group II – CHEMOTHERAPY AND CLINICAL STUDIES

Room: SAMAR

Participants: Dr. Alfredo T. Santos, Jr., Chairman
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GROUP III -- SNAIL ECOLOGY AND MOLLUSCICIDE

Room: NEGROS

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 Ms. Rosario Devera
 Mr. Escolastico Fabella
 Dr. Rizal Velasco
 Dr. Hiroshi Ogonuki

ABSTRACT OF SCIENTIFIC PAPERS

AND DISCUSSIONS

AN EVALUATION OF
THE MODIFIED THICK SMEAR STOOL TECHNIQUE
FOR THE DIAGNOSIS OF *SCHISTOSOMA JAPONICUM* INFECTION

Bayani L. BLAS

Schistosomiasis Control and Research Project, Palo, Leyte

A comparison of the modified thick smear stool technique was made with the merthiolate-formaldehyde concentration (MIFC) technique in several places. It showed varying results. This may be explained by the difficulty of diagnosis based purely on the egg shell, which is not present when the technique is used for the diagnosis of *S. mansoni* infection since the spine of the egg shell is more prominent.

The difficulty of diagnosis based purely on a shell structure has been confirmed by about 15% positives by the Kato-Katz among plasma COPT negative individuals and by the difference in diagnosis by well trained technicians using the Kato-Katz technique or its modification arising from the results of the workshop in Sorsogon.

Dr. Abear (SCRS, Manila/MOH)

From the paper presented, especially from Table V wherein there was quite a variation in the interpretation of the technique in the diagnosis of the different egg shell, I can only gather from them, how unexperienced and untrained they are with technique. This is important because this whole thing actually boils down to one problem, that is the reliability of your technicians.

Dr. Blas (SCRIP, Palo/MOH)

These are the technicians that were trained at the Institute of Public Health. They are expert technicians at Palo.

Dr. Burio (SCRS, Manila/MOH)

You have mentioned that shell structures of *S. japonicum* egg cannot be distinguished from other eggs; but you have not mentioned that the size, shape, thickness of the shell of *S. japonicum* are different from other egg such as *Ascaris* and hookworms. The presence of miracidium is just one of the criteria in identifying *Schistosoma* egg. Eosin is used to provide contrast to the fecal materials against the egg, so that the latter could easily be identified.

Dr. Blas (SCRIP, Palo/MOH)

Size and shape of *S. japonicum* egg vary depending on how it is viewed, whether it is seen at the top or on its side. It may, therefore, be rounded or oblong. The presence of miracidium, therefore, to me, is the best criterion for the diagnosis. Others may indicate only that it is *S. japonicum* egg, but one cannot be certain that it is.

DETECTION OF ANTIBODIES IN SCHISTOSOMIASIS JAPONICA BY ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA)

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Julian S. NOSEÑAS³⁾ and Alfredo T. SANTOS, Jr.²⁾

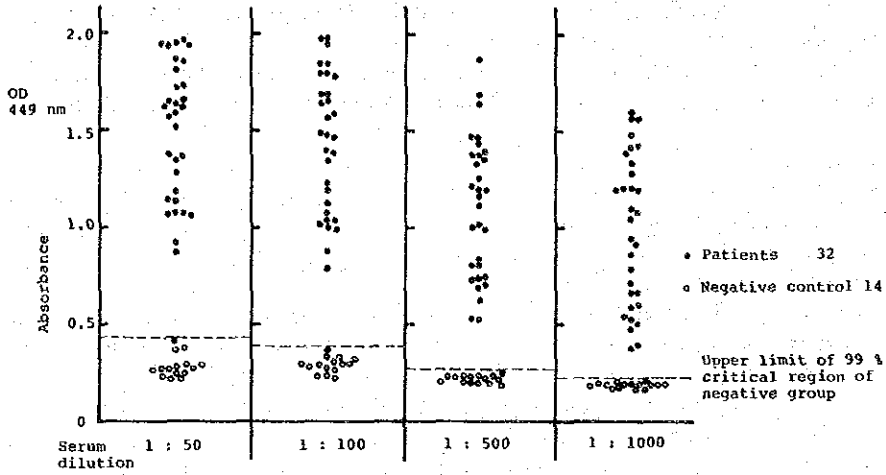
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- 2) Schistosomiasis Control and Research Project, Ministry of Health, Philippines
- 3) Health Component, National Irrigation Systems Improvement Project, Philippines

Since the first report of enzyme-linked immunosorbent assay (ELISA) in the quantitation of specific antibodies by Engvall and Perlman (1972), this technique has been applied for the detection of antibodies in *Trichinella spiralis* infection (Ljungström *et al.*, 1974; Engvall & Ljungström, 1975), malaria (Voller *et al.*, 1974), Chagas' disease (Voller *et al.*, 1975), toxoplasmosis (Voller, 1976) and schistosomiasis mansoni (Huldt *et al.*, 1975; Deelder *et al.*, 1977). ELISA was also used to study *S. japonicum* infections (Tanaka *et al.*, 1979).

The present study deals with establishment of a simple technique of ELISA for the field study of schistosomiasis japonica. Polystyrene microtiter plate with 0.3 ml flat bottom wells (Dynatech, M29ART) was used for antigen sensitization. The antigen was extracted from lyophilized adult worms or eggs of Yamanashi strain of *S. japonicum* in carbonate buffer (0.05M, pH 9.6). Peroxidase-conjugated anti-human IgG (MILES-YEDA) and 5-amino-salicylic acid were used for the conjugate and substrate, respectively. The enzyme reaction was stopped with 25 μ l of 1N NaOH. The reaction colored brown was read by a spectrophotometer at 449 nm or visual observation. For the purpose of establishing a stable, simple technique of ELISA, comparison of the antigenicity of adult worms and egg antigen, and condition of sensitizing and storing the plate with antigen, were examined. The egg antigen showed higher potency than the adult antigen. For the determination of the appropriate concentration of antigen and conjugate, blocktitration was performed using standard positive serum.

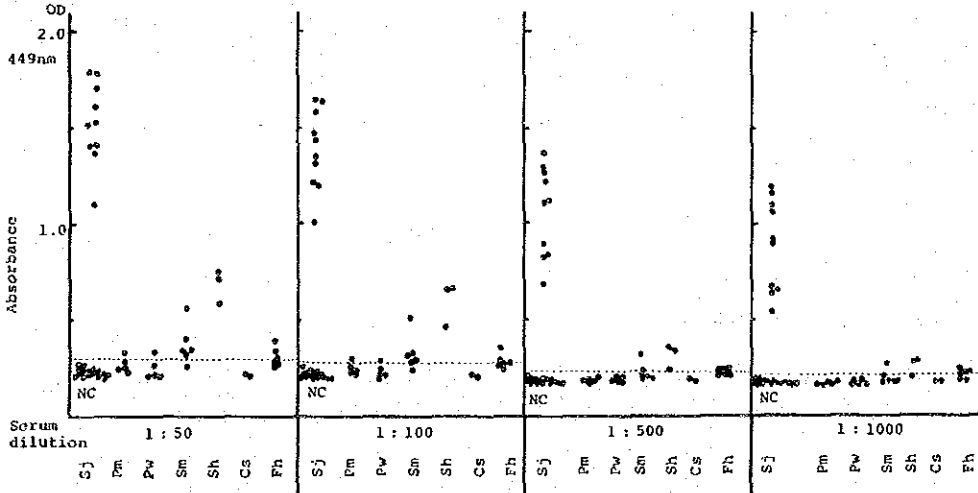
For the titration of antibody in patient sera collected in Leyte, Philippines, 80 μ g/ml of protein concentration of egg antigen was used to sensitize the plate for 2 hr. at 37°C. At first, each serum was diluted at serial two-fold dilutions from 1:60 and was placed in antigen sensitized wells. As a control, reaction with each serum at 1:60 in an antigen free well was examined. Degree of reaction at each well was determined by subtracting absorbance of the control from that in sensitized wells. Antibody titers of the 6 non-infected in Tokyo and the 6 non-infected in Leyte, Philippines were all lower than 1:60 while 6 patients in Leyte were higher than 1:3,840.

For simplification of the assessment for ELISA, an attempt was made to examine a single dilution of each serum sample in one well. Sera collected from 32 patients in the Philippines and the 6 non-infected in Tokyo and 8 in Leyte were diluted at 1:50, 1:100, 1:500 and 1:1,000. All diluted sera were examined by ELISA. With one exception (Treated with Fuadin), all the diluted sera from *S. japonicum* patients showed results above the upper limit of the 99% critical region of the negative group. Also an attempt was made to read the reaction of



Reaction of sera from *S. japonicum* infections and negative controls by ELISA at different serum dilutions.

Reactions of sera from various trematode infections with *S. japonicum* egg antigen by ELISA



Sj; *Schistosoma japonicum* Pm; *Paragonimus miyazakii* Cs; *Clonorchis sinensis*
 Sm; *Schistosoma mansoni* Pw; *Paragonimus westermani* NC; negative control
 Sh; *Schistosoma haematobium* Fh; *Fasciola hepatica*

these sera by naked eye. By this visual reading, positives and negatives were clearly distinguished at higher serum concentration than 1:100.

In the 2nd trial 38 sera from patients and 20 negatives were examined by ELISA at 1:100 dilution in one well. Thirty seven or 97.37% of the sera from patients showed positive reactions.

Cross reactions with crude *S. japonicum* egg antigen were examined using sera from infections with *S. japonicum*, *S. haematobium*, *S. mansoni*, *Paragonimus westermani*, *P. miyazakii*, *Fasciola hepatica* and *Clonorchis sinensis*.

In sera diluted at 1:50 or 1:100, reactions of *S. japonicum* infections were remarkably higher than negative controls.

The cross reactions were most prominent with *S. haematobium* followed by *S. mansoni*, *F. hepatica* and the two *Paragonimus* sera. These cross reactions, however, were minimized when the sera were diluted more.

At 1:500 dilution, positive reactions with infections other than *S. japonicum* occurred in *S. haematobium*, *S. mansoni* and *F. hepatica*.

Since the former two are non-existent and *Fasciola* infections are rare in man in the Philippines, the diagnosis of *S. japonicum* is presumed to be useful by ELISA even with the use of the crude egg antigen.

At 1:100 serum dilution, differentiation of the reactions between positives and negatives was much clearer. The weak positive reactions at this serum dilution with *Paragonimus* infections, however, may not cause a problem inasmuch as most of the schistosomiasis-infested areas of the Philippines are free from *Paragonimus*, except for two endemic foci of paragonimiasis, in Jaro, Leyte and Irosin, Sorsogon, Luzon.

The results indicated that the ELISA can be used to distinguish between schistosomiasis patients and non-infected persons from small amounts of serum or plasma collected with a capillary tube. Thus, ELISA can be applied in the sero-epidemiological survey in schistosomiasis endemic areas.

Dr. Lewert (Univ. of Chicago)

Did you determine any relationship between clinical state or egg production and ELISA titer?

Dr. Matsuda (Univ. of Tokyo)

We have not yet tried the comparison between clinical state and ELISA titer, and there was a rather poor correlation between egg counts and ELISA values in patients.

EVALUATION OF IMMUNODIFFUSION TEST FOR THE DIAGNOSIS OF SCHISTOSOMIASIS IN LEYTE, PHILIPPINES

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Skin test, complement fixation test, circumoval precipitin (COP) test and immunodiffusion tests have been used for the diagnosis of schistosomiasis. Among these tests, Ouchterlony test is one of simple procedures and has the advantage of being able to distinguish false positive from true positive.

Recently the Ouchterlony test has presented the successful results for the identification of some species among helminths. We applied micro-technique of the Ouchterlony test to detect infected people in endemic areas of *Schistosoma japonicum* in Leyte, Philippines.

For this test 0.1% saline extracts of egg and adult worm of *S. japonicum* were used as antigens and agar plate was prepared by 0.9% agarose in veronal buffer at pH 8.2. The size of wells for both of antigen and serum was 2 mm in diameter and the distance was 3 mm; 5 μ l of the antigen or serum was placed in the wells.

It is desirable to investigate the sensitivity of antigens in order to evaluate the Ouchterlony test. From this point of view, the protein content of the antigens was determined by Lowry method, and subsequently they were adjusted to 500 - 16,000 γ /ml. The adjusted antigens were applied to patient serum with *S. japonicum*. The result is shown in Fig. 1. Because egg antigen proved significantly higher sensitivity, this antigen is believed to be useful in the further study for the detection of moderately infected people in endemic areas. To achieve the desirable result, 8,000 γ /ml of protein content was appropriate for the diagnosis of schistosomiasis as well as paragonimiasis and fascioliasis.

The investigation of cross reaction between *S. japonicum* and other helminths was carried out. Egg antigen of *S. japonicum* was applied to the sera of 10 patients with *Paragonimus miyazakii* and 4 rabbits with *Fasciola hepatica*.

There were no cross reactions in these sera. Moreover, the antigens of *Schistosoma* egg, 2 other trematodes and 3 nematodes were applied to the sera of 34 patients with *S. japonicum*. All sera were positive against egg antigen and one sample was also positive against the antigens of *Toxocara canis*, *Dirofilaria immitis* and *Trichinella spiralis*. However, cross reactions were not seen against the antigens of *P. ohirai* and *F. hepatica*. Judging from the result, double infection of *T. canis* was suspected.

The comparative studies of the Ouchterlony test, COP test and fecal examination for the screening of schistosomiasis were also carried out. The COP and Ouchterlony tests were performed on the sera of 124 out-patients at SCRIP in Leyte, Philippines. The results of immunological tests were summarized in Table 1. Out of 26 egg positive cases, 24 were positive and

2 were negative in both tests. However, out of 98 egg negative cases, 49 showed positive in combined tests. Even in the egg negative cases, some schistosomiasis patients could be detected from immunologically positive cases by further fecal examination.

From these results, micro-technique of the Ouchterlony test was believed to be useful for the diagnosis of schistosomiasis in endemic areas.

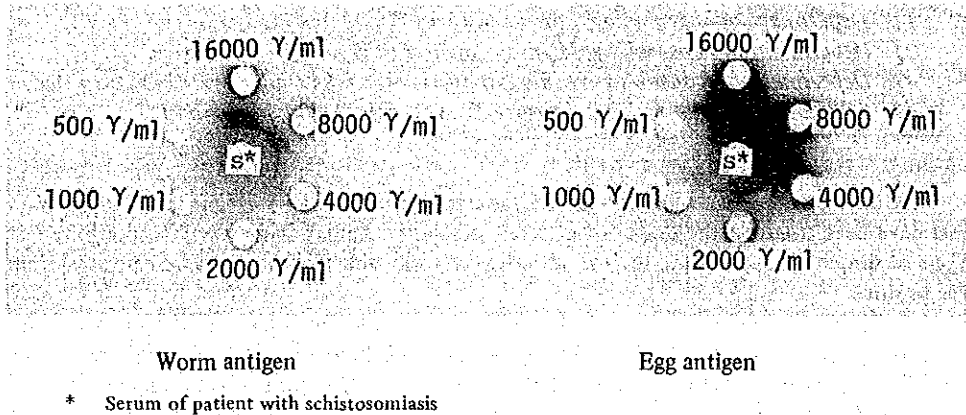


Fig. 1. Comparison of the sensitivity between worm antigen and egg antigen

Table 1. Comparison of the immunological tests between egg positive and egg negative cases

Case	No. examined	Immunological tests							
		COP (+)	ID* (+)	COP (+)	ID (-)	COP (-)	ID (+)	COP (-)	ID (-)
		No.	(%)	No.	(%)	No.	(%)	No.	(%)
Egg positive	26	24	(92.3)	0		0		2	(7.7)
Egg negative	98	34	(34.7)	11	(11.2)	4	(4.1)	49	(50.0)
Total	124	58	(46.8)	11	(8.9)	4	(3.2)	51	(41.1)

* Ouchterlony

Dr. Yogore (Univ. of Chicago)

What is the rationale of using the Ouchterlony technic when other technics like counter electrophoresis are available for diagnostic purposes?

Dr. Araki (Inst. of Public Health, Tokyo)

The Ouchterlony test is simple to perform and has the advantage of being able to distinguish false positive from true positive.

In human schistosomiasis, the counterimmunoelectrophoresis appears to be considerably more sensitive than the Ouchterlony test. However, further investigation will be necessary to distinguish the false positive of this test before its use for diagnostic purposes.

**A TECHNIQUE FOR SERO-DIAGNOSIS OF
SCHISTOSOMA JAPONICUM INFECTION
BY THE INDIRECT FLUORESCENT ANTIBODY (IFA) TEST
USING CERCARIAE-STUCK SLIDE ANTIGEN:
A PRELIMINARY REPORT**

Masanori KAWANAKA¹⁾ and Bayani L. BLAS²⁾

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2) Schistosomiasis Control and Research Project, Ministry of Health, Philippines

The application of fluorescent antibody technique is widely known and has been used both as a diagnostic tool and in experimental work on parasitology.

In 1960, Sadun *et al.* introduced the indirect fluorescent antibody test for schistosomiasis with *Schistosoma mansoni* cercariae as antigen. This test since then has been used both for laboratory diagnosis and in epidemiologic surveys.

The standardized procedure in test tubes is highly sensitive and relatively simple to perform, but it is time consuming and other reagents are necessary. The cercarial-antigen adhered to the slide in IFA test for avian schistosome dermatitis has been described recently (Kawanaka *et al.*, 1979). Since all the reactions can be performed in cercariae-stuck slides without using test tubes, this antigen seems to overcome some of the problems encountered with the original antigen.

In the present study, *Schistosoma japonicum* cercariae from endemic areas were prepared as cercarial antigen adhered to the slide. An application of the technique for the diagnosis of *Schistosoma japonicum* infection was then tried.

Table 1. Distribution of IFA titers in cases of egg positives, egg negatives and from non-endemic residents

Sera IFA titer	Palo		Manila
	Egg +	Egg -	
640	13 (11.8%)	0	0
320	19 (17.3%)	0	0
160	26 (23.6%)	2 (8.6%)	0
80	19 (17.3%)	2 (8.6%)	0
40	18 (16.4%)	6 (26.1%)	0
20	15 (13.6%)	8 (34.8%)	1 (1.6%)
10	0	2 (8.6%)	1 (1.6%)
< 10	0	3 (13.0%)	60 (96.8%)
	110 (100%)	23 (100%)	62 (100%)

Sera collected from 133 outpatients visiting the SCRIP at Palo, Leyte and from 62 individuals who live in non-endemic areas coming to the BRL (Bureau of Research and Laboratory), Manila, were examined during the period from October to November 1979. The stool samples of 133 outpatients were also examined for parasite eggs at SCRIP laboratory.

The test results are summarized in the table. The titer of the test serum was expressed by a reciprocal of the highest dilution which gave the specific fluorescence of any intensity.

With the sera from egg positives all of their titers ranged from 1:20 to 1:640. In contrast, among 62 sera from Manila, only one reacted positively at dilution of 1:20. Of 23 sera from egg negatives, 18 sera reacted at a dilution of 1:20 or above.

A criterion of positivity of a titer of 1:20 or greater may tentatively be considered. The possibility of false positive should be further investigated with residents in the highly endemic area of Leyte island.

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Japan J. Parasitol. 28:229-234

Dr. Ruben Umaly (College of Arts & Sciences, UP)

What is the advantage of cercaria antigen in IFAT as compared to sections of adult worms?

Adult worm section can easily be obtained by cryostat sectioning of adult worms artificially rolled in diaphragm muscle or adultworm in liver. Several sections can be placed on a slide and so the serum titer can easily be obtained. This would not endanger technician i.e., they would not be infected from handling the specimen.

Unlike the one with cercariae, one does not have to maintain live culture of infected snail. The specimen is easier to locate under the microscope because of bigger size and there is lesser chance of the section falling off during the processing. The chemicals involved are the same and the sensitivity and specifications of sections with cercariae are comparable. So what is the advantage of using cercariae?

Dr. KAWANAKA (NIH, Tokyo)

Some investigators have recommended the use of frozen-sectioned adult antigen in the IFA test for schistosomiasis. This antigen was prepared by sectioning the worm tissues at 4 - 6 μ m thickness by cryostat, and had to be stored at -70°C .

This procedure can be performed only in a well equipped laboratory.

In contrast, the cercariae antigen adhered to the slide can be prepared easily at any laboratory in the endemic areas.

Dr. Roque Burio (SCRS, Manila/MOH)

I'm interested with the preparation of antigen. Do you think the process or procedure in antigen preparation will change the chemical structure of antigen?

Dr. Kawanaka (NIH, Tokyo)

I cannot answer that question in reference to change of chemical structure of antigen.

I am also interested in the preparation of antigen for diagnosis of *S. japonicum* infection by IFA test, and have been using 1% acetic acid in ethanol for fixation of cercariae.

Our preliminary investigation with this fixation procedure indicated that neither denaturation of cercarial antigen nor loss of specificity took place within 2 months at 4°C.

**PRODUCTION OF COPT ANTIGEN
FOR SCHISTOSOMIASIS JAPONICA
WITH REGARDS ON THE ESTABLISHMENT
OF LABORATORY MOUSE COLONY IN THE TROPICS**

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2) *Merk Sharp and Dohme Limited Company (Japan)*

3) *Schistosomiasis Control and Research Project, Department of Health, Republic of the Philippines*

COPT (circumoval precipitin test) is useful and specific for the diagnosis of schistosomiasis japonica (Yokogawa *et al.*, 1967; Yogore *et al.*, 1968; Tanaka *et al.*, 1975; Matsuda *et al.*, 1977). It is obvious that the production of good COPT antigen is hardly carried out without the good supply of healthy experimental animals and the production of infected animals. Those works, however, have somewhat difficulties to be performed in the tropics.

1. Establishment of mouse colony for the infection of schistosome cercariae

It is difficult to make the ideal condition for breeding the experimental mouse in the tropics. Several hundred mice (ddY strain), which were not so healthy, were kept in Schistosomiasis Control and Research Project, Leyte, for the first time. Diseases caused by *Hymenolepis microstoma* (parasite in bile duct), *H. nana*, ectoparasites and HVJ (virus pneumonia) were eliminated by using antibiotics. Yomesan and Negvone. And then breeding method was being improved under the following schedules:

1. Mouse cages were exchanged once or twice a week.
2. Wooden chips as the litter were sterilized in drying oven.
3. Mouse cages, feeders, water containers and other equipments were disinfected.
4. The mice, 1 male and 3 to 5 females, for breeding were put in a cage, and pregnant mice were transferred to the other cages.
Date of birth was recorded.
5. Suckling mice have to be weaned at 4 weeks after birth.
6. Drinking water must be fresh.
7. Negvone was sprayed once a month.
8. Mouse feeds probably contained plenty of beetles as second intermediate host of *Hymenolepis* spp. Those feeds were used after they were dried and put on a sieve to remove the beetles.

The number of mice amounted to more than 2,000 within 6 months after this primitive program for breeding and management of mice has been carried out. And then, 50 to 100 healthy mice were being supplied for antigen production every week.

2. Production of infected mice with *S. japonicum* cercariae

It is also important to produce and maintain the infected mouse in the laboratory for production of good COPT antigen. It appeared that Philippine strain of *S. japonicum* is more pathogenic than other strains. Therefore, reasonable number of cercariae injected to a mouse was studied. The cercariae were collected by crushing the naturally infected snails, *Oncomelania quadrasi*, in Leyte. Infection was established by subcutaneous injection. Table 1 shows relationship among duration of infection, number of cercariae injected, survival rate of infected mice and infection rate. According to Table 1, the survival rate was suddenly going down 7 weeks after infection. It was 78.2% 6 weeks after infection and then went down to 28.3%, 27.95%, 10.17% 7, 8 and 9 weeks after infection, respectively. And it is obvious that the number of cercariae injected also affected the survival rate. Consequently, for COPT antigen production, mice infected with 30 to 50 cercariae should be sacrificed 6 weeks after infection, or mice infected with 15 cercariae should be sacrificed 8 weeks after infection.

Table 1. Relationship among duration of infection, no. of cercaria injected, survival rate and infection rate (October 1978 - January 1979)

Weeks after infection	No. of cercariae	Survival rate (%)			Infection rate (%)
		Male mouse	Female mouse	Total	
6 weeks	30	65/80 (81.25)	57/76 (75)	122/156 (78.2)	122/124 (98.4)
7 weeks	30	16/71 (22.54)	16/42 (38.10)	32/113 (28.30)	32/34 (94.1)
8 weeks	30	10/45 (22.22)	29/69 (42.03)	39/114 (34.21)	39/39 (100)
	25	32/158 (20.25)	55/135 (40.74)	87/293 (29.69)	87/94 (92.55)
	20	51/261 (19.54)	77/294 (26.19)	128/555 (23.06)	128/143 (89.51)
9 weeks	15	9/26 (34.62)	35/78 (44.87)	44/104 (42.31)	44/46 (95.65)
	20	6/31 (19.35)	0/28 (0)	6/59 (10.17)	6/6 (100)
Total		189/672 (28.13)	269/722 (37.26)	458/1,394 (32.86)	458/486 (94.24)
6 weeks				122/156 (78.2)	
7 weeks				32/113 (28.3)	
8 weeks				298/1,066 (27.95)	
9 weeks				6/59 (10.17)	

3. COPT antigen production

Fresh schistosome eggs were used for COPT by Oliver-Gonzalez (1954). And then, Rivera de Sala *et al.* (1952) showed that the lyophilized eggs had good antigenicity for COPT.

The procedure to make COPT antigen is shown in Figure 1. Infected intestine and liver of mice were digested by using 0.2% trypsin and 0.05% collagenase solution. Collagenase digestion was applied to remove minute host tissue attached with egg shell, which is liable to be confused with micro-precipitin of Type I according to Yokogawa *et al.* (1967). Before lyophilization, digested eggs were examined for its viability. Antigenicity of lyophilized eggs was also examined by the reaction with lyophilized rabbit serum 12 weeks after infection. And its index as parameter of antigenicity was calculated by the formula written in Figure 1. Eggs with high antigenicity could be supplied for the diagnosis and studies of schistosomiasis japonica. Antigens were preserved in a refrigerator at 4°C with silica gel to prevent the decline of its antigenicity.

Antigenicity of eggs and percentage of matured eggs from mice 4 to 7 weeks after infection were investigated. The eggs isolated 6 weeks after infection had good antigenicity for COPT.

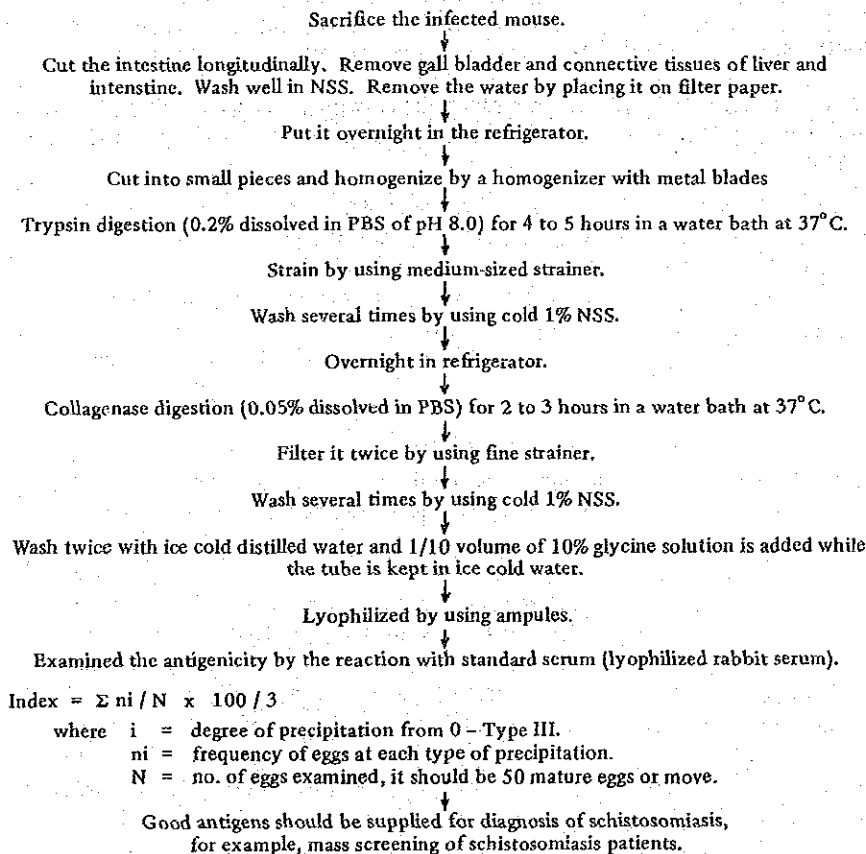


Fig. 1. Procedure of COP antigen production

Dr. Zerrudo (SCC)

1. Why do you inject subcutaneously the cercariae instead of infecting the mice naturally?
2. Do you infect them better this way?

Dr. Kamiya (Hokkaido Univ.)

1. It needs much more effort to establish the infection of *S. japonicum* in mice by skin penetration than by subcutaneous injection.
2. Subcutaneous injection is a simple way but difficult to infect the exact number of cercariae.
For COPT antigen production, however, the subcutaneous injection is the practical way in the Philippines.

Dr. Yasuraoka (Univ. of Tsukuba)

When we want to infect experimental animals with an exact number of *S. japonicum* cercariae, our cover-slip method (Yasuraoka *et al.*, Japan, J. Exp. Med., 48, 53-56) is strongly recommendable.

**SALIENT NOTES ON THE JOINT RP-JAPAN RESEARCHES
ON THE CIRCUMOVAL PRECIPITIN TEST (COPT)
FOR SCHISTOSOMIASIS**

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From 1972 to 1975 at least six researches on the circumoval precipitin test (COPT) for schistosomiasis, that is, four on its immunological aspects and 2 on its application in epidemiological survey, were jointly undertaken by four Japanese experts from JICA and an equal number of senior staff from the Schistosomiasis Control and Research Project in Palo, Leyte, under the Ministry of Health of the Republic of the Philippines. The immunological researches include the comparison of the sensitivity of the test using whole serum and serum extracted from filter paper with the MIFC technique of stool examination which showed the superior sensitivity of the whole serum over the extracted serum from the filter paper. The latter was just as sensitive as that of a single fecal examination by the MIFC technique. A technique of COP test using blood taken on filter paper was also found to be more sensitive than a microtiter technique of complement fixation test of schistosomiasis japonica. Likewise in the evaluation of COPT reaction for schistosomiasis between undiluted sera and among three criteria of interpreting the precipitates, it was observed that stronger reactions occur with undiluted serum than diluted serum and that the percentage of false positives by COPT can be minimized by considering only as positive reactions falling under Type II and III classification. Evaluation of the COPT using blood on filter paper for epidemiological survey of schistosomiasis showed indications of its usefulness and applicability.

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Dr. A.T. Santos (SCRS, Manila/MOH)

On the basis of the apparent good results with the COPT, would you recommend the use of the COPT for:

- 1) Epidemiologic surveys?
- 2) Case detection on a big scale?
- 3) Evaluation of treatment cases?

Dr. Noseñas (SCRS, Manila/MOH-NISIP I)

- 1) Yes, especially plasma COPT and when not available, the COPT filter paper method can substitute for MIFC stool examination since efficiency is about the same in epidemiological survey, but COPT has no use in recently treated cases because COP reaction remains positive.
- 2) Yes, since the method is simple and results are reliable.
- 3) Not practical in evaluation of treatment because COP reaction remains positive within 1 year after a successful treatment.

Dr. Burio (SCRS, Manila/MOH)

Since you have recommended the use of COPT in epidemiology, do you also recommend the use of different types of reaction in COPT for evaluation and/or correlation with the intensity of infection?

Dr. Noseñas (SCRS, Manila/MOH-NISIP I)

No, because it has not been established that strength of COPT reaction is always related to intensity of infection.

**SCHISTOSOMIASIS JAPONICA
IN BARRIO SAN ANTONIO, BASEY, SAMAR:
STUDIES WITH THE CIRCUMOVAL PRECIPITIN (COP) TEST***

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- 2) *SCRIP Palo, Leyte*

We have employed the COP test as a major immunodiagnostic procedure in our studies on the epidemiology of schistosomiasis japonica in Barrio San Antonio, Basey, Samar. Aside from the epidemiologic information that this test has provided, we have been able to gain a better insight on the use of the COP test as a field diagnostic tool and to assess its practicability, usefulness and limitations. This assessment has led to a proposal for the adoption of the plasma COP test for epidemiologic use in the Philippines.

Our initial studies showed that in human schistosomiasis japonica sensitivity of the COP test and serum reactivity as indicated by precipitate length, rises with increasing intensity of infection as measured by fecal egg output. False negative tests among known egg excretors are confined to those with very low egg outputs. COP sensitivity declines among infected individuals 50 years or older. Based on the examination of 193 stool-positive individuals, the COP test sensitivity employing whole serum was 92% as opposed to 49% when the eluate from dried blood on filter paper - the filter paper technic - was used. These results give reason to not use any blood collection technic that will result in significant dilution of antibody in COP tests. The identification of segmented precipitate in the COP test slide should be the basis for a positive COP test with the single exception of the reaction seen in recently acquired infections. If these criteria are used, no false positive reactions are found.

On COP tests of sera from more than 300 barrio residents, atypical precipitates not resembling the usual form were found in 7. These distinctive, atypical precipitates when bleb-like are characterized by the presence of vacuolation and when elongated, the precipitates are vacuolated and without the segmented appearance characteristic of the typical reaction. We found that 5 of the 7 individuals were recent migrants to the endemic area while another was only 5 years old at the time of examination.

If recently acquired schistosomiasis japonica is to be uncovered in an endemic area, it might be expected that this would most likely be detected among younger children shortly after initial contact with the infection in the environment. Consequently, school children were studied using a plasma COP test and it was found that 25% of 115 children in grades 1 - 3 exhibited these atypical precipitates. More than 100 COP-negative children had repeated examinations after 3 - 5 months and again after another 3 months. During this period the COP test converted to positive in 11 of these children with 8 showing only the atypical precipitates

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without segmented precipitates. One showed a mixed reaction with both types of precipitates and two showed only segmented precipitates. Thus, the atypical precipitate was the most frequently observed reaction in these positive conversions among the children and we have labelled the atypical precipitate as the reaction of recent infection (RRI). The potential usefulness of a diagnostic technic that can differentiate between recent and old infections in epidemiologic studies is obvious; it may find its most important application in the measurement of incidence and evaluation of control programs.

The study on school children in Barrio San Antonio described above would not have been possible except for the use of the plasma COP test which we have therefore proposed as the standard serodiagnostic test in the Philippines. Blood is collected by finger prick as in the filter paper technic thus overcoming the all-pervasive objection (in the rural Philippines) to venipuncture. Blood is collected in heparinized capillary tubes to allow separation of the red cells by sedimentation alone; the addition of a minimal amount of sodium azide to the separated plasma with sealing of each tube end allows storage of the plasma for up to two months at ambient temperatures without loss of COP reactivity. We have also proposed criteria for the reading of the COP tests to include the typical segmented and RRI reactions.

Finally, we must remark while the value of the COP as an immunodiagnostic procedure is questioned and apparently even dismissed in some quarters, recent studies have indicated that its specificity and sensitivity equal or exceed that of the most sophisticated and more expensive methods currently being employed for *Schistosoma mansoni* diagnosis. We should like to suggest at this meeting that a mechanism be set up to collect and store sera from well-documented positive *S. japonicum* infections as well as from those unequivocally uninfected and from individuals with a variety of diseases including infections by various parasitic agents. In this way, any investigator can be provided with small amounts of serum as unknowns for a completely unbiased evaluation of any immunodiagnostic method being developed. We foresee a need for such a mechanism when highly purified antigens are prepared and utilized in RIA, DASS and ELISA methods for the diagnosis of schistosomiasis japonica as is presently occurring with other infections.

Dr. Tanaka (Univ. of Tokyo)

1. When you compared the plasma COPT with filter paper blood COPT, did you use the same reading criterion for the plasma COPT?
2. You said that NaN_2 was added to the plasma in capillary tubes for preservation. Could you keep antibody for COPT in plasma at a room temperature in the tropics outside of refrigerator?

Dr. Yogore (Univ. of Chicago)

1. The filter paper COPT was performed by SCRIP personnel and therefore, was read according to Yokogawa's criteria. We performed the serum and plasma COPT and these were read according to our criteria. (Yogore *et al.*, 1968)
2. Yes, plasma tubes were kept at room temperature in Leyte and at room temperature in Chicago during this study. The plasma tubes were therefore kept at ambient temperature before tests at 30 and 60 days.

**CURRENT STATUS OF SCHISTOSOMIASIS JAPONICA
IN SORSOGON PROVINCE, REPUBLIC OF THE PHILIPPINES**

**Benjamin D. CABRERA¹⁾, Francisco VALEZA¹⁾,
Alfredo T. SANTOS, Jr.²⁾ and Ildefonso CRUZ¹⁾**

- 1) *Institute of Public Health, Univ. of the Philippines*
- 2) *Schistosomiasis Control and Research Service, Ministry of Health*

A resurvey of Irosin and the eight municipalities surrounding it for schistosomiasis japonica using COPT and FECT was done in order to determine the status of the disease thirty years after it was first reported in the town of Irosin in 1947. In Irosin, the results by FECT showed that there was a decrease in prevalence from 5.7% to 2.8%, however, if by COPT, then there was an increase from 5.7% to 12.2%. There is a definite trend of the disease to spread from Irosin into the surrounding municipalities. Whereas in 1951, only Irosin and Juban have been established as endemic foci for schistosomiasis, the result of previous surveys by the schisto-unit of Irosin and the present study seems to indicate that the disease has spread into seven additional towns surrounding Irosin. In like manner, the snail intermediate host, *Oncomelania quadrasi* has a tendency to spread to outlying areas outside of Irosin and Juban.

Mr. Escolástico Fabella (SCRS, Manila/MOH)

Has there been some surveys conducted before as to whether schistosomiasis cases are present in the outlying areas in Juban and Irosin? Is it possible that it is not the disease that is spreading but only our knowledge of it?

Dr. Cabrera (Inst. of Public Health, UP)

Dr. Santos can explain on this since I got these data from the SCRS and Dr. Santos is a co-author of this paper.

**SCHISTOSOMIASIS JAPONICA
IN BARRIO SAN ANTONIO, BASEY, SAMAR:
EPIDEMIOLOGY AND MORBIDITY**

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- 2) *The Philippine Ministry of Health, Schistosomiasis Research and Control Project, Palo, Leyte*

Although there have been a number of studies on the epidemiology of *Schistosoma mansoni* and *Schistosoma haematobium* in recent years, dealing with population or segments of populations continuously under risk of exposure, there have been few comparable studies of a comprehensive nature on the epidemiology of *Schistosoma japonicum*. The early reports of Tubangui, Wright *et al.* and Pesigan and his co-workers are of great importance but have not been supplemented by observation of the current disease status in areas other than Leyte and most are in the nature of prevalence surveys. Studies in the Celebes and Laos have been limited and the most recent investigations in Japan have dealt primarily with chronic infections, as in this area there are no longer population groups with a high endemicity, or ones in which transmission or risk of exposure is currently great. In the type of situation in the endemic areas of the Philippines where transmission may occur throughout the entire year and where exposure risk is high, there is much that still unknown concerning the status of the infected individual, or the impact of the infection on the population and there is a little quantitative information of the morbidity experienced by such a group. In addition, there have also been no epidemiological studies in the Philippines in which such a population has been monitored over an extended period of time.

The study reported here was initiated in September of 1976 under agreement with the Bureau of Laboratories of the Philippines Ministry of Health as a collaborative study with the Schistosomiasis Control and Research Project at Palo, Leyte.

Since we proposed to obtain baseline information for a possible longitudinal study, a small stable unstudied community was sought with accessibility to the Schistosomiasis Control and Research Project (SCRP) at Palo, Leyte. We selected Barrio San Antonio of the municipality of Basey, Western Samar Province, a relatively isolated coastal settlement located 1.7 kilometers across the San Janico Strait directly north of Tacloban City, Leyte.

Barrio San Antonio had a population of 1,788 with 298 dwellings in the census of 1975. If the growth rate in this barrio conforms with the Philippines national population growth rate the population at the time of this study can be estimated at 1,900. The number of dwelling units actually found in our house-to-house survey reached 3.20. The endemicity of *S. japonicum* in the municipality of Basey was originally established in surveys in 1951 when 156 of 519

This study was supported by the US-Japan Cooperative Medical Science Program administered by the National Institute of Allergy and Infectious Disease of the USPHS under Grant No. AI 07724.

individuals examined (30 percent) were found stool positive. At that time 17 percent of children in grades 1 through 3 were found to be infected, based on this single stool examination.

The survey reported here included (1) interviews with the head and older members of the household to gather personal and family data, (2) a physical medical examination, (3) the submission of stools and urine specimens, (4) a collection of blood by finger prick for blood counts and hemoglobin determinations, and (5) collection of blood by venipuncture from adults and older children. This was followed later by periodic stool examinations and serodiagnosis. The survey team included at a minimum a clinician from SCRIP, a medical history recorder, medical technician, laboratory helper and a driver. Usually one or two other professional personnel were also team members.

Initially 851 residents (45 percent of 240 households) participated in this survey to determine prevalence and intensity of *S. japonicum* infection and morbidity as indicated by associated hepatomegaly and splenomegaly. Subsequently nearly 80 percent of the barrio population have been examined and multiple examinations have been made of many residents. As a result of the initial single stool examination of 1 ml by a modified formalin concentration technique, 40% of this population was found to be infected. On subsequent examinations, with the addition of serologic techniques and recording the history of therapy, approximately 70% of this population was found to be infected with *S. japonicum* after the age of ten years. If judged by the number of eggs produced per milliliter of feces, infection intensity in this population might be considered to be low. However, 25% (73 of 391 positives on single examination) exhibit schistosomal hepatomegaly or hepato-splenomegaly and have a mean egg count of only 10.9. Those infected but without hepatomegaly have a slightly lower mean egg count of 8.4. Of the infected males with hepatomegaly, 75% are 19 years of age or less and 45% of these are producing less than 10 eggs per ml. Abdominal pain, distress, diarrhea, and dysentery are significantly more frequent in the infected than uninfected, and this frequency is related to egg output. In addition the heights and weights of these infected individuals are significantly less than those of the uninfected members of this population and are also significantly less than the Filipino norm.

We have a great deal of additional detailed information on this small population that time does not permit us to discuss; there are however some generalizations that can be made. Barrio San Antonio may be considered an example of a relatively moderately infected population with its members having diverse occupations not totally confined to agriculture. If it is representative we can conclude that the estimated prevalence of Philippine *S. japonicum* infections made in the 1950's and based on single stool examinations was low and with modern techniques the figure should probably be doubled. With the increase in population in these areas in the last 25 years the number of infected individuals may well be doubled again suggesting that well over a million individuals are involved. The infection rate in children is high even in primary school grades 1 to 3; and in this barrio is over 35%. Fourteen percent are infected on entering school with an increase to 50% during the next two years. By age 10 prevalence of infections in males is over 70% (this figure is even higher in other areas we are studying). More than 25% of the entire population infected has recognizable schistosomal morbidity as judged by hepatomegaly or hepato-splenomegaly. It should be emphasized that in the group with such pathology more than half are producing less than 20 eggs per gram of feces. This contrasts with the findings in other schistosomal infections elsewhere in the world e.g. *S. mansoni*. In other words egg excretion rate is not a good correlate of schistosomal pathology in this group. It follows that

techniques for diagnosis that will not reliably detect less than 20 eggs per gram such as the Kato method, or partial sampling of concentrates, are unsuited in this area.

The current study provides good baseline information on the status of infection and disease in a well defined group. In the schistosome endemic area of the Philippines programs of control utilizing various approaches are being instituted and there is increasing use and availability of a spectrum of chemotherapeutic agents. For most endemic areas where these techniques may be employed, baseline information on the infection and disease status of the infection and disease status of the population does not exist. As a consequence, the impact of these methods, as in the past, will be difficult if not impossible to assess. The information now available on this relatively stable population in Barrio San Antonio can be of great value in allowing us to determine the impact and relative efficacy of the control measures if instituted in this area. The data should also be examined to aid in planning control and therapeutic measures to direct these at the segments of the population at greatest risk. For example, it may be reasonable that the main thrust of efforts towards prevention and control should be directed toward the age cohort 10 years and below and their activities in this environment, since by the age of 10 most of this population are infected.

Dr. Zerrudo (SCC)

1. Is there a correlation between the height and weight of infected individuals with that of intensity of infection as indicated by the number of eggs per/unit volume (ml. or gram)?
2. Would you suggest anthropometric studies?

Dr. Lewert (Univ. of Chicago)

1. Only very roughly since we do find in those less than 20 years of age the individuals with lowest heights and weights and those producing the largest number of eggs. The groups studied are too small to say whether or not a direct statistical relationship exists.
2. Certainly, prior to control, to give an additional assessment of the results of control at a future date.

Dr. Abear (SCRS, Manila/MOH)

The most striking feature that I've noticed about your paper is the very, very low egg counts, way below those that other studies have indicated. Perhaps, its because you have utilized a procedure (MFCT) which is poorly quantitative. If your technicians have examined each specimen, then you are missing more than 58% of these eggs.

Dr. Lewert (Univ. of Chicago)

I admit the egg counts are generally low and these were the findings by Palo technicians, but I believe the figures are correct.

Dr. Salazar (IPH, UP)

How representative is Bo. San Antonio of other prospective schistosomiasis endemic areas in the Philippines?

Dr. Lewert (Univ. of Chicago)

We believe it is a good example of a moderately infected area. Other areas are certainly more heavily infected and have a greater prevalence and morbidity. It is an excellent area in which to assess the efficacy of a control program because of its stability and diversity of occupation.

**CASE MONITORING OF *SCHISTOSOMA JAPONICUM* INFECTIONS
AMONG SCHOOL CHILDREN AT DAGAMI, LEYTE**

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The incidence of schistosomiasis has been studied by Pesigan *et al.* (1958) in the Philippines, by Farooq & Hairston (1966) and Farooq *et al.* (1966) in Egypt, by Schiff (1977) in Rhodesia and by Jordan (1977) in St. Lucia. Although the incidence has been emphasized to be an appropriate parameter to evaluate the effect of control measures (Farooq *et al.*, 1966, Jordan, 1977), the follow-up study of inhabitants in the endemic area has rarely been performed because of the difficulty of having necessary resources for the mass examination and of lacking a simple procedure.

In the present study, about 700 school children at Dagami area, Leyte, Philippines have been examined yearly since 1974. All children at 9 schools in the area were examined by fecal examination by MIFC method and by circumoval precipitin test (COPT) using blood taken on the filter paper by finger prick. Every year, new children were registered to give an individual number and data of examinations were processed by the computer. In the main file in a magnetic tape, data were arranged in the order of the individual number and of the yearly record. Since the interval of re-examination differed by individuals, the number of negatives to be turned positive after 12 months was calculated at each group of different intervals and from the total positives, the incidence rate was calculated in a whole population.

In the examinations of 4 school years (SY), 1974/75, 1975/76, 1976/77 and 1977/78, ratios of children re-examined after 1 year were 31.6%, 29.9% and 60.3%, respectively.

The incidence rate by fecal examination during 3 years fluctuated much. By COPT, it went up in the 2nd year and maintained at the same level in the 3rd year. The combined results by fecal examination and COPT showed relatively stable values with increasing tendency in these 3 years.

The results of prevalence rate fluctuated much in 4 years with special high prevalence rate by COPT and consequently by the combined result in SY 1974/75. Among 3 methods of examination, the result of fecal examination was comparatively stable, probably due to its stability of detection even though the sensitivity is not so high.

In the present study, a method was established to calculate the incidence rate using the data of routine examination. The incidence was stable by the combined results of fecal examination and COPT.

Snails were controlled by draining the water around a school, Dagami Central II. However, the incidence of children in this school was slightly increasing from 15.7% to 19.3%. This may indicate that children get more infection in the other areas than around the school.

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**Prevalence and incidence rates of *S. japonicum* infections
among school children at Dagami, Leyte observed by fecal examination and COPT**

Examina- tion	SY 1974/75		SY 1975/76		SY 1976/77		SY 1977/78	
PREVALENCE:	No. exam.	% +	No. exam.	% +	No. exam.	% +	No. exam.	% +
Egg	552	33.7	577	30.5	554	26.7	1,255	37.9
COP	624	77.1	673	21.1	732	25.3	1,506	37.9
Egg/COP	638	77.7	690	33.5	741	34.1	1,515	47.4
INCIDENCE:			- no. *	%	- no.	%	- no.	%
Egg			157	25.6	127	41.3	396	36.9
COP			131	10.7	162	21.3	441	21.5
Egg/COP			141	22.1	137	24.2	373	27.0

* The number of negatives at the previous examination.

Dr. Burio (SCRS, Manila/MOH)

There are similarities between your computer-oriented data and our research data in Sorsogon under the WHO Workshop 1978; but there are also differences like in our identification number. Our identification number has seven digits, the first 2 digits refer to the place or barrio where the individual came from, the next three digits refer to the household number and the last 2 digits to the order in the family of the individuals.

The reason for the differences perhaps, is due to our goal which is to expand the study throughout the municipality of Irosin, Sorsogon. Whereas, your study is limited to a few individuals in Leyte.

Dr. Sy (IPH, UP)

1. What other parameters have you used in monitoring your cases?
2. Did you follow-up the height and weight of these school-children?

Dr. Tanaka (Univ. of Tokyo)

1. Intensity of Infection or EPG is recorded in my main file in the magnetic tape. No other parameters have been used.
2. The height and weight were not taken into consideration.

Dr. Lewert (Univ. of Chicago)

What are intervals between examinations -- any relationship to planting and harvesting?

Dr. Tanaka (Univ. of Tokyo)

It was difficult to determine the fixed interval between two examinations. The incidence was calculated using the data examined at different time intervals.

Dr. Yogore (Univ. of Chicago)

Do you have any figures for any place in the Philippines which indicate that annual incidence is decreasing?

Dr. Tanaka (Univ. of Tokyo)

I do not know, since school children in Dagami area are the only population in my study. No other information has been yet available.

HEALTH KNOWLEDGE, ATTITUDES AND PRACTICES RELATED TO SCHISTOSOMIASIS

T. V. TIGLAO

Institute of Public Health, University of the Philippines

A study on the knowledge, attitudes and practices related to schistosomiasis was conducted in Leyte in 1978 as basis for planning the educational component of the schistosomiasis control program.

Using the multi-stage cluster sampling, four municipalities were randomly selected from 22 endemic municipalities; four barangays were then randomly selected from each municipality and the total households from the 16 selected barangays were then interviewed. In addition the municipal officials and the teachers in the sample municipalities were interviewed and given questionnaires respectively. All in all, 1,935 households, 172 teachers and 49 municipal officials served as respondents.

Majority (62.7) of the sample householders belong to the low income bracket; 77.4% have low educational attainment (elementary education), with only one third (34.3%) gainfully employed.

The areas included in the interview schedule and questionnaire used were on the knowledge on common community health problems, on the cause, transmission and control of schistosomiasis, the attitude toward common diseases in the community as well as on schistosomiasis as measured by their rating on their seriousness, actions taken when sick with diseases mentioned, and reasons for such action. Attitudes towards and utilization of the Rural Health Units and the Palo Schistosomiasis Control Project were also included.

The study revealed that the people of Leyte are knowledgeable about their community health problems and are aware that schistosomiasis is one of such problems. However, about 1/4 (23.5%) are not aware of the disease.

The municipal officials, on the other hand, have a wider range of knowledge about community health problems and ranked schistosomiasis as the first of such problems. The teachers are the most knowledgeable of the three categories of respondents.

In the same manner, the respondents generally know the systems of the disease, the parts of the body affected, the contributory factors, and the needed action to take when sick with schistosomiasis. However, such knowledge of what to do is not translated into action. Of the 307 households respondents with schistosomiasis cases, 10% did not consult anyone. Of those who consulted, only 7% do so at once, while one fourth (24%) wait more than one year. Delay in action is attributed to financial and economic constraints.

Majority of the respondents consider the disease "serious" to "very serious". Households respondents who have not had the disease consider schistosomiasis more serious than those who have not had the disease.

Knowledge is limited on the transmission and control of the disease. About half (44.4%) of the 1,935 household respondents do not know. Those who know emphasize contact with bodies of water but little attention was given to improper waste disposal. Misconception regarding the cause of the disease was expressed. By the same token, knowledge on control measures gave emphasis to avoiding water contact with only 8% mentioning environmental sanitation.

Hardly do the respondents know about the snail (*Oncomelania quadrasi*). Only 8.9% of the 1,935 households respondents and 38.8% of municipal officials know the role of the snail in schistosomiasis transmission. Some believe the snail to be edible.

People's knowledge about the role of the snail in schistosomiasis control is a pre-requisite to their willingness to participate in snail control.

While people know that schistosomiasis is acquired through water contact people still continue to frequent such bodies of water as: rivers (42.7%); beach (24.7%); streams (18.6%); ricefields (13.5%). More than 40% go daily bathing, and laundering, crossing, farming, fishing, gathering vegetables, and defecating.

Only 10.6% of the population are served by piped municipal water. Therefore, the river still serves as their source of domestic water for laundering (24.9%), bathing (15.9%) and even for drinking (1.9%).

Toilets, even if in existence, are not utilized. While 82.2% have adequate toilets, only 41.5% "always use" such, with 24.7% being maintained very poorly. Open fields (13.0%), bodies of water (10.0%), public toilets (10.3%), or pit toilets (0.8%) are used by those without toilets.

People also do not realize that domestic animals can serve as reservoirs of infection in schistosomiasis. Hence 39.1% of pigs, 89.6% of dogs and 16.1% of carabao are left astray.

The attitude of the respondents towards their Rural Health Units is favorable. Only about 5% rated the RHU services as not satisfactory. More than 70% have availed of its services. However, only 26.8% of those who availed of its services say they were given health information and an even smaller percentage (4%) say they received information on schistosomiasis.

A smaller percentage of the respondents (27.6%) have availed themselves of the services of the Palo Schistosomiasis Control Project, understandably because not all are sick with schistosomiasis. Of these, 26.6% acknowledge having received schistosomiasis information. Majority of those who used the services rated the services satisfactory.

The ANOVA test of significance show that the knowledge of the households respondents on common community health problems, and the transmission, prevention, treatment and control of schistosomiasis is affected by sex, age, educational attainment, occupation, economic status and experience with the disease.

Age, educational attainment and economic class exert significant influence on the attitude towards the elimination of snail. On the other hand, age, prevalence of the disease and experience with the disease are significant in influencing attitude towards willingness to participate in snail campaign.

With regards to health practices, economic class, educational attainment and occupation make a difference in the health practices of the sample population.

It is evident that educational attainment and economic status are the common factors that influence health knowledge, attitudes and practices related to schistosomiasis.

Dr. Salazar (IPH, UP)

If age, sex and other socio-cultural determinants as observed do not affect the epidemiology of any disease, what will? — since these are the main areas of concern of human life in general. Anyway, do you feel that you are now in a position to make recommendations that will serve as guidelines in the formulation of effective, preventive and control measures against schistosomiasis in the Philippines?

Mrs. Soldevilla (OHEPT/MOH)

Follow-up of question of Dr. Salazar on target group for health education -- Clarification/ Illustration

- Findings of the study will provide specific baseline data on which target group would health education efforts be directed. For example -- Toilets, even if, etc.
- 82.2% -- with adequate toilets
- 41.5% -- always "use"
- 40.7% -- target group for more sustained health education to translate knowledge into practice

Dr. Umaly (College of Arts & Sci., UP)

Answer to difference 82.2 and 41.25% of those with toilets and those using it may not be in education but in availability of water supply to make the use of toilets more pleasant, e.g. less odorous and more convenient.

Dr. Sy (IPH, UP)

Of the 40.7% who have toilets but do not use them, did you try to find out the reasons for not using them? I think, this is not only due to the unavailability of water supply but also cultural in nature.

POPULATION EPIDEMIOLOGY OF *S. JAPONICUM*

Arturo C. REYES
W.H.O. Consultant

Certain observations during the past few years have markedly influenced the methods and techniques used in schistosomiasis epidemiological field studies. One of them is the growing awareness of the focality of schistosomiasis transmission in endemic areas emphasizing the need for studies in small communities. The other is an appreciation of the advantages of using quantitative rather than qualitative egg examination techniques in determining morbidity and mortality of infection. As a result, the study of the distribution of an infectious endemic disease such as schistosomiasis in whole populations (population epidemiology) using quantitative measurements is now considered to be a relatively new TDR method.

The advantages of conducting epidemiologic studies of whole populations of small communities are:

- (1) the entire population can be examined, baseline and other pertinent data necessary for further studies or evaluation of control measures can easily be gathered and updated as required;
- (2) it serves as a useful first step to determine etiologic associations;
- (3) short term follow-up is facilitated;
- (4) small communities in endemic areas serve as the ideal population in which to provide practical experience in the detailed organization, execution and field analysis of epidemiologic studies;
- (5) the use of local community organization not only in the conduct of field research but also as the mechanism of operational control could be explored;
- (6) guidelines for the control programme may be formulated and tested.

Although epidemiological studies on whole populations using quantitative methods have been done in endemic areas of *S. haematobium* and *S. mansoni*, reports of similar studies in endemic areas of *S. japonicum* are lacking. Such a study was therefore conducted as part of the Workshop on Population Epidemiology of *S. japonicum* held in Manila and Irosin, Sorsogon from July - November 1978.

The workshop was a joint activity of the NSCRS of the Ministry of Health, the Institute of Public Health and the College of Medicine, UP and the WHO.

The study will soon be published hence only excerpts of the methodology and results are given.

The area consisted of 2 barangays, Bolos and Gumapia in the municipality of Irosin, Province of Sorsogon.

Detailed scale maps of the 2 barangays with all the houses numbered were made and a household census was undertaken.

Labeled plastic containers were systematically distributed to all household members and collected the following morning. Each stool specimen was examined in the field laboratory using a modified thick smear and the MIFC method. The presence of occult blood was made by the Hematest method.

Morbidity questionnaires were administered to persons 10 years and older. Physical examinations were made on individuals 5 years and older with special attention being given to liver and splenic enlargement.

There were 795 persons distributed in 127 households. Of these, 755 (95%) were examined.

Of the 755 individuals examined, 326 (43.2%) were positive for *S. japonicum* by the modified thick smear method. An additional 48 persons (6.4%) negative by thick smear were positive by MIFC procedure, thus giving an overall prevalence rate of 49.5%. The prevalence rate in males (54%) was significantly higher than that in females (30.2%). The peak prevalence in males is in the age group 20 - 24 years, while in females it is in the age group 35 - 44 years.

The age group 15 - 19 years (both sexes) registered the highest output of 6,600 eggs/gm as well as the highest prevalence rate. Four and one tenths per cent (4.1%) of the total study population or 9.5% of those infected, excreted 50% of the eggs counted. The age range of this group is 6 - 53 years.

A history of dysentery was significantly more frequent in persons with high egg count (> 400 egg/gm).

The overall prevalence of hepatomegaly was 73% and was significantly associated with *S. japonicum* infection. The prevalence of hepatomegaly was consistently higher in males than in females in the infected than the non-infected for all age groups except in those 55 - 64 years of age. Hepatomegaly of 5 cm and greater tended to be associated with increasing egg counts.

Splenomegaly was significantly associated with *S. japonicum* infection; all individuals with splenic enlargement had also liver enlargement.

There was no correlation between *S. japonicum* infection and neurological defects, anemia, ascitis peripheral edema, superficial venous enlargement and elevated blood pressure.

Clustering of individuals with high egg counts was present: 38.2% of persons with high counts resided in 20.9% of the households with at least one highly infected person.

Of the 42 individuals (7 - 54 years of age) who had received treatment during the past 5 years, 31 (73.8%) were found to be passing eggs.

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Dr. Hayashi (Kofu City Hospital)

1. Do the words of neurological defects mean by paroxysmal symptoms such as generalized convulsion, Jacksonian and psychomotor?
2. According to our study on chronic cerebral schistosomiasis in Leyte, the ratio of incidence of paroxysmal symptoms is apparently higher than in non endemic areas.

Dr. Reyes (WHO Consultant)

1. Yes.
2. Our finding, probably due to small sample size, is that there is no significant difference in occurrence of neurological defects between infected and non-infected.

ANNUAL OCCURRENCE OF
SCHISTOSOMA JAPONICUM INFECTIONS IN THE WILD RAT,
RATTUS RATTUS MINDANENSIS, IN LEYTE, PHILIPPINES

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- 2) Merk Sharp and Dohme Limited Company (Japan)
- 3) Department of Parasitology, Institute of Medical Science, University of Tokyo
- 4) Schistosomiasis Control and Research Project, Department of Health, Republic of the Philippines

Annual prevalence of *Schistosoma japonicum* infections in wild rats, *Rattus rattus mindanensis*, in the pilot control area was investigated. It was supposed that the prevalence was useful as a parameter to evaluate the control works of schistosomiasis, since the rat has short life span.

One hundred wire-cage traps were set for one week every month from February 1978 to February 1979, in and around Central Elementary School II, Dagami, Leyte. The prevalence rates of *S. japonicum* in rats are shown in Table 1 and Figure 1. 163 out of 199 rats, 81.9%, were infected. No significant difference between infection rates in male and female rats. Infection rate increased from February to April and also it was high until July. All male rats were infected from April to July. And then, the prevalence rate decreased to September and fluctuated until December. Subsequently, it was going up to February 1979.

The prevalence of schistosome cercariae in *Oncomelania quadrasi* at the same area from July 1978 to March 1979 was shown in Table 2. It was going up from September 1978 to January 1979. This result showed the interrelation with the fluke prevalence in rats.

Table 3 shows the distribution of *S. japonicum* eggs in various organs of wild rats. Eggs were deposited in the lungs, brain, pancreas and so on. The frequent presence of eggs in the pancreas caused necrosis of pancreas tissues. And also we found the presence of eggs in the pancreas in 53 mice out of 458 experimentally infected mice. It is suggested that it may cause any symptoms in human schistosomiasis.

Table 4 shows the result of COP reaction in rat sera from Dagami. It shows 2 cases of false positive and 8 false negative cases out of 144 cases examined. Generally speaking, COP reaction is weak in sera of infected rats. Table 5, however, suggested that COP reaction was strongly exhibited in sera from rats deposited eggs in its spleen.

Consequently, it can be concluded that the rat is not so good definitive host, but it involves in agglomeration and dispersal of *Schistosoma japonicum* in nature.

Table 1. Prevalence of *Schistosoma japonicum* in rats of Dagami

Month of Investigation	Prevalence (%)					
	Male rat		Female rat		Total	
1978						
February	5/6	(83.3)	7/12	(58.3)	12/18*	(66.7)
March	7/8	(87.5)	5/6	(83.3)	12/14	(85.7)
April	3/3	(100)	2/2	(100)	5/5	(100)
May	9/9	(100)	4/5	(80)	13/14	(92.9)
June	9/9	(100)	11/13	(84.6)	20/22	(90.9)
July	6/6	(100)	12/12	(100)	18/18	(100)
August	8/10	(80)	8/9	(88.9)	16/19	(84.2)
September	4/7	(57.1)	1/2	(50)	5/9	(55.6)
October	3/5	(60)	7/8	(87.5)	10/13	(76.9)
November	7/9	(77.8)	6/7	(85.7)	13/16	(81.2)
December	3/5	(60)	3/7	(42.9)	6/12	(50)
1979						
January	12/16	(75)	7/9	(77.8)	19/25	(76)
February	4/4	(100)	10/10	(100)	14/14	(100)
Total	80/97	(82.47)	83/102	(81.37)	163/199	(81.9)

* No. infected rats/examined.

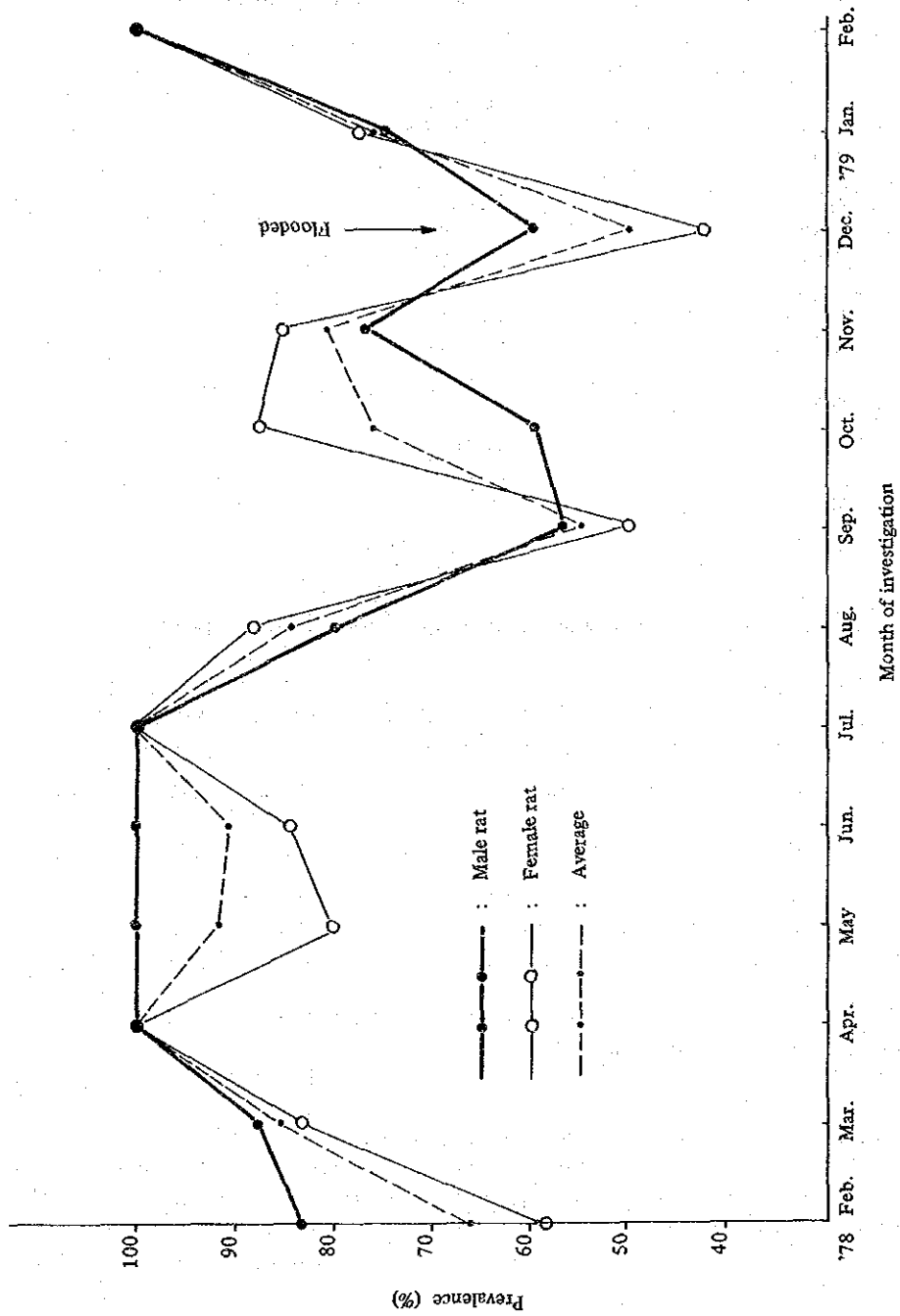


Fig. 1. Monthly fluctuation of the prevalence of *S. japonicum* infection in wild rats of Dagami

Table 2. Prevalence of schistosome cercariae in *Oncomelania quadrasi* of Dagami

Month collected	No. positive snails/Examined	Prevalence (%)
1978		
July	17/100	17.00
August	80/2,295	3.49
September	19/1,000	1.9
October	195/3,686	5.29
November	357/5,420	6.59
December	124/1,680	7.38
1979		
January	108/1,050	10.29
February	15/200	7.50
March	151/3,398	4.44

Table 3. Distribution of *S. japonicum* eggs in various organs of wild rats

Sex of rat	Liver	Intestine	Lung	Spleen	Kidney	Brain	Pancreas
Male	78/80	65/80	63/80	29/65	4/65	2/65	7/19*
Female	79/82	61/82	58/82	28/68	1/68	5/68	5/19
Total	157/162	126/162	121/162	57/133	5/133	7/133	12/38

* No. of egg-positive cases / No. examined.

Table 4. Result of COP reaction in rat sera of Dagami

No. of rats examined	Type of COP**				
		No reaction	I	II	III
Male: 75	Schisto. +* = 62	6	7	16	33
	Schisto. - = 13	12	1	0	0
Female: 69	Schisto. + = 58	2	8	17	31
	Schisto. - = 11	10	1	0	0
Total: 144	Schisto. + = 120	8	15	33	64
	Schisto. - = 24	22	2	0	0

* Examination of *S. japonicum* fluke by autopsy

** Criteria according to Yokogawa *et al.* (1967)

Table 5. COP reaction of sera from rats deposited eggs in the spleen

No. cases examined	Type of COP reaction			
	No reaction	I	II	III
Male rat 26	0	1	4	21
Female rat 24	0	1	5	18
Total 50	0	2	9	39

Dr. Lewert (Univ. of Chicago)

What is the meaning of statement "Rat is not a good host"?

Dr. Kamiya (Hokkaido Univ.)

In rats the number of eggs deposited in the intestine was not so many. In addition, few ulceration due to the egg deposition in intestinal mucosa was observed.

Furthermore, the percentage of degenerated eggs deposited in the various organs was higher and the number of flukes found in the rat were usually less than those in the mouse and the rabbit experimentally infected.

ANIMAL SCHISTOSOMIASIS: A REVIEW

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Bureau of Animal Industry, Ministry of Agriculture

Schistosomiasis is caused by any trematode species of genera *Schistosoma* and *Ornithobilharzia*. It is an important parasitic disease in man and animals in scattered but somewhat localized geographical regions of the world.

Schistosomiasis has long been recognized as an important disease among domestic animals in many parts of the world, including Asia, Europe, North and South America and Africa affecting cattle, goats, water buffaloes, horses, mules, dogs, pigs, rabbits and occasionally cats. Among wild animals cases have been reported in antelopes, zebra, and monkeys (Lapage, 1956) and experimental infections has been produced in opossums, capybaras, and pecaries (Torrealha *et al.*, 1958).

In the Philippines its occurrence in domestic animals was first reported by Tubangui and Pasco (1941). Of the 6 dogs, 6 pigs, and 21 carabaos examined, results showed that 2 dogs (33.3%), and 3 pigs (50.0%) were found positive for *S. japonicum*, but all the carabaos were negative. Hunter, *et al* (1946) reported that 13 pigs were found infected with *S. japonicum* in the region west of Naujan Lake in Oriental Mindoro. Pesigan, *et al.* (1953) surveyed Palo, Leyte and found that 31 dogs (18.2%), 1 goat (1.4%) and 14 rats (22.7%) positive for *S. japonicum*. Recently Oshima, *et al.* (1978) reported that among 45 field rates examined. In *Rattus mindanensis* (Hearns, 1905), 39 (86%) were found to be positive for *S. japonicum*. In an ongoing survey in Dagami, Leyte (Dumag *et al.*) found that among 1,473 animals (486 pigs, 323 dogs, 657 carabaos, and 7 goats) examined only 3 pigs (0.6%) and 32 dogs (9.9%) were positive for *S. japonicum* while all the carabaos and goats were found negative. As this study is still in progress it is premature to make conclusion.

The schistosoma species of public health and veterinary importance have been reviewed and enumerated, *S. mansoni*, *S. haematobium*, *S. japonicum*, *S. intercalatum*, and the mekong schistosome. So far, only *S. japonicum*, causes infections under natural conditions both in man and animals. Other species are specific for animals and accidentally develop in man (Hoeden *et al.*, 1964). In Taiwan, *S. japonicum* was found to infect only domestic and wild animals (Hsu *et al.*, 1954) and fails to develop to maturity in humans. The schistomes of veterinary importance may infect a wide range of animal hosts and cause considerable morbidity in livestock but are of little or direct public health importance. However, a case of *Schistosoma bovis* infection in man was reported by Roper (1951) in East Africa.

Cases of schistosomiasis among domestic animals have been long reported in many parts of the world. However, in the Philippines though carabaos, cattle, goats, pigs and dogs have been reported infected with *S. japonicum*, the disease was never incriminated as the cause of mortality among livestock and never considered as a serious disease among domestic animals. However, Yason (1975) reported she was able to produce the disease in pigs and that dramatic clinical changes were seen characterized by loss of appetite, rapid loss of weight, lethargy, paleness of the mucous membranes, diarrhea, muscle weakness, progressive emaciation and dehydration.

Pathogenesis and pathology of the disease in cattle have been studied by several authors

abroad but so far researches in the Philippines have been directed only on their role as reservoir hosts in the transmission of the disease. However, Yason (1975) studied the pathological changes experimentally in pigs and observed that the changes ranged from petechial hemorrhages to endophlebitis, periphlebitis, thrombophlebitis, and parasitic granulomas or pseudo-tubercles.

Since symptoms and history of the disease are not enough to distinguish schistosomiasis from other debilitating disease, diagnosis should be confirmed by the presence of eggs in the feces of infected animals.

Prevention and control of schistosomiasis is difficult, therefore several methods should be combined.

1. Destruction of the snail intermediate hosts.
2. Removal of snails by mechanical barriers or snail traps as practiced in Africa, but their efficacy is doubtful, even when combined with molluscicides.
3. Biological control has been tested on a limited scale in Kenya, but the results obtained are inclusive.
4. Efficient drainage, removal of water weeds and increased water flow, make the survival of the snails difficult (Pesigan, 1958)
5. Treatment of infected animals has its place in the control of schistosomiasis.

A successful control of *Schistosoma* infections in domestic animals which are considered the reservoir hosts in the transmission of the disease in man will in no doubt contribute a great deal in the prevention and control of schistosomiasis in man.

Dr. Yasuraoka (Univ. of Tsukuba)

Since 1975, we have examined a lot of fresh water snails including *O. quadrasi*, and found approximately 40 species of cercariae so far. No cercaria belonging to the genus *Schistosoma* has been found except that of *S. japonicum*.

This may indicate that we have no animal schistosomes other than *S. japonicum* in the Philippines.

**STUDIES ON THE CERCARIAE FROM *ONCOMELANIA QUADRASI*
IN LEYTE ISLAND, PHILIPPINES**

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The snail, *Oncomelania quadrasi* (Möllendorff, 1895), is a well-known snail because it is the only intermediate host of *Schistosoma japonicum* in the Philippines. In the course of epidemiologic studies of this fluke, many senior investigators have encountered some other cercariae aside from *S. japonicum*. Thus from *Oncomelania nosophora* in Japan, besides the cercaria of *S. japonicum*, three other species were reported; namely, *Cercaria longissima* (Suzuki et Nishio, 1914) Faust, 1924, *Cercaria okabei* Ito, 1949, and cercaria of *Maritreminoides caridinae* (Yamaguti et Nishimura, 1944) Chen, 1957. From *Oncomelania hupensis* in China, only one species, *Cercaria sensa* Komiya, 1952 was reported. But from *O. quadrasi* in the Philippines no such report has been made up to the present time.

During the past two years of 1975 and 1976, the present authors examined a lot of the snails, *O. quadrasi* in Leyte, Philippines. These snails were collected from nearly all of the endemic areas in Leyte, increasing the number to 6,423. Six species of cercariae including that of *S. japonicum* were found to be infected. These cercariae except that of *S. japonicum* are surmised to be non-pathogenic for the human body. By artificially increasing these five species of non-pathogenic cercariae there may result a decrease in the number of snails, because it is known that when a snail harbours some cercariae, this snail will be destroyed as a result of parasitic castration. So the study of these cercariae is very necessary, not only for the biological study but also for the biological control of schistosomiasis.

In this study the detailed morphological descriptions of each cercariae, with some remarks on their presumptive life history, were made and illustrated for the convenience of future study. Altogether, six species of cercariae including that of *Schistosoma japonicum* were found, namely two furcocercariae, one monostome cercaria, two xiphidiocercariae and one tail-less cercaria as shown in Table 1.

Studies are now under way to seek a new approach to biological control of *S. japonicum* through the competitive and predatory activities of one of these 5 species of larval trematodes within the snail host, *O. quadrasi*.

Table 1. A list of cercariae from *Oncomelania quadrasi* in Leyte Island, Philippines

(Results of 6,423 snail examination during 1975 - 1976)

Species	Presumptive adult form	Number of snail infected	Body size	Locality
<i>Cercaria leyteensis</i> No.1	Schistosomatidae (<i>S. japonicum</i>)	193 (3.00%)	160 x 64 μ m	Everywhere of surveyed area
<i>Cercaria leyteensis</i> No.2	Diplostomatidae (<i>Diplostomum</i> or <i>Alaria</i>)	5 (0.08%)	114 x 62 μ m	Palo, Tanauan
<i>Cercaria leyteensis</i> No.3	Notocotylidae	8 (0.12%)	433 x 214 μ m	Palo, Santa Fe, Pastrana
<i>Cercaria leyteensis</i> No.4	Lecithodendriidae	1 (0.02%)	97 x 55 μ m	Santa Fe
<i>Cercaria leyteensis</i> No.5	Microphallidae (<i>Maritreminoides</i>)	4 (0.06%)	75 x 34 μ m	Palo, Santa Fe
<i>Cercaria leyteensis</i> No.6	Monorchidae?	2 (0.03%)	267 x 103 μ m	Pastrana

Dr. Francisco Sy (Institute of Public Health, UP)

Have you tried infecting cercariae leyteensis No.2 to No.6 to experimental animals and try to recover adult schistosome?

Dr. Yasuraoka (University of Tsukuba)

Not yet.

Dr. Kawanaka (NIH, Tokyo)

Cercaria leyteensis No.3 encysts easily in the outside without any second intermediate host. During the past eight months we attempted to feed 8 ducklings and 2 chicks with this metacercaria, but we could not get the adult worm yet.

We found three more species of cercaria from *Oncomelania quadrasi* in Leyte Island.

We found a cercaria belonging to the family of Gymnophalidae in two snails collected from Dagami. This cercaria is alike to *Cercaria sensa* from *Oncomelania hupensis* in China in many points, but differs from it because of its possessing a shorter tail, in the aspect of the excretory canal and a few other points. The Cercaria encysts in the same host snails.

The second cercaria was found in two snails from Alcaraz, near Palo. This cercaria is a tail-less without stylet. The body size of this cercaria is slightly larger than *Cercaria leyteensis* No.6 that is tailless cercaria with a short stylet.

We found another monostome cercaria in only one snail from Alcaraz. The body is ellipsoidal in shape without acetabulum. One pair of pigmented eyespots is present, and adhesive organs are located on both posterolateral parts of the body. This cercaria does not encyst in the outside.

CONVERSION OF *SCHISTOSOMA JAPONICUM* CERCARIAE
TO SCHISTOSOMULA IN SERUM-SUPPLEMENTED MEDIA,
AND SUBSEQUENT CULTURE *IN VITRO*

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Techniques which adequately support the growth of schistosomes *in vitro* may provide us many informations on the physiology, nutrition, and immunology of the parasites. They may also be used to study the mode of action of antischistosomal drugs. Although many attempts have been made to culture *Schistosoma mansoni* *in vitro*, there have been only a few studies on the cultivation of *S. japonicum*.

We have found that *S. japonicum* cercariae, axenized by washing in NCTC 109, transformed to schistosomula when incubated directly in NCTC 109 containing human or rabbit serum at 37°C. The resultant schistosomula were grown *in vitro* to adults which mated, although the females did not produce eggs.

In medium with human serum tail shedding took place, and by 8 h approximately 50% of the organisms had lost their tails. After 24 h the tailless larvae were very active and assumed the elongated shape typical of the lung form in the mouse. Evacuation of preacetabular glands was observed in almost all tailless larvae after 4 h incubation. Based on their morphology, preacetabular gland depletion, characteristic muscular contraction and motility, the tailless larvae could be described as "schistosomulum-like". After 72 h a population which initially contained almost exclusively whole cercariae converted to a population containing 70 - 80% schistosomulum-like larvae and only 10 - 20% dead larvae.

In medium with 50% rabbit serum more than 80% of the larvae were tailless after 72 h incubation. Most were comparable to the lung stage. In control experiments in NCTC 109 without serum, the intact cercariae remained active for approximately 24 h after which time they became motionless and opaque, and were all dead by 72 h incubation.

Definitive proof that the larvae produced *in vitro* without a membrane are true schistosomula would be their ability to develop to adult worms; we therefore continued our cultures in the same medium, which still contained free tails, nontransformed and semitransformed organisms. One percent washed, packed blood cells was added on day 4, and the medium replaced twice weekly. The schistosomulum-like larvae or even larvae with shrunken tails begun feeding on red blood cells on day 7 and reached the gut-closed stage by day 12, an equivalent rate of development to that in the mouse. They attained a relatively late stage of development by day 30 at which time males produced sperm in the anterior testes and mated with females but the females did not produce eggs.

To determine the threshold concentration of serum necessary for induction of the cercaria-schistosomulum transformation, *S. japonicum* cercariae were incubated in media with different

concentrations of human serum in NCTC 109. The results showed that 5%, 10%, 25% and 50% serum-supplemented media were equally effective. Subsequently, the effect of more diluted concentrations of human serum was tested. In the lower concentrations of the serum, i.e., 0.25%, 0.5% and 1.0%, almost all cercariae remained intact and all the worms were found dead by 96 h incubation. The 2.0% concentration of serum, however, enhanced the transformation of cercariae to schistosomula, although the rate and extent were lower than those in 4.0%.

In another series of experiments, intact *S. japonicum* cercariae were incubated in medium with 50% human serum at 27°C and 37°C. Following 4 h incubation at 37°C more than 40% of the larvae were tailless and approximately 60% at 24 h. However, the larvae incubated at 27°C became tailless more slowly than those at 37°C.

In all the experiments so far described, intact cercariae were incubated in NCTC 109 supplemented with unheated human or rabbit serum. To determine whether heat labile factors in serum affect the cercaria-schistosomulum transformation, we used human and rabbit serum heated to 56°C for 30 min. The results showed that in 50% heat-inactivated serum supplemented media, both *S. japonicum* and *S. mansoni* cercariae transformed to schistosomulum-like larvae at a slower rate than in unheated serum. However, by 72 h incubation, the proportion of schistosomulum-like larvae in media with heat-inactivated serum was similar to that in media with unheated serum.

Dr. E. Garcia (IPH, UP)

1. Have you tried RPMI 1640?
2. How fast is the turnover of the schistosome membrane?

Dr. Yasuraoka (Univ. of Tsukuba)

1. Not yet. In NCTC 109 alone, schistosomula can survive for more than 4 weeks, though no growth can be observed.
2. During the course of cultivation of schistosomula *in vitro*, the turnover of the tegument membrane may take place very frequently.

Dr. Francisco Sy (IPH, UP)

1. What possible factors in the medium induce the transformation of cercariae to schistosomula?
2. For how long were you able to maintain the schistosomula and up to what stage of development?

Dr. Yasuraoka (Univ. of Tsukuba)

1. It is possible that lecithin and/or phospholipids in serum could have participated in the process.
2. You can culture *S. japonicum in vitro* in media containing equal volumes of NCTC 109 and human serum for more than half a year. The schistosomula can grow to adults which mate, although the females do not produce eggs.

THE EMERGENCE OF *SCHISTOSOMA JAPONICUM* CERCARIAE
FROM *ONCOMELANIA QUADRASI* IN LEYTE, PHILIPPINES

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There have been many observations on cercarial emergence of human *Schistosoma*, including a few reports on that of *S. japonicum*. Isobe (1923), observing the shedding of *S. japonicum* cercariae from *Oncomelania formosa*, as well as Osaka (1936), Komiya & Ishii (1954) and Gumble *et al.* (1957), observing that from *O. nosophora*, reported that no periodic emergence took place. On the other hand, Mao *et al.* (1949), who observed the shedding from *O. hupensis*, reported that the shedding occurred during the daytime. Bauman *et al.* (1958), observed with *O. quadrasi*, and concluded that the natural shedding was of a definite nocturnal periodic nature. And Pesigan *et al.* (1958), observing with *O. quadrasi*, almost agreed with Bauman *et al.* Kifune & Takao (1970) observed the shedding *O. nosophora*, reported that initial emergence began within 2 hours after the submergence of the snails and the next release was usually observed at the following night irrespective to the hour of the submergence. There seemed to be strain differences in the shedding of *S. japonicum* cercariae.

The present study has been undertaken to know whether the shedding of *S. japonicum* cercariae from *O. quadrasi* shows periodic nature, as Bauman *et al.* (1948) observed.

Before experiments, the snails were kept in a petri dish with a wet filter paper at the bottom for a few days, so that the snails barely released cercariae. Four infected snails were put into a small dish with 1 cm diameter and 1.5 cm height containing 0.8 - 0.9 ml of yesterday's tap water. All cercariae in dishes were counted every 2 hours under a dissecting microscope, if numerous, after fixing by formalin. Light conditions used in this study were diffused sunlight near window. Room temperature was controlled between 24°C and 26°C. The observation lasted at least 4 days, although one group of 4 dishes was observed for the 13 successive days from Jan. 13 to 26, 1979.

Results in table and figure are summarized as follows: The shedding of *S. japonicum* cercariae from *O. quadrasi* snails was observed quite unlike the previous report by Bauman *et al.* (1948). This schistosome cercariae showed two patterns in the emergence. One was the initial non-periodic emergence after the start of submerging the snails. Another was the following periodic emergence in the afternoon which was almost of a diurnal nature. The peak of the periodic emergence occurred mainly between 2 PM and 4 PM. This periodic emergence seemed to be influenced in daily number of cercariae by not only exogenous light intensity

but also endogenous potential emergence capacity in which cercarial reproduction was of a cyclic nature in the snail host.

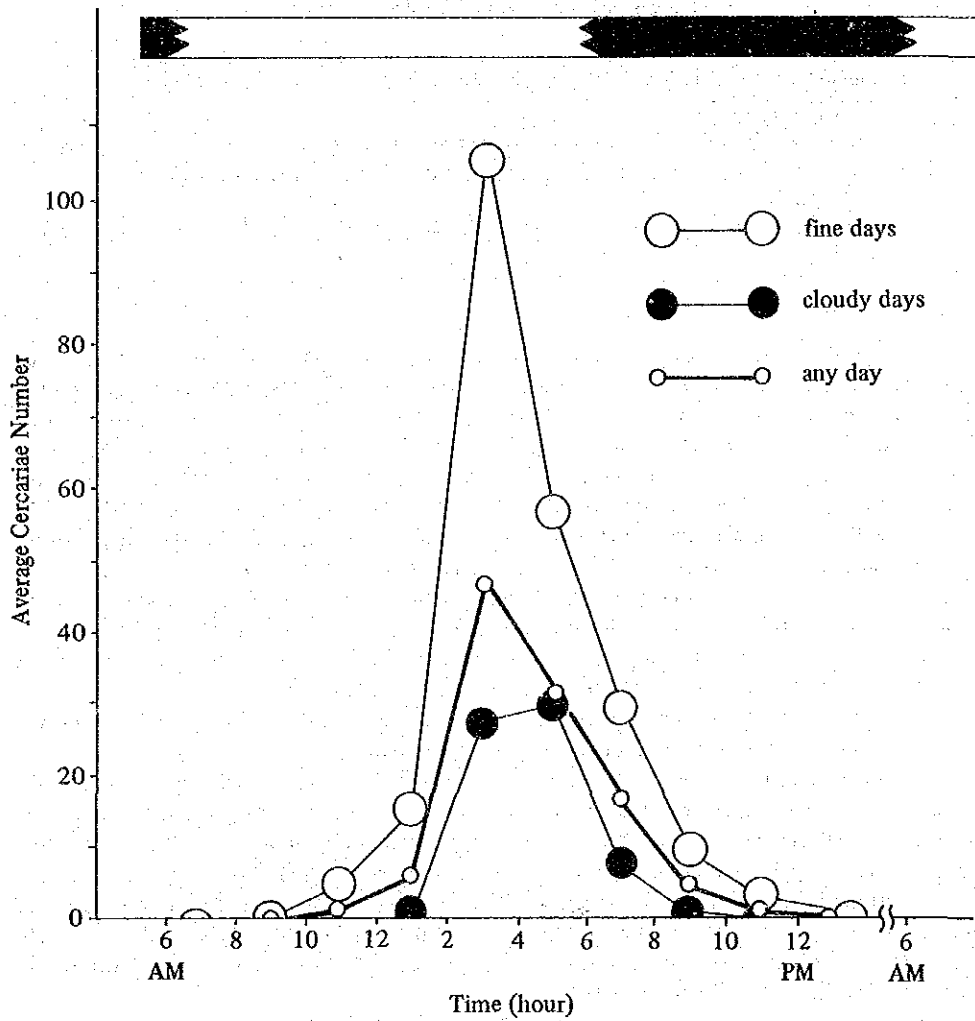


Fig. 1. Effect of light intensity on the periodic emergence of *S. japonicum* cercariae from *O. quadrasii*

Table 2. The periodic emergence of *S. japonicum* cercariae from *O. quadras* for the 12 successive days

Date	Weather	No. of cercariae from 16 snails												(Total)
		AM 6	AM 8	AM 10	AM 12	PM 2	PM 4	PM 6	PM 8	PM 10	PM 12	AM 6		
Jan. 13, '79	fine				† 1,031	318	121	45	18	4	4	4	1,541	
Jan. 14, '79	fine	0	0	0	0	7	20	14	7	2	0	0	50	
15	*	0	0	0	0	0	0	17	7	9	4	4	37	
16	cloudy	0	0	0	0	0	0	0	0	0	0	0	0	
17	cloudy	0	0	0	6	81	81	24	7	0	0	0	199	
18	fine	0	2	0	32	308	113	78	26	8	4	4	571	
19	fine	0	1	0	1	18	16	3	0	0	0	0	39	
20	cloudy	0	0	0	0	0	0	0	0	0	0	0	0	
21	cloudy	0	0	0	4	53	14	1	0	0	0	0	72	
22	**	0	0	0	0	0	0	31	5	1	0	0	37	
23	*	0	1	4	0	5	1	1	0	0	0	0	12	
24	fine	0	0	15	29	87	76	20	4	0	0	0	231	
25	cloudy	0	0	0	0	0	55	12	0	1	0	0	68	
14 - 25	any	0	4	19	72	559	376	201	56	21	8	1,316		
	av.	0	0.3	1.5	6.0	46.6	31.3	16.8	4.7	1.8	0.7	109.7		
14, 18, 19, 24	fine	0	4	19	62	420	225	115	37	10	4	896		
	av.	0	1.0	4.8	15.5	105.0	56.3	28.8	9.3	2.5	1.0	244		
16, 17, 20, 21, 25	cloudy	0	0	0	6	134	150	37	7	1	0	335		
	av.	0	0	0	1.2	26.8	30.0	7.4	1.4	0.2	0	67		

Experiment 4

† : start of submergence

* : fine in the morning and cloudy in the afternoon

** : cloudy in the morning and fine in the afternoon

DRUG TRIALS FOR SCHISTOSOMIASIS JAPONICA IN THE PHILIPPINES: A REVIEW

Bayani L. BLAS

Schistosomiasis Control and Research Project, Palo, Leyte

A number of parenteral and oral preparations in the chemotherapy of *Schistosoma japonicum* infection have been tried. The parenteral preparations are all antimonials which have shown relatively good efficacy but with severe toxic side reactions which are alarming in nature.

Among the oral preparations tried, the suppressive management with Ambilhar for 10 days which may be repeated from 1 to 3 months for 3 doses may be considered as a stop gap measure in the meantime that data on a greater number of patients are being gathered with a single day dose of Biltricide or praziquantel.

Dr. Yogore (Univ. of Chicago)

The basic philosophy of suppressive treatment is to lessen the number of eggs reaching the environment and interfere with transmission. Is there any available evidence that tends to show that there has been any effect on transmission with the suppressive therapy?

Dr. Blas (SCRIP, Palo/MOH)

We have not actually determined the effect of suppressive doses on the transmission of the disease. The suppressive dose in Ambilhar was thought of in order to reduce its side effects.

NIRIDAZOLE FOR THE TREATMENT OF SCHISTOSOMIASIS JAPONICA IN THE PHILIPPINES : A REVIEW

Bayani L. BLAS

Schistosomiasis Control and Research Project, Palo, Leyte

Initial trials with niridazole at 20 to 25 mg/kg/day for 10 to 14 days was found to be toxic. Subsequent trials was reduced to 10 to 15 mg/kg/day. Under this dosage regime, a total of 309 patients were treated for 24 days. An average of 78.8% stool negative conversion rate was obtained 1 to 6 months after treatment. Among those with high or low egg output, a total of 50.8% dropped out or discontinued treatment due to a variety of causes, the most common of which was the long duration of treatment.

A suppressive 10-day course of treatment was tried first in 35 patients with an average egg reduction of 84.6% one to six months after treatment. Percent becoming negative was 28.6% during the first month which was subsequently reduced the following months finally becoming zero in the 6th month. An additional 332 patients were further treated with this 10-day suppressive course of treatment. Seven patients had to stop the medications due to side reactions especially hallucinations, convulsive seizures and insomnia. Children generally tolerate the drug better. Retreatment of patients at 3 months interval maintained the egg reduction and negative egg conversion rates up to the 6th month of stool follow-up.

Deworming of patients reduced significantly by the vomiting and abdominal pain arising from the administration of the drug.

Based from the above findings the following can be recommended:

1. Patients who can tolerate the drug can be given 10-15 mg/kg/day for 24 days. To prevent wasting of the drug and to be able to follow-up the patient, tablets of Ambilhar good for 5 to 10 days should only be given with instructions for the patients to return for more tablets after the drug has been consumed.
2. For those who cannot tolerate the drug, a suppressive course of management for 10 days can be given which may be repeated at 1 to 3 months interval for 3 courses depending on the clinical and parasitological improvement of the patient.
3. Prior deworming before Ambilhar treatment is recommended to reduce the abdominal side reactions such as vomiting and abdominal pain.

Dr. Domingo (College of Med. UP)

Did you stratify your patients as to severity before treatment?

Dr. Blas (SCRIP, Palo/MOH)

No, except for Biltricide where patients were divided into different groups based on their respective egg counts. All patients are without hepato-splenomegaly for fairness in the comparison of the various drugs tried.

Dr. Degremont (Swiss Trop. Inst.)

1. Did you try to reduce preventively side effects due to Ambilhar by adjuvants like Valium or Phenobarbital?
2. After a radical cure of *S. haematobium* or *S. mansoni* by Ambilhar, black eggs (dead eggs) are still eliminated for 6 to 12 months. Is it the same with *S. japonicum*?

Dr. Blas (SCRIP, Palo/MOH)

1. No Valium or phenobarbital were given for symptomatic relief of side reactions, particularly hallucinations and convulsive seizures.
2. Our patients were only followed up for 6 months after treatment and we have not noticed such effect on *S. japonicum* eggs in this span of time.

Dr. Tanaka (Univ. of Tokyo)

How do you define the deworming by the drug in schistosomiasis?

Dr. Blas (SCRIP, Palo/MOH)

Deworming is not actually for the treatment of schistosomiasis. It was done to see whether the abdominal reactions such as nausea, vomiting and abdominal pain can be reduced.

Dr. Cruz (IPH, UP)

1. Will you please explain what you mean by deworming?
2. Did you do deworming on all your patients?

Dr. Blas (SCRIP, Palo/MOH)

1. By deworming, we gave combantrin or pyrantel pamoate before treatment with Ambilhar.
2. No, about half of the cases in one trial were dewormed and the other half were not dewormed. Results were then compared as to their reactions to Ambilhar treatment.

**TOXICITY AND EFFICACY STUDY ON EMBAY 8440 (PRAZIQUANTEL)
IN EARLY HUMAN *SCHISTOSOMA JAPONICUM* INFECTION
IN THE PHILIPPINES**

Alfredo T. SANTOS, Jr., Bayani L. BLAS, Julian S. NOSEÑAS,

Gerundio P. PORTILLO and O. M. ORTEGA

Schistosomiasis Control and Research Service, Ministry of Health

A durable blind clinical trial on Embay 8440 (praziquantel) using two dosage schemes both of which are administered orally in one day was conducted on 60 hospitalized early schistosomiasis cases to evaluate its toxicity and efficacy. Thirty patients received a single dose of 50 mg/kg body weight and the other 30 patients received 3 doses of 20 mg/kg each every 4 hours. A control group of 30 patients were given placebo. Side reactions to the drug were generally mild and well tolerated with the divided dosage showing lesser and milder reactions than the single dose. No adverse effects to the cardiovascular, hematopoietic, hepatic and urinary organs were observed. The stool follow-up one year after treatment revealed that praziquantel could render stools negative and/or suppress egg production significantly. With its apparently low toxicity and high efficacy and short treatment course, praziquantel promises to be a drug suitable for the mass treatment of schistosomiasis in the Philippines.

Dr. Domingo (College of Med., UP)

1. What is the reason for the placebo group?
2. What do you mean by complaints? What complaints do you consider due to *S. japonicum*?
3. You classify fever as a side effect of praziquantel, how did you exclude other causes of fever?

Dr. Santos (SCRS, Manila/MOH)

1. The use of placebo in the initial trials with praziquantel is necessary in order to assess more carefully drug related toxicity and to a certain extent efficacy, since egg output normally fluctuates.
2. Since most of the common complaints of schistosomiasis patients could also be caused by common helminthic infections and diseases, it is difficult to attribute symptoms specific to schistosomiasis.
For this study pre-treatment complaints of patients were used as a reference point during the follow-up. It is felt that since there was no other attempt to treat other conditions, it was presumed that the disappearance of pre-treatment complaints was due to the drug.
3. Fever in this study was considered drug-related if it was not present before treatment.

Dr. Lewert (University of Chicago)

What is the basis for terming these cases "early" when they may have been infected for 10-15 years?

Dr. A. T. Santos, Jr. (SCRS, Manila/MOH)

In this study, early refers actually to mild cases irrespective of duration of infection, which include patients with hepatomegaly of not more than 3 inches below the xyphoid process.

The use of the term "early" is actually intended to differentiate patients from the "late" manifestations of the disease, like those with hepato-splenomegaly.

Dr. Sy (IPH, UP)

1. What dosage of praziquantel is being used in your mass treatment?
2. Have you tried using this drug in single dose with concomitant symptomatic therapy during this mass treatment?

Dr. A. T. Santos, Jr. (SCRS, Manila/MOH)

1. We are using a dose of 60 mg/kg body weight administered either in 2 or 3 divided doses.
2. No, this has not been done since severe reaction occur only in a significantly fewer number of cases.

CLINICAL STUDY OF CEREBRAL AND HEPATOSPLENOMEGALY CASES ASSOCIATED WITH SCHISTOSOMIASIS IN LEYTE ISLAND

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Gerundio P. PORTILLO²⁾ and Bayani L. BLAS²⁾

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2) *Schistosomiasis Control and Research Project, Paló, Leyte, Philippines*

Since February 1975, we have been studying the clinical symptoms of cerebral and hepatosplenomegaly cases associated with schistosomiasis and their electroencephalographic (EEG) findings as well.

We have also tried to treat these cases with an anticonvulsant and antischistosomal agents such as Fuadin, niridazol and praziquantel.

Seventy-five subjects with cerebral schistosomiasis (CSJ) were selected randomly from 300 and some patients with suspected CSJ who showed symptoms of the central nervous systems such as convulsion, attack like disturbance of consciousness, dysphasia and hemiparesis.

The ages of the subjects ranged from 14 to 63 years, with a mean of 33. The ratio of males to females was 48:27.

As for the clinical pictures of the subjects, 71 patients showed the paroxysmal disease. Of the 71 patients, 54 showed convulsion, and 13 showed psychomotor seizure and one autonomic seizure. Of the convulsive group, Jacksonian was observed in 33 patients. That is to say, 58 patients or 82% of the paroxysmal disease group showed the localized lesion of the brain. The patient with late onset paroxysmal disease in which the initial attack occurred after the age of 20 were present in 49 to 69% of this group.

The frequency of attacks, when cases with the clinical type was excluded, was 1-3 times a day in 16 patients, 1-3 times a week in 19 patients and 1-2 times a month in 16. There were 51 patients having attacks more than once a month, and they represented 72% of the paroxysmal disease group.

The result of EEG was normal in 24 to 32%, borderline in 13 to 17%, and abnormal in 38 to 51%. The characteristic abnormal or borderline findings of EEG was the random and paroxysmal slow waves with asymmetry.

For hepatosplenomegaly cases, the subject of our study were 78 patients having primary hepatosplenomegaly who were selected from the list of schistosomiasis patients recorded by Schistosomiasis Control and Research Project.

The ratio of men to women was 75 to 3. Subjects ranged in age from 5 to 57 years, with a mean age of 17, and with a mean onset age of 14. Subjects were composed of 7 patients under 10 years of age, 56 patients between the age of 10 to 19 and 9 patients over 20 years old.

The pattern of the occurrence of hepatosplenomegaly was almost the same in all the patients. Abdominal enlargement occurred within 3 to 12 months after the appearance of bloody mucous stools. Hepatosplenomegaly had been present for 3 years or less in 74% of the patients and for 7 years or more in only 13%.

Based on the degree of hepatosplenomegaly, the patients were classified into the three categories of hepatomegaly (H), hepatosplenomegaly (HS) and splenomegaly (S). The clinical

timespan was less than 3 years in 86% of the patients with the H type and in 72% of the HS type. However, in the S type, their clinical timespan did not show any particular tendencies.

Hepatosplenomegaly was characterized by an elastic and hard liver having a smooth surface, obtuse edge and distinct border. In most of the cases, H was located in the center of the epigastrium, being symmetrical in the tip of the ensiform process. The mean size of the liver by palpable was 9 cm in both of the H and HS types.

Hardness of the S type was slightly more consistent than that of the liver. The surface of the spleen was smooth and the edge was obtuse. The mean size of the spleen was 11 cm in the HS cases, and 16 cm in the S cases.

In the relationship between hepatosplenomegaly and the results of the laboratory examination, of the 38 patients who underwent liver function tests, 5 patients with H and 3 patients with HS had slight liver impairments. On the other hand, peripheral blood examinations revealed marked anemia in 30 patients with the H and in as many as 23 patients with the HS type. All of the patients with marked anemia showed less than 200×10^4 per cubic millimeter. Leukopenia was observed in only 7 patients and in which the degree of leukopenia revealed less than 3000 per cubic millimeter. Thrombopenia was observed in only 3 patients.

The result of EEG findings in hepatosplenomegaly was normal in 63 patients, borderline in 10 patients and abnormal in 5 patients. There was no special relationship between hepatosplenomegaly type and abnormal or borderline EEG findings.

During the course of our study, we had an impression that many subjects were afflicted with anemia and/or malnutrition, and were accompanied with slow secondary sex traits. Height of the subjects was compared with the average height obtained from 2,620 pupils of 13 elementary schools in Leyte Island. Thirty-five boys with the ages of 7 to 14 years were selected and studied; 11 were within the normal range, 7 were comparatively small and 17 were remarkably small. In addition, of these 24 small boys, 22 were also found to be smaller than their healthy counterparts.

As to familial factors, the 78 patients in this study were from families having more than two patients in the same family.

We found 12 cases of familial aggregation of hepatosplenomegaly, i.e. 8 and 4 families had 2 and 3 patients in the same family, respectively. In two cases, however, no splenomegaly but hepatomegaly was seen in youngsters.

We checked neurological symptoms such as finger tremors, muscle rigidity, episodic or paroxysmal disturbance of consciousness and convulsion in the subjects. However, none of them had any sign of the above mentioned symptoms, i.e. there were no cases of hepatocerebral type in the subjects.

Dr. Cruz (IPH, UP)

How did you rule out the other neurologic causes in your suspected cerebral schistosomiasis cases?

Dr. Hayashi (Kofu City Hospital)

Unfortunately, we haven't had any autopsy and necropsy cases. In my personal opinion, some abnormal lesion should be located at motor area or temporal lobe areas of the brain. However, I do not know what kinds of lesion is present.

THERAPEUTIC STUDIES OF CEREBRAL SCHISTOSOMIASIS IN PALO, LEYTE

Lilian C. TORMIS

Schistosomiasis Control and Research Project, Ministry of Health

Seventy-one cases of cerebral schistosomiasis were examined in Palo, Leyte and 56 patients were treated with either anti-schistosomal or anticonvulsant drugs.

Compared with the results prior to therapy, the ratio of abnormal EEG to borderline was remarkably improved. Seizures completely disappeared in 41% of the treated patients.

With the lack of more effective and non-toxic drugs for schistosomiasis, it can be stated that anticonvulsants would complement antischistosomal drugs in the treatment of cerebral schistosomiasis. In the more difficult cases wherein seizures continue even after treatment with antischistosomal drugs, it is quite impossible to obtain an improved EEG pattern, hence, it is of utmost importance that their symptoms or the frequency of the seizures should be controlled with the proper use of anticonvulsants and specific chemotherapy.

With the advent of Biltricide or praziquantel which is an apparently better drug, several cerebral cases were treated with mild to moderate side-reactions such as fever, abdominal pain and vomiting. In two patients, both grand mal cases, an abortive type of convulsion developed. More cases are intended to be treated and follow-up of treated cases will be made to determine whether seizures will be reduced or will entirely disappear.

Dr. Domingo (College of Med. UP)

How did you verify the diagnosis of cerebral schistosomiasis?

Dr. Tormis (SCRIP, Palo/MOH)

Our diagnosis for cerebral schistosomiasis was based on laboratory examination as well as clinical and EEG examination, in as much as we do not have adequate facilities for further and complex procedures as C-T scan, etc.

Dr. Abear (SCRS, Manila/MOH)

In giving the drug to these cerebral cases, did you expect these cases to be improved or cured of their symptoms? I'm asking this because, what causes the symptoms is the granuloma formation around the eggs and this drugs are not effective on the granuloma, so that you can not expect that those anti-schistosomal drugs will have any effect at all.

Dr. Tormis (SCRIP, Palo/MOH)

Our investigation revealed improvement for complete disappearance of seizures in 18 of 28 cases after Fuadin therapy. Previous studies also showed the satisfactory response of cerebral cases to Fuadin and this was attributed to the initial egg-suppression effect of this

drug which probably prevents the formation of new granuloma or resolution existing of new ones. Although there are untreated cases with spontaneous improvement, it must be noted that a greater percentage of improvement is obtained after therapy than without treatment.

Dr. Burio (SCRS, Manila/MOH)

1. How significant is prevalence of cerebral schistosomiasis from prevalence of seizure in the general population?
2. Is EEG pattern conclusive of a space occupying lesion among cerebral schistosomiasis cases?
3. Did you rule out paragonimiasis from your cerebral cases?

Dr. Tormis (SCRCP, Palo/MOH)

1. The world wide distribution of epilepsy or seizures is 0.3 to 0.5%. In Palo, Leyte where population is about 26,000 there are probably 285 cases of suspected cerebral schistosomiasis or patients with paroxysmal disease and this corresponds to about 1.1% of inhabitants which is 2 - 3 times higher and could be traced to exogenous factors, such as the endemicity of *S. japonicum* in this area.
2. The EEG pattern of a progressive space occupying lesion such as brain tumor is quite different from that of cerebral schistosomiasis. However, in cases where the size of brain tumor is still small, EEG pattern looks like in cerebral schistosomiasis, but it does not show any diffuse alpha pattern. The EEG pattern should be correlated with laboratory and clinical findings to be conclusive of the diagnosis of cerebral schistosomiasis.
3. Paragonimiasis was ruled out by the absence of history of respiratory symptoms and absence of characteristic ova in the sputum.

Dr. Sy (IPH, UP)

1. Is there any typical EEG pattern of these cerebral schistosomiasis cases?
2. What is the characteristics (age, sex, stay of disease) of the three patients who died? Were they under any form of antischistosomal therapy?

Dr. Tormis (SCRCP, Palo/MOH)

1. The typical EEG pattern commonly encountered in cerebral schistosomiasis is a diffuse alpha pattern, however, a more interesting finding is slight asymmetric theta waves predominant in the posterior leads and occasionally at the temporal area.
2. One case was a 17 yr. old male who died of status convulsion; second case was 37 yr. old male with jaundice and the third case was a 43 yrs. old male who presented such symptoms as severe headache, frequent vomiting and coma before death. All were not under any form of antischistosomal therapy.

STUDIES ON THE TREATMENT OF HEPATOSPLENIC SCHISTOSOMIASIS JAPONICA WITH PRAZIQUANTEL

Gerandio P. PORTILLO

Schistosomiasis Control and Research Project, Palo, Leyte

Thirty-eight hepato-splenic cases of schistosomiasis were given a one day treatment course with praziquantel to determine whether the drug would produce any untoward reactions referable especially to the central nervous system. The patients were divided into 2 treatment and one control group. One group received a single dose schedule of 1 x 50 mg/kg body weight, one group in divided doses of 3 x 20 mg/kg body weight given every 4 hours and the last received placebo. The placebo group subsequently received praziquantel.

No clinical or encephalographic evidence was encountered which denoted central nervous system irritation, neither adverse effects referable to the various organ systems were observed. Side effects were generally mild to moderate and transient.

Results of the 6th months post-treatment stool follow-up showed significant parasitological cures and/or reduction in egg output.

On the basis of the effectivity and the absence of undesirable clinical or laboratory evidence of toxicity to the central nervous system or other organ system which could be attributed to praziquantel, it is apparently safe to administer the drug in hepato-splenic schistosomiasis.

Dr. Abear (SCRS, Manila/MOH)

Did you give anthelmintics to your patients prior to treatment with praziquantel?

It is possible that praziquantel might irritate parasites other than *Schistosoma*, like *Ascaris* or hookworm producing those side reactions like abdominal pain.

The abdominal pain might not be due to gastric irritation because the nature of pain described was colicky.

Dr. Portillo (SCRIP, Palo/MOH)

No, we did not give any anthelmintic before treatment. Yes, I agree with you that some of the side effects could be attributed to other parasites.

Dr. Martin-Ranada (SCRS, Manila/MOH)

Noticing the papers reported on praziquantel, the most common side effect is gastric irritation manifested by abdominal pain, nausea, and vomiting immediately after tablet intake. Is it possible for the drug manufacturers to produce tablets which will be absorbed in the lower gut for better patient tolerance?

Dr. Portillo (SCRIP, Palo/MOH)

Yes, I agree with you, that entevic coating might eliminate or deminish the side effects which denoted gastric irritation.

Dr. A. Degremont (Swiss Tropical Institute, Switzerland)

In Shanghai and Wushi China doctors have treated more than one thousand patients with praziquantel and reported that the more frequent side effect is arhythmia just after abdominal pain. I would like to know if such side effect has never occurred among your patients.

Dr. Portillo (SCRIP, Palo/MOH)

In this study, no such changes were noted among the subjects either clinically or in the ECG tracings.