

Schistosomiasis control in the 21st century Proceedings of the International Symposium on Schistosomiasis, Shanghai, July 4–6, 2001

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Abstract

A total of 120 papers were presented at the International Symposium on Schistosomiasis which was held in Shanghai, July 4–6, 2001 with the theme of Schistosomiasis Control in the 21st Century. In order to focus more attention on the new challenges in control programmes for schistosomiasis as well as show the priority of research areas in new century, we summarize the advances of control programmes and researches in nine areas, including (1) Status of schistosomiasis control programmes; (2) Progress in applied field research; (3) Biology and control approaches of snail hosts; (4) Novel approaches for schistosomiasis control; (5) Pathogenesis and morbidity of the disease; (6) Immunology and vaccine development; (7) Screening of population for chemotherapy in low transmission areas; (8) Sustainable intervention methods in different endemic settings; (9) Impact of animal schistosomiasis on agricultural development and importance of its control; (10) GIS/RS application and environmental changes. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

The International Symposium on Schistosomiasis was held in Shanghai, July 4–6, 2001, sponsored by the Ministry of Health, People's Republic of China. The theme of the symposium was Schistosomiasis Control in the 21st Century with the following aims: (1) Exploration into and

exchange of experiences in the control of schistosomiasis; (2) Promoting friendly communication among scientists in all countries, and (3) Giving impetus to the cooperation among scientists in the world involved in the control and research of schistosomiasis. The conference was partially supported by WHO, TDR and the Swedish International Development Cooperation Agency.

A total of 200 participants from 18 countries, including Japan, France, United States, Germany, Egypt, Brazil, Denmark, Zimbabwe, United

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Kingdom, Australia, Switzerland, Philippines, Indonesia, and representatives from the World Health Organization (WHO), Special Programme on Research and Training in Tropical Diseases (TDR) attended the symposium. Among all the papers submitted to the conference committee, 120 papers were presented in the conference with 12 contributions in a plenary session, and others in group sessions including (1) Epidemiology and control, (2) Biology and ecology, (3) Chemotherapy and diagnosis, and (4) Immunology and molecular biology. In addition, a round-table discussion was arranged on the topic of “Challenges and opportunities of schistosomiasis control in the new century in China—control and elimination of schistosomiasis in low transmission areas”. The presentations covered the following aspects: (1) Status of schistosomiasis control programmes; (2) Progress in applied field research; (3) Biology and control approaches of snail hosts; (4) Novel approaches for schistosomiasis control; (5) Pathogenesis and morbidity of the disease; (6) Immunology and vaccine development; (7) Screening of population for chemotherapy in low transmission areas; (8) Sustainable intervention methods in different endemic settings; (9) Impact of animal schistosomiasis on agricultural development and importance of its control; (10) GIS/RS application and environmental changes.

2. Status of schistosomiasis control programmes

A total of six papers described the current status of schistosomiasis control programmes at national or regional levels. The global status of schistosomiasis was presented by Engels. The distribution of schistosomiasis has changed over the last 50 years and there have been a number of successful control programmes. However, overall, the number of estimated infected persons and those at risk of infection have not been reduced. In several endemic countries, where control has been successful, the number of people infected and at risk of infection is very small, whereas in most other endemic areas, the situation has not changed significantly, especially in Africa. Successful schistosomiasis control requires in the first place a long-term commitment.

The current status of the schistosomiasis control programme in China was presented both by Jiang et al. in a plenary session and by Chen in the round-table discussion. After continued efforts over the past five decades, schistosomiasis has been successfully eliminated in the provinces of Guangdong, Fujian and Zhejiang, in the municipality of Shanghai, and in the autonomous region of Guangxi. *Schistosoma japonicum* has been eliminated from one third of the original endemic areas, and is under control in another one third. According to available data, by the end of 1999, there were a total of 409 counties endemic for schistosomiasis. Among them, 238 counties have reached the criterion of transmission interruption, 56 counties have reached the criterion of transmission control and in the remaining 115 counties, the disease is still endemic. The combined approaches of snail control, chemotherapy, health education and hygienic movement were integral components of the control strategy engaged in China. In spite of the substantial progress against schistosomiasis that has been made, the national programme on schistosomiasis control is facing new challenges. It will be difficult to maintain the prevalence or morbidity at a low level after mass chemotherapy has been used for many years. More effort is required to consolidate the achievements gained and to further minimize the transmission areas as well as the intensity of infection. In particular, the following new problems need to be tackled in the near future. (1) With the completion of the World Bank Loan Project (WBLP) on schistosomiasis control in the country by the end of 2000, schistosomiasis transmission still occurs in large areas. The coverage rate and intensity of chemotherapy will decline because of limited resources. (2) After the serious flooding in the Yangtze River valley in 1998, both snail-infested areas and the possibility of infection with *S. japonicum* through water contact have been increased. Furthermore, in order to reduce the impact of floods, the State Council adopted a policy for anti-flooding of “returning cultured land into the lake and relocation of farmers from endemic areas to newly established towns”. It is one of the new issues in the control programme that needs investigation, since the pol-

icy may contribute to an increase of snail habitats on a large scale and increase the possibility of people coming into close contact with infested water, thus increasing prevalence of schistosomiasis in some areas. (3) The impact of the Three Gorges Dam project on transmission of schistosomiasis in the middle and lower reaches of the Yangtze River is still unclear. There is a need to strengthen the investigation and surveillance on the impact of water levels to the distribution and dispersal of *Oncomelania* snail in the Yangtze River valley.

Leornado reported that in the Philippines, of the total population affected by the disease 6.7 million people are at risk and 1.8 million are directly exposed to the disease. The pattern of *S. japonicum* infection has become more localized in the high rainfall areas of the southern Philippine islands. Since the World Bank loan for schistosomiasis control to the Philippines ended in 1995, a longitudinal study has shown the potential for a rebound increase of morbidity when an annual treatment is missed; prevalence, intensity of infection and morbidity may increase, especially in the poorer and more isolated communities within the endemic regions.

In Indonesia, a schistosomiasis control programme has been carried out since 1981 in Napu and Lindu Valleys (Izhar). The control measures were mass treatment using praziquantel (PZQ) and snail control with the aim being to reduce the prevalence to less than 1%. The average prevalence of schistosomiasis in 1999 was 0.46 and 1.55%, respectively, for Lindu and Napu valleys. Nowadays the schistosomiasis control programme is integrated into the Central Sulawesi Integrated Development Area and Conservation Project (CSIAD & CP) funded by ADB. After the project was implemented in the year 2000 the schistosomiasis prevalence was further reduced.

Urbani reported that the districts of Khong and Mounlapamoh, in the southern province of Champassak in Laos, and all the villages along the Mekong River and its tributaries in the provinces of Kratie and Stung Treng in Cambodia, have been recognized as endemic areas for *Schistosoma mekongi*. In Laos, control activities started in 1989, supported by WHO. The inter-

vention, based on annual universal treatment with a single dose of PZQ (40 mg/kg), and health education, resulted in a dramatic fall in the prevalence of the infection, now around 2% in Khong district and 0.4% in Mounlapamok district. Since 1991, the entire population in the two endemic districts was targeted with mass drug administration. A surveillance system is now under evaluation by the MOH to prevent any resurgence of the infection. Today, still 60 000 people are estimated to be at risk of infection in Laos and about 90 000, in Cambodia.

In Egypt, both *Schistosoma haematobium* and *Schistosoma mansoni* have been endemic for many centuries. The government of Egypt, together with the World Bank and the African Development Bank, established the National Schistosomiasis Control Programme (NSCP) in 1977, with the main objective of morbidity control. The operational components include chemotherapy, health education, focal snail control and environmental improvement. NSCP succeeded in lowering the prevalence, intensity of infection and thereby the morbidity due to schistosomiasis significantly.

In sub-Saharan Africa, where transmission is high and control resources generally limited, WHO is now advocating aiming for morbidity control in the most strict sense. At present, most of the available information is limited to numbers of infected individuals. Here, where there have been few attempts at control and where the population has increased by approximately 70% over the last 25 years, a significant number of people are infected or at risk of infection. It has been estimated that over 80% of schistosomiasis cases, and almost all of those individuals most severely affected in the world, are now concentrated in Africa.

In Brazil, the objectives of the Schistosomiasis Control Program (SCP) were a reduction in the most severe clinical forms and the number of deaths caused by the disease. In spite of this, the research undertaken to investigate the impact of the activities of the SCP has been limited to mere prevalence analysis, or to a parasitic burden analysis.

3. Progress in applied field research

Effective schistosomiasis control is one of the main components of applied field research. In view of the different strategies applied in high and low transmission areas, WHO has redefined its research agenda in the field of schistosomiasis control. For high transmission areas, it was thought essential to further investigate issues such as the burden of disease due to schistosomiasis and its economic impact, to further develop methods for rapid epidemiological assessment, to search for a more optimal use of PZQ, to develop new drugs, and to document the cost-effectiveness of the different components of control interventions. For low transmission areas, the evaluation of sensitive diagnostic methods and their further development into field applicable assays is defined as the highest priority.

In China, a new strategy was formulated and the following activities are to be implemented in the future: (1) Continuing the activities on strengthening the control programme under government leadership, with involvement by relevant departments, and insisting on the policy of taking comprehensive control with scientific approaches. (2) The control strategy has been adjusted in time after the completion of the WBLP. Different control strategies will be implemented in different endemic areas based on the local situation. Environmental modification will be continued in combination with construction activities in agriculture and water resources. (3) Epidemiological surveillance systems will be strengthened in order to understand the changes of transmission and prevalence in time and provide reliable information for decision making. (4) More attention will be paid to research such as the impact of environmental changes on transmission of schistosomiasis.

Zhao reported on the national schistosomiasis surveillance system used in China. A total of eighteen longitudinal surveillance sites for schistosomiasis was set up covering seven provinces where the disease was still endemic in 2000. In each site, the infection rates of residents and domestic animals were examined by ELISA, COPT, IHA, Kato–Katz and the miracidial

hatching method, and the intensities of infection were evaluated. Much attention has been paid to the control of schistosomiasis in mountainous regions of Yunnan and Sichuan. A control strategy was developed focusing on chemotherapy and health education, associated with mollusciding and cercariciding in contaminated environments. The strategy can effectively interrupt transmission of schistosomiasis in 3–4 years in the plateau endemic areas where snail control has not been feasible.

In the lake region of China, a study was carried out in eight villages heavily endemic for *S. japonicum* in Hunan Province from 1998 to 2000. It was demonstrated that mass chemotherapy should still be the choice in areas where prevalence of infection and frequency of contact with infested water by residents are high. Targeted chemotherapy i.e. treatment of those with water contact and/or symptoms, could be a useful alternative to mass chemotherapy, especially when the frequency of water contact is not high. Chemotherapy based on fecal screening was the least cost-effective of three schemes in the study areas. Epidemiological factors and the control strategy for newly identified schistosomiasis–endemic areas in three cities of Hunan province were reviewed by Li. Urban schistosomiasis has become an important aspect of the control program with an increase in the mobile population. Guo tested the cost-effectiveness of sustainable chemotherapy. In the experimental village where mass chemotherapy was given only once in 2 years, the total cost for the mass chemotherapy was 7042.6 Chinese yuan, with 106.3 yuan for 1% reduction of prevalence and 15.5 yuan for 1% reduction of prevalence per 100 persons. The strategy of using mass chemotherapy once every 2 years achieved a similar effect in reducing prevalence but was less expensive than annual drug administration.

Immunodiagnosis, due to its rapidity, affordability and ease of acceptance, has been integrated into the control program in China since the early 1980s as a way of improving epidemiological surveys and identifying targets for treatment. Wu reviewed the progress of diagnostic technology in China over the past 50 years. With the appear-

ance of the intradermal test (ID) in early 1950s in China, the other immunodiagnosis methods, such as CHR, COPT, IHA and other agglutination tests with soluble antigens, were developed and applied in late 1960s. In the late 1970s, the ELISA with crude antigens of the parasite and many modified testing systems of ELISA were developed, e.g. Dot-ELISA, SPA-ELISA, ABC-ELISA, K-ELISA, PVC-ELISA etc.

Almost all serologic techniques developed so far for antibody detection exhibit about 90% or more sensitivity compared with parasitological findings. Since the mid 1980s, a number of defined antigens fractionated from eggs and worms have been tested, including MSA1, TCA-S-A, 31/32 kDa diagnostic protein, SIEA 26–28 kDa etc.

A new example is the 107–121 kDa antigen, which in field trials revealed 95.74% in sensitivity and 100% in specificity without cross-reaction with sera from individuals with paragonimiasis, clonorchiasis or fasciolopsiasis. Some cloned and expressed molecules for the construction of assays for antibody-detection, e.g. SjGST26, GST-HD fusion protein etc. were also developed. The ELISA constructed with NP30 of the mimic GAA, substituting for antigen, has proved to be both sensitive and specific as well as very fast in detecting the conversion of seropositives into seronegatives one-year after treatment (100%). Exploration of detecting the circulating anodic antigen (CAA) for immunodiagnosis of *S. japonicum* infection was initiated in China in the early 1980s. It is still not possible to expect that the existing immunodiagnostic approaches can meet the requirements for epidemiological studies and control programs of schistosomiasis due to the imprecision of available tests which often result in erroneous conclusions. Updates of ongoing researches in the Philippines were provided by Acosta who discussed human immune responses in ‘susceptible’ and ‘resistant’ groups in endemic areas and also detailed the course of *S. japonicum* infection in monkey experiments.

The important role of applied research in control programs was stressed by Bergquist. The utilization of artemether for control purposes is a good example of how research and control can advance hand in hand. The development of

artemether is one of many successful projects initiated by the Joint Research Management Committee (JRMCC), the advisory body created for the research component of the World Bank Loan. Thanks to the investment made by JRMCC in 1994, a series of successful controlled human trials were carried out leading to mushrooming research in this area. Political must be mobilized to fund implementation research defining the limits in terms of target groups and/or endemic settings for artemether in controlling schistosomiasis and elucidating the advantages of combining artemether and PZQ.

4. Biology of snail hosts and parasite

A total of 11 papers were presented on this topic, including two on genetics, three on population dynamics, two on sampling surveys of snails, and four on the biology of parasites. In the genetics, Davis discussed the genetic diversity of *Oncomelania* throughout China following experiments on allozymes and COI gene sequences of *Oncomelania*. The results show that there are three allopatric subspecies; *O. h. hupensis* found below the Three Gorges of the Yangtze River; *O. h. robertsoni* above the Three Gorges in Yunnan and Sichuan Provinces; *O. h. tangi* in Fujian Province, isolated from the Yangtze River drainage by a mountain range. *O. h. hupensis* may have either smooth or ribbed shells. Analyses of COI haplotypes indicates that isolated populations with little or no immigration are genetically stable and thus are true populations. Where snails are transported by the annual floods and deposited as aggregates as the flood subsides, true population structure does not occur. Infection rates are affected by population structure. As *S. japonicum* has coevolved with tight linkage with *O. hupensis*, the patterns of genetic divergence and population structure of *Oncomelania* has great implications for divergence of *S. japonicum* throughout China and the rest of Asia. The variation on response of *O. hupensis* populations, collected from 37 field sites in endemic areas in southern China, to niclosamide in the laboratory was reported by Dai. The largest differences in

response after 24 h were found to niclosamide with death rates varying between 0 and 100%. LC₅₀ values ranged from 0.032 to 0.19 mg/l with a mean value of 0.0920 mg/l. Since snails with the lowest and highest LC₅₀ values came from collecting sites which were geographically close, it is unlikely that the differences found represent only natural variation between geographically distinct populations.

In the population dynamics of snails, Ndlela introduced the effects of conspecific overcrowding on growth and reproduction of *Bulinus globosus*, an intermediate host snail for schistosomiasis, and *Bulinus tropicus*, a potential snail competitor. The overcrowding in *B. globosus* and *B. tropicus* snails resulted in reduced growth and fecundity. Diaw presented the population dynamics of the snail host in the Senegal River. A new malacological colonization was found until the recent outbreak in 1989–1990 in Richard–Toll of the River. This was the first sign that ecological changes resulting from the dam's construction had an impact on the prevalence of schistosomiasis in the Senegal River Basin. The overall infection rate in *B. pfeifferi* was 52%, *B. truncatus* 5%, *B. globosus* 14%. Olufemi presented the distribution and ecology of two recently introduced *Australasian pulmonate* snails to Nigeria: *Indoplanorbis exustus* (Deshayes, 1843) and *Amerianna carinata* (H. Adams, 1861) in Nigeria. *I. exustus* serves as host to *Schistosoma* spp. (*S. spindale*, *S. indicum* and *S. nasale*), and *Angiostrongylus cantonensis*, which can induce eosinophilic meningitis in man.

In the sampling survey on snail populations, Davis introduced a new quantitative sampling method for *Oncomelania*. The traditional method of sampling snails using a 0.1 m² frame is suitable for reducing the negative binomial. The new sampling technique involves placing 10 000 m² measured SQUARES over representative areas of a grassland; there may be 4–10 such SQUARES depending on the area of grazing land for a given village. The SQUARE is divided into 100 numbered cells of 10 × 10 m. Twenty of the numbered cells were chosen at random to be sampled for snails. A frame of 4 m² (= 36.66 quan) is placed in the center of the cell to be sampled and all snails are collected. The living snails are separated

from the dead and the living snails crushed to determine if they are infected with *S. japonicum*. From this random sample covering a number of 90 909 quan areas, one can answer the questions asked. Meng reported a stratified sampling survey on *O. h. robertsoni* in ditches, by checking all the snails in one frame (0.1 m²) every 10 m in ditches in the mountainous area of Sichuan, in order to investigate the snail distribution. It was suggested that heavily infected snails are mainly distributed within the 200 m to the intersect of ditches at the 1st and 2nd level villages where the high-risk areas occur in the mountainous area of Sichuan.

Six papers were presented on the biology of *S. japonicum* and other trematodes. Dong and Jiang introduced the culture procedure and ultrastructural observations of cultured cells from *S. japonicum*. The cultured cells from adults could be divided into germ cells, vitelline cells, flame cells and nerve cells. Vitelline cells were most in number. The degenerative process of the cultured cells from *S. japonicum* consisted of necrosis according to the ultrastructural changes of the chromatin, vitelline globules, mitochondria and endoplasmic reticulum within the cells. The changes of the above structures could be used to estimate whether the culture conditions were appropriate. Sun reported the growing degree days (GDD) of *S. japonicum* developing in the intermediate snail host, *O. hupensis*, in the field. This indicated that the value of GDD at 1489.43 was long enough for *S. japonicum* to complete its development in snails from the Yangtze River Valley. Liu studied in heme-oxygenase in *S. japonicum* and the results indicated that the enzyme was expressed in different cells of *S. japonicum*, and was located in the cytoplasm. Xu reported natural nidi of *S. japonicum* were found in *Rattus norvegicus* in two islets located in Nanjing reaches of the Yangtze River with areas of 333 and 500 ha. It was suggested that great attention must be paid to eliminating wild rats in the schistosomiasis control program.

The diversity of larval trematodes infecting freshwater gastropods from the highveld and lowveld areas of Zimbabwe was reported by Chingwena. A total of 13 789 gastropods, representing ten species were collected from 21 sites

and 909 (6.6%) harboured trematode parasites. Altogether, eight morphologically distinguishable groups of cercaria were identified. The main intermediate host for amphistomes was *B. tropicus*. Infections of *B. globosus*, *B. pfeifferi* and *B. forskalli* with amphistome cercariae recorded in this study are new records in Zimbabwe.

Zhang presented on the molecular phylogenetics of *Orientobilharzia turkestanicum* based on nuclear and mitochondrial genes. Phylogenetic trees based on the data all suggested that *O. turkestanicum* lies within the genus *Schistosoma* which is therefore, as currently defined, a paraphyletic taxon. The presence of an Asian species basal to African species suggested that the lineage comprising *Schistosoma* and *Orientobilharzia* originated in Asia.

5. Novel approaches for schistosomiasis control

Novel snail control approaches have been tried in several investigations. The modified floodgate and subside pool has been designed to prevent snail dispersal in river systems, as presented by Xu. The facilities of control snail dispersal with subside pool and block net were set up in the field. The rate of dropping or broking snails from moving through the floodgate and subside pool was 100%. The new techniques are worthy of application widely in irrigation systems in endemic areas for schistosomiasis.

Another six papers were on novel snail control, including three on biological control, and three on plant molluscicides. Several biological control programmes in Venezuela were conducted mainly using two snail species, as introduced by Pointier, the ampullarid *Marisa cornuarietis* and the thiarid *Melanoides tuberculata*. These may prove useful for sustainable control of the snail hosts of schistosomiasis in this area. Mubila reported a study undertaken on the shores of Lake Kariba, Zambia to investigate snail-parasite compatibility as a factor in endemicity of urinary schistosomiasis around Lake Kariba in comparison to L. Bangweulu and Lusaka. Ecological factors could be the explanation for the observed low endemicity of urinary schistosomiasis, but investigations were

not sufficient to lead to conclusive results. Paul examined the behaviour of two aquatic snails, *B. globosus* and *B. tropicus* when exposed to water conditioned by *Tilapia rendalli* and an indigenous cichlid fish, *Sargochromis codringtonii*. Increasing the number of fish in a tank did not change the response of snails when exposed to water conditioned by *S. codringtonii*. *B. globosus* reacted more to water conditioned by feeding fish compared to non-feeding fish.

Three kinds of plant components extracted from rapeseed, *Solanum xanthocarpum* and *Eucalyptus* leaves were tested as plant molluscicides. The molluscicidal active ingredient was isolated from rapeseed with 0.24–0.3% of the yield rate. Comprehensive spectral analysis demonstrated that this compound was recognized as 2-hydroxyl-3-butenyl-thioglucoside. Molluscicidal testing in the laboratory showed that the LC_{50} was 28.43 ± 1.38 mg/l. The extract from *Solanum xanthocarpum* showed that, at room temperature (25 °C) for 48 h, the LC_{50} of *O. hupensis* was 0.332 mg/l, *B. gabarata* was 0.858 mg/l, *L. Stagnalis* was 0.747 mg/l. LC_{50} of *S. xanthocarpum* for rare minnow was 2.02 mg/l. LD_{50} of *S. xanthocarpum* in mice was 794 mg/kg. While the molluscicidal effect of extracts from *Eucalyptus* leaves showed that all the three kinds of extracts (water, alcohol and oil extracts) of *Eucalyptus* had a strong molluscicidal effect on *Oncomelania* snails, as well as a certain degree of lethal effect to snail eggs, but low toxicity to fish. In alcohol extraction, the LD_{50} of *Eucalyptus cordata* f. *Lonceolata* were 16.0 and 12.2 mg/l after 48 and 72 h immersing; while the LD_{50} of *E. camaldulensis* were 19.4 and 15.5 mg/l after 48 and 72 h immersing.

Two new drugs, artemether and artesunate, have been recommended to be widely applied in endemic areas and have high promise due to high prophylactic efficacy and safety, and they have both proved useful in protecting soldiers during recent floods in China. Dai observed a total of 12233 people (army men, policemen, etc.) who contacted infested water during flood fighting in 1998 and were administered with artesunate (300 mg) once per week for 3 weeks, and another 2038 people were treated only with PZQ as a control.

No acute cases occurred among those people administered with artesunate. The stool-positive rate was 0.22% 3 months after taking artesunate. However, among those people only treated with PZQ, the stool-positive rate was 8.15%. Yi also evaluated the effect of artesunate to prevent infection following short-term exposure (7–8 days) to infested water during flood fighting in 1998. The ‘double blind test’ was performed and results showed that two cases were stool-positive with the positive rate 1.19% in 240 cases of the experimental group, while 22 cases were stool-positive with the positive rate 11.0% in 200 cases of control group. The protection rate was 89.18%.

On the optimal use of artesunate for prophylaxis of schistosomiasis japonica, Lin described a ‘7 d interval’ scheme carried out in seven endemic villages around the Poyang Lake, Jiangxi province. Zhu reported that there were significant differences between a control group and artesunate-treated groups in 300 head of cattle, grazing in marshland of Wucheng township, Yongxiu county, with the protection reaching 75–100%.

For Artemether, a collaborative effort between Chinese, European and African scientists with support from TDR, was made to investigate further the anti-schistosomal effects of artemether. Xiao and N’Goran reported that artemether can be used to prevent schistosomiasis. The drug does not prevent infection but the development of adult worms, and hence egg production—the cause of morbidity—is precluded. Artemether is active against *S. japonicum*, *S. mansoni* and *S. haematobium* larvae.

Seven field trials with control groups were carried out between 1994 and 1996 in Hunan, Yunnan, Anhui and Jiangxi provinces. Areas endemic for schistosomiasis in the mountainous, marshland and lake regions around the Dongting and Poyang lakes were selected. Wang tested a total of 175 cattle from a heavily endemic village in the lake region by giving artemether with the first dose of 4 mg/kg within 15 days after contacting with infested water, followed by three repeated doses every 15 days. All observations indicated that artemether was effective both in humans and in cattle.

Laboratory studies suggested that *S. mansoni* infection could be partially prevented in humans by administering artemether once every three weeks. Results from field trials in an endemic area in western Cote d’Ivoire showed that the prophylactic efficacy was 50% (95% confidence interval: 35–71%) and the intensity of infection among those re-infected was significantly lower in artemether-treated individuals when compared to the placebo recipients. A randomized, controlled trial among children living in a highly endemic area for *S. haematobium* in central Côte d’Ivoire is being undertaken similar to the trial with *S. mansoni*. To compare the efficacy of the two drugs, Tu did a comparative study of therapeutic effects of artemether and artesunate on *S. mansoni* adult worms in mice. The results showed that the therapeutic efficacy of artemether on *S. mansoni* in mice was better than that of artesunate. Further studies are needed to verify these results.

A field clinical study on the therapeutic efficacy with lower dosage (25 mg/kg) of PZQ showed that the lower dosage of PZQ still had a good efficacy with less side effects and less expenditure in the treatment of chronic schistosomiasis, especially if it was used in mass chemotherapy. Liu studied a new plant-originating cercaricide (‘Fangyouling’), a cercaricide extracted from the seeds of *Jatropha curcas*. The population protection rate of ‘Fangyouling’ for schistosomiasis was high, with the infection rate 1.43 and 9.09% in the experimental and the control groups, respectively.

Three papers described modeling methods in the transmission of schistosomiasis. One was reported by Williams that extended Barbour’s model to allow for further heterogeneity within the two major definitive hosts and incorporates necessary parameter estimates, appropriate to lake/marshland ecology, from the Poyang Lake area in Jiangxi Province in China. A worm-burden model using two ordinary differential equations to characterize disease transmission and control in risk groups defined by residence and occupation through epidemiological and statistical analysis in Sichuan was reported by Liang. Danso-Appiah and De Vlas introduced META analysis to elucidate the effects of major determinants, such as chemotherapy, animal manage-

ment, vaccine application and environmental modifications, for forecasting the impact of different control strategies.

6. Pathogenesis and morbidity of the disease

Three investigations were related to pathogenesis or morbidity in animal models. The immunomorphology of the hepatic egg granuloma in *S. japonicum*-infected pigs was investigated by Hurst. All developmental stages of the hepatic *S. japonicum* egg granuloma in the pig manifest MHC class II-dependent CD4+ T cell activity concomitant with infiltration of CD8+ T cells. Antibody, mainly IgG, is produced within the granulomas, whereas the primary site for activity of mature B cells preceding the effector cell stage appears to be granuloma-associated lymphoid nodules. Iburg reported on the pathogenesis of congenital infection with *S. japonicum* in pigs. In the experiment, a schistosomulum found in meconium 109 days post infection had inflammatory reactions in the livers, and modulation of the infection occurred from 54 to 69 days post infection. The synthesis and degradation of collagen kept dynamic balance at the early stage of schistosomiasis japonica, while later the quantity of collagen synthesis was higher than that of collagen degradation. It was confirmed at the transcription level that when the quantity of collagen synthesis was higher than that of degradation, liver fibrogenesis may result.

Since histopathological examination can provide useful information to identify hepatic diseases, histopathological examination on the liver and spleen during splenectomy in a total of 38 cases of advanced schistosomiasis associated with ultrasonography and serum biochemistry was conducted. Upon histopathological examination, in 34 out of 38 cases, schistosome eggs were found. Schistosomal liver fibrosis was shown in 23 cases and mixed hepatic cirrhosis i.e. schistosome and hepatitis in origin, was seen in 14 case. Post-hepatitis cirrhosis was seen in one case. Ultrasonography is important in the diagnosis of liver fibrosis/cirrhosis. The impact on physical fitness and working capacity and distribution of patients

with advanced schistosomiasis in Susong county, Anhui province were described by Wu. The physical fitness and working capacity were reduced in advanced cases. Thirteen individuals (28.3%) in the case group had moderate reduction of working capacity or were even unable to work, but only seven (12.7%) individuals in the control group had moderate reduction of working capacity, and none was unable to work ($P < 0.01$). In the previous year, the average of working days lost was 4.11 days in the case group and 0.86 day in the control group. Physical fitness scores showed the control group (score 71.84) was significantly fitter than the case group (score 61.09, $P < 0.01$).

The records of 3547 cases with advanced disease registered between 1988 and 1998 were analysed and these showed that 610 subjects had died. The average fatality was 8.6% per year. Among the causes of death, 30.1% were due to severe ascites, 36.6% due to hemorrhage of upper digestive tract, 28.4% due to hepatic coma, and 2.9% were complicated with peritonitis. Among all causes of death other than schistosomiasis, hepatitis B or A accounted for 44.7%. The complications with hemorrhage of upper digestive tract, hepatic coma, and peritonitis were the main causes of death for the disease.

7. Immunology and vaccine development

With increased interest in genome projects, the expressed sequence tag (EST) approach has become one of the most important strategies for novel gene discovery. The genome size of *Schistosoma* is 270 Mb, with the total number of genes estimated at about 15 000–20 000, many of which need to be identified. At present, several institutions in China are launching programs to screen gene libraries and to identify novel schistosome genes. Feng presented a total of 10368 clones from four *S. japonicum* cDNA libraries (SJA—both male and female adult worms, SJM—male adult worms, SJF—female adult worms and SJEP—eggs) and sequenced them for generating ESTs. A total of 101 cDNA clones was obtained from a cDNA library constructed from *S.*

japonicum cercarial RNA which was used to generate ESTs, reported by Fung from Hongkong. Wu presented the EST approach that has provided partial sequences of 531 clones. Of them, 59 clones (11.1%) represented irrelevant sequences. The remaining 472 clones were grouped as 378 different expressed genes of *S. japonicum*. 472 useable sequences have been deposited in dbEST of GenBank. Bao also introduced an EST approach to isolate and identify novel genes from a cDNA library of adult *S. japonicum*; 429 recombinant clones were isolated from the cDNA library, and the inserts of cDNA were identified by PCR, and 127 ESTs were generated by PCR direct sequencing.

McManus reported the complete sequences for the coding proteins of the mitochondrial genomes of *S. mansoni* (NMRI, Puerto Rico; 14 415 bp), *S. japonicum* (Anhui, China; 14 085 bp) and *S. mekongi* (Khong Island, Laos; 14 072 bp). There was a high level of identity (87–94% identity at both the NC and AA levels) for all protein-encoding genes of *S. mekongi* and *S. malayensis*.

To identify some immunogenic antigens, Song studied the single chain fv gene of anti-idiotypic monoclonal antibody NP30 of *S. japonicum*. And, Yu described a miracidial antigen protein composed of 116 amino acids, with a molecular weight of 12913.3 Da, and isoelectric point (PI) of 4.49. Single base mutations exist among the members of miracidial antigen family. As the miracidial antigen is an excreted antigen, and expressed at higher level in the egg, there might be an important relationship between the miracidial antigens and fibrosis formation. The SEA-stimulated IFN- γ level of 79 'resistant' (not reinfected) group was significantly higher than that of the 14 'susceptible' (reinfected) group ($P = 0.0079$) and was significantly, negatively correlated with SEA-specific IgG4 level ($P < 0.05$), as presented by Zhang. Multiple and non-conditional logistic regression analysis showed that the individuals with the higher level of SEA-specific IFN- γ were 6.5 times less susceptible than those with the lower level. This suggested that SEA-specific IFN- γ might associate with the resistance to the reinfection with *S. japonicum*. Yi reported that the levels of detected antibody isotypes in sera pre-

and post-chemotherapy from an area with repeated chemotherapy for *S. japonicum* were higher than those from a newly-identified endemic area, though the differences for some isotypes were not significant. In the area with repeated chemotherapy, the mean levels of anti-AWA IgE rose at the beginning after chemotherapy and then descended slowly and remained at the higher level one-year later; the level of anti-SEA IgE decreased at the beginning after treatment and then rose slowly to a level similar to that pre-treatment.

For design of new bioengineering drugs, immuno-prevention and immunodiagnosis of schistosomiasis by its blockage of signal transduction and immune reactions, Shen obtained two β -galactosidase-Sj14-3-3 fusion proteins. Induced by IPTG and identified by SDS-PAGE followed by Western blot, both showed a predominant band corresponding to a molecular weight of approximately 32 kDa. Kikuchi described the HLA-class II region and polymorphic immune response related genes (TNF- γ promoter, IL-4R, IL-13 promoter, IL-13 region); HLA-DRB1*1101 and HLA-DRB5*0101, and IL-13 promoter A/A genotypes were revealed to be associated with protection and susceptibility to fibrosis. Moreover, HLA-DRB5*0101 and IL-13P- A/A both of which were susceptible markers to fibrosis were synergistically elevated as shown by the odd's ratio. This effect was considered to be mediated though IL-13 production and up-regulation in the antigen specific CD4+ T cells stimulated by HLA-DRB5*0101. Wang obtained a cDNA clone from an adult *S. japonicum* cDNA library by immunoscreening using specific human high-titer IgE antisera of *S. japonicum*. The recombinant plasmid pGEX-6p-1/BL 21, which included the novel gene encoding the IgE identified protein, was successfully constructed.

Epidemiology and immune correlates for human susceptibility to *S. japonicum* in the Dongting Lake region, described by Li, provided evidence that susceptibility/resistance correlates with antibody isotypes against native schistosome antigens. Wu presented influence on immunological functions after splenectomy in patients with advanced schistosomiasis with splenomegaly. The

levels of IgG, CD₃⁺, CD₄⁺, CD₄⁺/CD₈⁺ in patients after splenectomy were significantly higher than in patients before splenectomy ($P < 0.05$ or $P < 0.01$). Splenectomy can improve the immunological function in patients with advanced schistosomiasis and splenomegaly. Xia found Tyrophostin-25 significantly inhibited the expression of IL-2, IFN- γ and IL-4 ($P < 0.01$), D-sphingosine mainly inhibited the expression of IL-4 and Wortmannin mainly inhibited the expression of IFN- γ ($P < 0.01$). The Th2 response was reduced by using D-sphingosine, and Th2 response was enhanced while Wortmannin was used. The findings suggested that signal transduction inhibitors could modulate Th1/Th2 immune deviation. Yoshida found *S. mansoni* infection caused A/J mice escape from lethal *P. chabaudi* infection through the induction of increased IFN- γ production. As a consequence of upregulated IFN- γ , NO as effector for the resistance against *P. chabaudi* would be provided by activated macrophages. When *S. mansoni* infected mice were inoculated with *C. parvum* oocysts, the peak of oocysts per gram of feces was elevated and oocyst excretion were extended in double-infected mice.

Chemotherapy has been the cornerstone of anti-schistosomiasis control activities, but after 20 years of large-scale use of PZQ, the spectre of drug-resistant parasites is looming and it is time for a new approach using supplementary tools. At present, development of a vaccine is a public health priority. There were several papers on the investigation of vaccine candidate. McManus described a series of vaccination/challenge experiments undertaken in mice and water buffaloes using a recombinant form of Paramyosin (Sj-97) expressed in bacteria and subsequently purified. The vaccine efficacy results obtained were similar and consistent in mice and buffaloes with a significant (ranging from 40 to 66%) decrease in liver eggs, indicating an anti-fecundity effect. Mathematical modelling indicates that, at these current estimates of vaccine efficacy, control could be possible by combining drug treatment of the human population with vaccination of bovines living in close to humans. Grzych found mice nasally immunized with Sj26GST liposomes display a significant reduction in worm burden after a chal-

lenge infection: (39% $P < 0.002$) by comparison to control animals (47% $P < 0.005$). Hu reported the recombinant protein (rSj338) had potential as a candidate vaccine antigen against *S. japonicum* and four epitopes of rSj338 were partially protective against *S. japonicum*. When the epitopes were mixed with the epitopes of another vaccine candidate rSj22.6, a 45.4% ($P < 0.01$) worm reduction and 59.1% ($P < 0.01$) liver egg reduction were obtained. It was suggested that mixing multiple epitopes from different antigens may be more effective for vaccine design. Katz presented on mice immunized with rSm14 and challenged with 100 *S. mansoni* cercariae of the LE strain showed 55.3% ($P < 0.03$) and 45.4% ($P < 0.05$) worm reduction respectively in relation to the non-immunized control group. However, rSm14-immunized mice challenged with 100 cercariae of the MAP strain did not show significant worm reduction in two experiments.

Several DNA vaccine studies have been undertaken recently. Fu studied a P23 peptide of the Sj23 membrane protein of *S. japonicum* (Chinese mainland strain), and found the polypeptide was antigenic and may play an important role in inducing immune protection against schistosomiasis. Shi studied a pCD-sj32 DNA vaccine that can induce substantial protective immunity against infection of *S. japonicum* and anti-fecundity efficacy, with a worm reduction rate of 32.4–52.4% and an egg reduction rate of 54.2–57.7%. Yi performed seven separate vaccine trials with recombinant sj32, a *S. japonicum* protease, in the mouse model and demonstrated a statistically significant reduction of 40–50% in adult worm burden. Protection was observed in three different species of mice and with different adjuvants: Quil A, IL-12, MPL and Freund's complete adjuvant. The triose phosphate isomerase of *S. japonicum* Chinese strain (SjCTPI) was tested in mice as a DNA vaccine in combination with IL-12. SjCTPI protein was shown to be expressed in the membrane and plasma of the muscle cells of C57BL/6 mice. The worm and egg reduction rates of the TPI group and TPI + IL-12 group were 27.9, 13.7 and 31.9, 18.6%, respectively, in comparison with the pcDNA3.1 control group. Zhu found the worm and egg reduction rates were 32.4 and

46.9%, respectively, indicating significant protection induced by vaccination with pcDNA3 + SjGCP1, an expression product of the gynecophoral canal protein gene of *S. japonicum*. Liu reported a 600 bp DNA fragment amplified by PCR from an adult *S. japonicum* cDNA library, containing an *S. japonicum* Chinese mainland strain fatty acid binding protein (Sj14FABP) gene. The purified recombinant protein from the *Baculovirus* silkworm system was immunogenic in mice, rats and sheep, and 37.7, 31.8 and 59.2% worm reductions were obtained in outbred Kunming mice, Wistar rats and sheep respectively, when vaccinated with Sj14/GST, compared to a control group. Mean 42.9% reductions in faecal egg count and 44.9 and 69.6% in tissue egg counts in the liver and small intestine, respectively, were recorded in the sheep experiment.

Several investigators undertook some basic studies related to vaccine development. The active immunity to Kunming mice with NP30 resulted in protection with levels ranging from 22.4 to 50.5% depending on the different immunization procedures. The active immunity in sheep with NP30 produced 42.8% protection. The number of eggs in the liver of the group immunized with NP30 were decreased by 35.8%. The size and number of egg granulomas in the liver were also reduced significantly. Lee established a transgenic mouse model which can express the TH1 and TH2 specific surface markers to investigate the protective immune mechanisms brought about by the 26 kDa GST vaccine antigen from a Taiwanese strain of *S. japonicum*. The application of transgenic mice model can directly measure TH1/TH2 and other effector cell production conducted by flow cytometric assay and the protective immune mechanisms of 26 kDa GST were further clarified. Allam undertook parasitologic, histopathologic, and immunologic studies that demonstrated that the co-administration of MLV with rIL-12 as an adjuvant to mice could elicit highly significant levels of protective immunity against challenge infection. Among 129 human schistosomiasis cases, cytokine levels were found to be much higher in the individuals who were egg-negative than those who were egg-positive. Also, cytokine levels were increased significantly after treatment

in the infected group, especially IL-5 and IFN- γ ($P < 0.01$). These results suggested that the level of human cellular immune responses in schistosomiasis japonica endemic areas may be down-regulated generally (both Th1 and Th2 responses) and can be elevated after PZQ treatment. Zhou prepared short peptides mimicking antigenic epitopes of attenuated cercariae. As compared with the control group, significant levels of specific antibodies were induced in mice vaccinated with mixed phage clones, and the worm and the liver egg reduction rates were 33.6 and 56.1%, respectively, ($P < 0.001$). This indicated that antigenic epitopes of attenuated cercariae can be prepared by immunoscreening of a random peptide library and protective immunity against *S. japonicum* can be stimulated by these epitopes in mice.

8. Screening of population for chemotherapy in low transmission areas

Four new diagnostic methods were assessed in screening of target populations after chemotherapy. In field evaluation, a rapid simple dipstick dye immunoassay (DDIA), introduced by Zhu, showed positive rate by DDIA of 96.69% in 121 cases of schistosomiasis, but 90.08% obtained by COPT. As the antigen conjugated with dye was stable at room temperature for at least 6 months, the DDIA was more useful for screening purposes on a large scale in endemic areas compared with other immunoassays. A non-invasive immunodiagnostic technique to assess the feasibility by using saliva and urine in diagnosis of schistosomiasis japonica was reported. The sensitivity of antibody detection in rabbit saliva and serum was 94.7% (18/19) and 100% (19/19), respectively. The sensitivity of antibody detection was 90.6% (29/32) in patient saliva and 100% (32/32) in serum. Both antigen and antibody presented 3% false positivity in 100 urine samples of healthy individuals. Therefore, either detection of specific antibodies in saliva or combined detection of both circulating antigens and specific antibodies in urine can be used as a noninvasive immunodiagnostic method for schistosomiasis.

Field applicable assays using the Magnetic Bead Antigen Capture Enzyme Immuno-Assay (MBAC-EIA) in the immunodiagnosis of infection with *S. haematobium* was presented by Ndhlovu. The specificity of the detection of CAA was 19% while the sensitivity was 100%. The specificity for CCA in urine samples was 19.2% while the sensitivity was 93.8%. For SEA, figures were 48.5 and 81% for specificity and sensitivity, respectively. Questionnaires have also been used for screening populations for chemotherapy in the field. Danso-Appiah presented a study carried out in a mixed urinary and intestinal schistosomiasis endemic area along the Weija Basin in the Greater Accra Region of Ghana, to determine through a questionnaire whether or not individuals with schistosomiasis signs and symptoms (fever for comparative purposes) self reported in the regular health services. A reasonable number of subjects with swollen abdomens (10%) and blood in stool (5%) who went to the hospital as a first action still self medicated afterwards. Compared to blood in urine, a significant number of subjects did not have any idea about the cause of bloody diarrhea.

Two papers described the immunodiagnosis used for evaluation of chemotherapy efficacy in *S. japonicum* infection. Two antigens, the 66 kDa from adult worms and the 67 kDa from immature eggs were isolated from gels and tested in an ELISA with sera from 60 uninfected and 90 infected individuals. The antibody response to the 66 kDa antigen was more short-lived than that to SEA. At 12 months, 91% of the serum samples had become negative while only 52% of the SEA reactivity turned negative ($P < 0.01$). Likewise the antibody response to the 67 kDa antigen was negative in 85% of the samples at 12 months post treatment while only 51% of the SEA reactivity changed to negative. Additional antigens used in these studies were adult worm membrane antigens (SjMAg) and Keyhole Limpet Hemocyanin (KLH). Sera from non-endemic areas did not recognize the antigens but 95% of the sera samples from chronically infected individuals did. IgG4 detection demonstrated that the negative rate of infected subjects at 6 and 12 months post-treatment was 50, 93% for SjMAg; 36, 93% for KLH while the SEA antibody response took a

longer time, with negative conversions of 27, 60% at the two time points. Finally, recombinant Sj32 kDa protein was also applied to ELISA for detecting IgG and showed a specificity of 100%, cross-reactivity of 0–5.7% and sensitivity of 93% for chronic *S. japonicum* infection. Negative rates were 46, 77 and 90% at 6, 12 and 24 months post-treatment, respectively. These studies suggest that specific antibody responses could be used as an indication for drug treatment and to monitor the efficacy of a chemotherapy program for *S. japonicum*.

The potential infection source in a non-target population was observed by Zhang in middle and high prevalence areas of schistosomiasis, since the population aged 6–60 defined as the target population were included in the control program, and those aged < 6 or > 60 as the non-target population were normally neglected in the control program. It was found that there were still a lot of infected cases in the non-target population in high (18.4%) and medium (5.0%) endemic areas. These cases were neglected in the current control program, in spite of the fact that faecal contamination from these people may contribute to transmission.

The basic knowledge for diagnosis was reviewed in two papers. A major advantage of serum CAA detection as compared to stool examination is that antigen levels show little fluctuation. Sensitivity can be increased by combining both 100% specific methods. In precise epidemiological analyses on worm population kinetics and host-parasite interactions, serum CAA levels appear to give important complementary information. Although serum CAA levels may be a better indication and a more stable measure of worm burden than egg counts, they are definitely not the ‘gold standard’. There are strong indications that although antigen levels are not strictly proportional with worm burdens, the underlying biological and/or methodological mechanisms are still unclear. More sophisticated analyses or complex modeling approaches to study the dynamics of schistosome infections are not helpful as long as these knowledge gaps persist. Variations in *S. japonicum* egg counts and the related epidemiology was presented by Yu, whose studies were

undertaken in the endemic areas for *S. japonicum* in both Jiangxi Province and Hubei Province. The distribution of *S. japonicum* eggs in the stool was not at random, with a clear trend in egg counts decreasing from the beginning of the stool to the end and from the outside layer to the center. Light and moderate infections were probably missed with a single or a few measurements. The positive rate increased by 20% more when comparing seven repeated measurements against only once. The negative binomial distribution could be used to describe the variations of egg count of inter- and intra-population variations, inter- and intra-individuals variations, and intra-stool variations. A mathematical model for *S. japonicum* egg count variations was established on the basis of the theory of negative binomial distribution. In the lightly infected population, the sensitivity of two slides increased from 47.7% by standard Kato–Katz method to 72.3% (average) by sampling from the head and/or outside surface of stool. Sampling from the head and/or outside surface of the stool can increase the sensitivity of Kato–Katz method in populations with light infection.

PZQ is currently the drug of choice for the treatment of schistosomiasis. Treatments of *S. mansoni* infection with the standard dose of 40 mg/kg body weight usually produce short-term parasitological cure rates of more than 70%. Recently, however, unusually low cure rates (18–40%) have repeatedly been reported and the emergence of PZQ resistance is feared. Several investigations were on the topic of resistance of schistosome populations to PZQ.

Low PZQ efficacy in Senegal has been reported. In a recently established, intense *S. mansoni* focus in northern Senegal, only 18% of the cases in an initial trial (1991) became parasitologically negative 12 weeks after treatment. Further epidemiological research by treating individuals from the area residing temporarily in non-endemic areas, as well as re-treating non-cured individuals within endemic areas, showed that under these conditions normal cure rates (80–87%) could be obtained. No epidemiological evidence for the occurrence of a PZQ-resistant strain of *S. mansoni* in Senegal has yet been established. Danso-Ap-

piah tested by Multi-level regression models and bootstrap analysis whether the poor cure rates in Senegal were really exceptional and could be attributed to the emergence of resistance.

In the laboratory, to understand the fecundity and biological adaptation of PZQ resistant isolates of *S. mansoni*, comparisons were made between four PZQ susceptible isolates and four resistant isolates including a laboratory selected isolate and three Senegalese isolates collected from uncured cases. It was suggested there may be significant differences in biology between PZQ resistant and susceptible isolates. The occurrence of isolates of *S. mansoni* that are tolerant/ resistant to PZQ requires the development of a quick and simple test for field or clinical use to determine the reason for failures of treatment. Liang did in vitro responses of PZQ susceptible and resistant isolates of *S. mansoni* to PZQ. The results showed that there were different responses to PZQ at the egg, miracidial, cercarial and adult stages of *S. mansoni* between susceptible and resistant isolates. To look for possible evidence of the development of resistance in *S. japonicum* to PZQ, Liang undertook a field survey in China. Importantly, there was no evidence for reduced susceptibility of *S. japonicum* to PZQ despite its extensive use in the main endemic areas of China for more than 10 years.

Variation in response to oxamniquine by *S. mansoni* has been observed in the outpatients' clinic of the Infectious and Parasitic Diseases Service in the Clementino Fraga Filho University Hospital in Rio de Janeiro, Brazil. Conceicao tested experimental resistance of *S. mansoni* isolates to oxamniquine to determine the experimental behaviour of *S. mansoni* isolates from patients with failure of treatment with oxamniquine. The results were similar showing higher number of males surviving and a possible resistance to oxamniquine. There was no case of patients with failure of treatment with PZQ.

Wang reviewed that among 38 species of mammals, *Microtus fortis* (Rodentia, Cricetidae, Muridae) is a non-permissive host for *S. japonicum*, in which most worms survive for less than 12 days. He suggested mechanisms of *M. fortis* resistance to *S. japonicum* infection. The

parasite death at the schistosomulum stage in *M. fortis* was not related to the property of the hemoglobin of this non-permissive host, and a possible cellular mechanism may be responsible for the worm death. The serum from infected *M. fortis* could recognize some specific antigens in an adult worm cDNA library of *S. japonicum*.

9. Sustainable intervention methods in different endemic settings

A few studies reported on the different interventions needed to be implemented in different endemic settings. Zhang reported the practical approach of chemotherapy combined with mollusciciding used in a heavily endemic area with a prevalence of 29.5%. Synchronous chemotherapy to both humans and cattle was carried out for three consecutive years with 40.8% average coverage rate. After 3-year intervention with the control approach the infection rate of residents and cattle decreased by 88.3 and 88.6%, respectively; new infection in children under 14 years of age decreased by 87.4%; and the snail infection rate and the density of infected snails decreased by 94.2 and 95.9%, respectively. Wang undertook a retrospective study on the effect of crop rotation in combination with chemotherapy in humans and cattle in the inner embankment regions and control area. The results showed that in crop rotation areas the snail habitats decreased from 762 000 m² in 1980 to 84 600 m² in 1995, and no snails were found in 533 300 m² of paddy fields in 1995 which used to be snail habitats; human infection rate decreased from 29.54% in 1980 to 3.87% in 1995, and cattle infection rate decreased from 19.10% in 1980 to 2.0% in 1995. In control areas, the snail situation and morbidity in humans had not significantly changed until crop rotation was carried out.

Surveillance on detection of snails and infection sources is still necessary after interruption of schistosomiasis transmission in Huangshan city, as presented by Fang. Based on the endemicity in history, geography, years since disease elimination and chronological records of prevalence, the surveillance on detection of snails either by inves-

tigation at key spots, reports from the masses, or survey on the flooding area, and on serological (COPT, IHA) or parasitological (stool) examinations for target groups, has been carried out. Although the mobile population increased remarkably and flooding occurred frequently, the situation after interruption of disease transmission has been stable.

Schistosomiasis control in the Poyang lake region was reviewed. From 1992 to 1998, a comprehensive strategy aiming at morbidity control in humans was adopted in eight counties around the lake region. Infection rate in humans dropped from 16.02% in 1992 to 4.94% in 1998 in high endemic villages, from 4.75 to 1.47% in moderate endemic villages. The strategies for schistosomiasis control in the Poyang Lake region have been formulated according to endemic characteristics. Main control approaches are selective chemotherapy to reduce human prevalence, focal snail control in areas with a high transmission potential, and chemotherapy for young bovines to decrease density of infected snails, and health education in medium and high endemic areas to raise the compliance to chemotherapy.

With economic development, more and more mobile population appeared in urban areas, for example, Zheng reported that more than 200 million surplus labors were immigrated from rural areas to city areas recently in China. Therefore, urban schistosomiasis was stressed in two papers. Hu reported urban schistosomiasis occurred in Huangshi city, Hubei province. The integrated control intervention has been undertaken since 1956. As a result, the prevalence rate in residents decreased from 10.1% before intervention to current 0 and no acute or advanced cases and no infected cattle were seen during the past 6 years. The environment changed greatly which ensured economic benefit. The average life expectancy was 35 years before intervention and is 72.8 years nowadays. Theron reported the observation carried out in the insular endemic focus of intestinal schistosomiasis in Guadeloupe where the black rat *Rattus rattus* acts as a reservoir host for the human parasite *S. mansoni*. All urbanized foci have been eliminated following several associated measures such as chemotherapy, health education,

improved sanitation and water supply. The murine focus was eliminated using biological control of the intermediate hosts by snail competitors. However, the swampy forest-cultivated focus where human and murine host adapted populations of schistosomes overlap, still remains active in spite of the control approaches.

Health education has been a major consideration in the control program since the implementation of a control strategy during the WBLP on Schistosomiasis Control in China. Sun presented the National Pilot Program on health education in China which tried to explore an effective model of the health education interventions. In the pilot areas, the communication methods were selected to promote the health education interventions combining mass media with other small media to the target population to influence their knowledge, attitude and behavioral practice (KAP). An evaluation questionnaire was conducted among 500 people. Compared with the results from a baseline survey, the awareness rate of the knowledge on schistosomiasis control of the target groups increased from 46.43 to 99.63%. The reduction rate of cercariae-infested water exposure and occurrences of the targets changed from 93.75 to 99.40%. The intervention effect on students was more significant than other groups because the prevalence rate in the population aged under 15 years decreased from 3.47% in 1994 to 1.05% in 1996. It indicated that the communication strategy must possess the following four principles: a special target, approachable objective, economical and unimpeded media application.

In Hubei, Liu reported that in the trial groups the pass rate of schistosomiasis control knowledge raised by 24.8%, the correct rate of health action increased by 29.5%, and the frequency of contacting infested water dropped by 22.1% after health education. In Jiangxi, Hu reported a field investigation carried out among 24687 inhabitants from 18 endemic villages of 18 endemic counties in Jiangxi province from 1992 to 1998. After the interventions, the pass-examination rates of anti-schistosomiasis knowledge among pupils, adult women and adult men rose by 90.5, 34.9 and 12.5%, respectively. The rate of adult women who washed clothes in infested water declined by

26.0%. This model can remarkably reduce the chance of infection with *S. japonicum* in two out of three inhabitants (pupils and adult women) in endemic areas, and increase chemotherapy compliance in whole population.

Health education was considered to be the main approach in combination with population chemotherapy in the control work. The main ways of water contact were listed among different target populations, such as amusement activities (swimming and playing) in pupils, the daily activities (washing clothes) in adult women, and the production activities (fishing, farming) in adult men. The main causes of infection among three target populations were as follows: swimming in infested water due to lack of knowledge in pupils, clothes-washing in infested water due to wrong concept of anti-schistosomiasis value in adult women, and exposure to infested water in production activities in adult men. The latter was hard to avoid when the old production style continues.

10. Impact of animal schistosomiasis on agricultural development and its importance for control

A note of the importance of the agricultural sector in control approaches to schistosomiasis was addressed by Willingham. He demonstrated a constraint for agricultural development and food security. 'Persisting' and 'emerging' zoonoses such as cysticercosis, echinococcosis, trichinellosis, fascioliasis, schistosomiasis japonica and toxoplasmosis have a significant impact on both agriculture and public health. These diseases usually receive very little attention from the governments of the affected countries. However, the evidence suggests that the impact of these diseases is more than proportional to the relatively low burdens of disease. More attention should be given to the impacts of these diseases on the health of both humans and their livestock, and the environments that they share.

In China and the Philippines the occupational groups at greatest risk of infection with *S. japonicum* are fishermen and farmers, and thus the diseases can have significant impact on important

sources of cereals and proteins. Compounding this is the impact of the parasite on the health and production (meat, milk, work capacity, reproduction, etc.) of livestock. Studies concerning the impact of *S. japonicum* on food security and agricultural development as well as the effects of the disease on the health and production of livestock have been very limited.

Zhang reported the animal hosts of *S. japonicum* and their roles in the transmission of schistosomiasis in the Poyang Lake region of Jiangxi. The definitive hosts of *S. japonicum* include humans, domestic animals and other wild mammals in the Poyang Lake region. According to the survey of stool contamination in some susceptible marshlands with *S. japonicum*, greater than 90% *S. japonicum* eggs came from bovines, about 6–8% from pigs. It was evident that infected bovines and pigs with schistosomiasis (especially the younger animals) are the main infective sources. Results from experimental epidemiological studies showed that the density of infected snails in marshlands could drop to 0 or close to 0 through mass chemotherapy of domestic animals.

11. GIS/RS application and environmental changes

The following aspect covering the impact of flooding and the Three Gorges Dam project on schistosomiasis transmission, and GIS/RS application in the prediction of transmission was one of the hot topics in the symposium.

11.1. Impact of floods

Since the serious flood that occurred in 1998 was the biggest in the 20th century in the Yangtze River valley, several presentations covered the topic of the impact of flooding on transmission of schistosomiasis along the Yangtze River. The impact of flooding causing epidemics of acute schistosomiasis in seven counties distributed along the Yangtze River in Hubei province in the flood years 1989, 1991, 1996 and 1998 was reviewed by Yu and Li. The total number of acute cases

reported in the seven counties in the 4 flood years was 7772, distributed in 1066 villages. The main way for people to get acute infection was swimming, which accounted for 61.89 and 46.41% of the total acute cases, in 1989 and 1991, respectively. The collapse of the Fushui River embankment in 1998 in Yangxing county caused the overflow of lake water with infected snails and most of the resident areas were inundated. A total of 108 cases of acute schistosomiasis were recorded during the flood season in 1998, increasing by 89.4 and 31.7% compared with cases reported in 1996 and 1997, respectively. In spite of 170 000 people exposed to infested water, no acute cases occurred during November and December, after the heavy flooding in 1998, due to the implementation of control activities.

The influence of flooding on transmission in Jiangxi and Hubei provinces was presented. The flooded areas in the Poyang Lake region in 1998 covered more than 400 million m² with the highest water level up to 22.5 m above sea level. Snail-ridden marshlands were flooded from early January in 1998, 120 days and 105 days earlier than in 1997 and in 1999, respectively. In 1998, the average standardized infection rate was 3.09% in residents of surveillance villages, lower than that in 1997 (4.57%) and 3.98% in bovines, similar to that in 1997 (3.89%). In 1999, the standardized infection rate in residents and in bovines was 3.97 and 2.91%, respectively, while the density of snails and infected snails increased from 0.474 and 0.0009/0.11 m² to 0.658 and 0.0012/0.11 m², respectively. So far, no snails have been found inside the embankment with abandoned dikes from 13 pilot sites. The main threat might arise from the policy of returning areas inside dikes into marshland.

In Hubei province, the counties suffering from the floods in 1998 and places where snails were dispersed were described. The dispersal of snail areas was increased in five counties, with the dispersal rate ranging from 2.75 to 67.59%, with an average of 19.77%. The prevalence in humans ranged from zero to 22.08% with an average prevalence of 14.57%, increasing by 1.68 times compared with that in 1997. Acute schistosomiasis cases in 1998 were 428, 4.41 times higher than

those in 1997. The prevalence in cattle ranged from zero to 31.67% with an average of 17.70%, 1.68 times higher than in 1997.

11.2. Impact of The Three Gorges Dam project

The Three Gorges Project is an integrated project on a large scale that will exploit and improve the environment of the Yangtze River. It will have a profound effect on improving and accelerating China's social and economic development. But, the transmission and prevalence of schistosomiasis is often aggravated by building new projects for water conservation and power generation in endemic areas, of which there were many examples reported in the world.

A study project to elucidate the relationship between these environmental changes caused by the Three Gorge Dam project and the transmission of schistosomiasis was carried out in collaboration with the Changjiang Water Conservancy Committee and Chinese Academy of Sciences. Zheng reported that owing to sedimentation of silts, some islets in the region of back-water of the reservoir will be formed after the Three Gorges project is built for 10–14 years. A total of 632 km² of land will be submerged after the dam is built, including 23 800 ha of farmland and 5000 ha of orange orchard. More than 1.13 million people will move to high altitude sites or to outside of the reservoir. If the farmland leaks heavily and water table is above 0.4 m, this type of environment will form new snail habitats. The appearance of the marshland in Dongting Lake will increase the chances of water contact activity for both residents and livestock, and increase the exposure risk to the infested water. After the Three Gorges reservoir is closed, the amount of mean sedimentation per year will be reduced from 145 to 20 million tons within the first 50 years. It will limit the enlargement trend of the marshland. But, the speed of expansion of the marshland or snail habitats will be accelerated 80 years later. Owing to less sedimentation of silts, a part of the marshland with reeds will change into grass beach or reed-grass beach, which will increase the areas of high transmission potential for *S. japonicum*. Water levels at Hukou station in Poyang Lake

will be elevated about 0.11–0.90 m during the period of January, February and March, and decline about 0.07–0.13 m in December after the dam is built. Whenever it is a wet year or a dry year, the water level will be lower than 13 m during these months. The survival and development of snail will be not affected, since no snail distributed under 13 m. A part of the marshland in the lower reaches of the Yangtze River will be submerged earlier than before after the dam is built. The difference range of water levels of the Yangtze River between the wet and dry seasons in Anhui and Jiangsu Provinces will be under the lowest water level at which snails occur. There will be no change in snail distribution. In the middle reaches of the Yangtze River, Xu reported that the water level of the Yangtze River will last for a longer period in the flood season, and the fluctuation of the riparian water table will follow the water level of the Yangtze River. The prevalence of people and snail density differed significantly between years and this correlated with the typical high, middle and low water levels in the Yangtze River.

11.3. GIS/RS application

With the development of novel technology in geographic information systems (GIS) and remote sensing (RS), more researches have undertaken to apply this tool in the schistosomiasis research and control. The forecast system for schistosomiasis transmission by application of GIS/RS in the middle and lower Yangtze River basin was investigated by a collaboration group, as presented by Zhou. This aims to rapidly predict the status of schistosomiasis in China and to assess the impacts of natural or social factors, such as floods, the Three Gorge Dam Project, and environmental modification, on transmission of schistosomiasis and distribution of snail habitats. The results indicated that the forecasting and monitoring of disease transmission has been improved after establishment of GIS databases and predicting models.

A global network on schistosomiasis information systems and control of snail-borne diseases (Gnosis), introduced by Malone, was established

in April 2000, sponsored by the Rockefeller Foundation in Bellagio, Italy. The organizational plan was conceived to create a global network of collaborating health workers and earth scientists dedicated to the development of computer-based models that can be used for improved control programs for schistosomiasis and other snail-borne diseases of medical and veterinary importance. More details on the work plan, compatible GIS data formats, minimum medical database can be searched on the website: <http://www.gnosisgis.org>, which enables seamless incorporation of results from each regional GIS project into a global model. Under the umbrella of GNO-SIS, the relevant GIS databases in China has been established consisting of epidemiological data on schistosomiasis and relevant environmental data from Jiangsu, Anhui, Jiangxi in the lower reaches of the Yangtze River, such as prevalence, incidence and number of the host, and the correlated climate and hydrology data, as presented by Yang.

Spear presented the integration and analysis of spatial and temporal data for schistosomiasis control, of which the ultimate goal is to model the spatio-temporal pattern of schistosomiasis infection by integrating the dynamic processes with spatial dispersion processes. By using global positioning system technology to map the irrigation ditches in support of snail population surveys at a small scale and the analysis of Landsat images for identification of snail habitat at a much larger scale, to use spatial statistics to study the spatial interaction of risk groups, and to examine the role of various environmental factors in disease transmission. The basic Anderson–May model was used to pertain to specific risk groups defined by residence and occupation and to parameterize the model in ways that can more directly incorporate field data including some spatially-related information.

The GIS/RS tool has been used in various purposes and regions. Brooker presented the mapping and prediction of schistosomiasis in Africa. Collating empirical data, using information from both published sources and ‘grey literature’ can go towards describing the distribution of infection, estimating population at risk and help iden-

tify where further information is required. Whilst reliable risk maps can be developed for *S. haematobium* in Cameroon, the models are shown to be inappropriate for Tanzania. In Tanzania, predictive maps were developed using detailed data for a coastal region. These maps allow the accurate prediction of infection patterns in coastal Tanzania, but do not predict accurately the patterns near Lake Victoria. Brillet reviewed the usefulness of medical geography for the control of schistosomiasis in Brazil.

More papers were presented on the analysis of satellite images. Xu presented the way to show the spatial pattern modeling of snail distribution and correlation analysis with land-cover types generated from Ikonos image in Xichang villages, Sichuan Province. Seto reviewed the application of RS to schistosomiasis, with the aim of better understanding spatial factors at the local level that affect disease transmission. Two studies in China based on RS data with different spatial resolutions were discussed. The first study attempted to identify *O. hupensis* habitats by classification of Landsat TM imagery. The results of this study suggested that remote sensing may be used to create maps of emerging snail habitats. The second study presented the use of high-resolution Ikonos imagery to identify spatial features associated with schistosomiasis prevalence.

The impact of the 1998 floods on snail distribution in the lower Yangtze River basin was assessed by Zhou. When compared with ground snail survey data collected in the spring of 2000, the correspondence rate between potential snail habitats identified by image analysis of the 1998–1999 Landsat TM data and ground survey data was over 90% in large marshlands in two regions, the Poyang Lake region and the Nanjing part of the Yangtze River. Guo presented a rapid method of snail habitat identification and assessment of high risk regions for schistosomiasis in the Poyang Lake by GIS/RS. The extracted image map was able to identify subtle ecotones (zones between grass-land that are optimal snail habitats, and lake water, mud flats, ponds that are too wet for snail breeding). All spots with infected snails were recorded with geo-code data, that is, longitude, latitude and the distance between the spots

to villages. A negative linear regression relationship was shown between prevalence of schistosomiasis and distance from village to positive snail sites. Zhang demonstrated the surveillance on snail habitats and snail dispersal during flooding seasons by using Landsat TM satellite data. The results showed that snail distribution was related to grass, bulrush, and willow areas. Lin reported the classification maps of the marshlands with different land cover in endemic areas of *S. japonicum*, created by Landsat TM data from Chayegang, Jiangxi Province and Liupo, Anhui Province. Wu collected field data before and after flooding from April 1999 to December 2000 in 100 survey sites in correspondence to the satellite images (Landsat TM) taken. Snail habitat was highly associated with grassland and sparsely covered grassland which was analyzed by CART classification. The sensitivity of classification ranged from 83.33 to 94.45%, with specificity being from 61.11 to 68.33%. All these results demonstrated that RS can contribute to studies on the distribution of snail habitats and the approach can become a promising epidemiological

method for schistosomiasis and other diseases related to ecology.

Malone reported a model on the environmental risk of *S. haematobium* in East Africa using a vegetation index and land surface temperature from the global land 1-km AVHRR dataset. Annual composite maps prepared from normalized difference vegetation index (NDVI) and earth surface maximum temperature (Tmax) satellite data from the 1992–1995 archives of the Global land 1-km program of the United States Geological Survey were studied for potential value, using GIS methods, as surrogates of climate data in development of environmental risk models for *S. haematobium* in East Africa. These results, and similar findings in an earlier report on *S. mansoni* risk in the same region, suggest that Global 1-km NDVI and Tmax, when used together, can be used as surrogate climate data for development of GIS risk assessment models for schistosomiasis in East Africa. This raised the question whether it is possible to use image analysis models to identify the habitats of amphibious *Oncomelania* snails.