CHAPTER 6

Schistosomiasis Japonica: Control and Research Needs

Xiao-Nong Zhou,* **Robert Bergquist,†**
Lydia Leonardo,‡ **Guo-Jing Yang,§** **Kun Yang,§**
Mohammad Sudomo,¶ and **Remigio Olveda#**

Contents

Abstract

Schistosomiasis japonica, a chronic and debilitating disease caused by the blood fluke *Schistosoma japonicum*, is still of considerable economic and public health concern in the People's Republic of

* National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention, Shanghai, People's Republic of China
† Ingerod, Brastad, Sweden
‡ Department of Parasitology, College of Public Health, University of the Philippines, Manila, Philippines
§ Jiangsu Institute of Parasitic Diseases, Wuxi, People's Republic of China
¶ Ecology and Health Status Research and Development Centre, National Institute of Health Research and Development, Ministry of Health, Jakarta, Indonesia
# Department of Health, Research Institute for Tropical Medicine (RITM), Muntinlupa, Manila, Philippines

Advances in Parasitology, Volume 72
ISSN 0065-308X, DOI: 10.1016/S0065-308X(10)72006-6

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China, the Philippines, and Indonesia. Despite major progress made over the past several decades with the control of schistosomiasis japonica in the aforementioned countries, the disease is emerging in some areas. We review the epidemiological status and transmission patterns of schistosomiasis japonica, placing it into a historical context, and discuss experiences and lessons with national control efforts. Our analyses reveal that an integrated control approach, implemented through intersectoral collaboration, is essential to bring down the prevalence and intensity of *Schistosoma japonicum* infections and disease-related morbidity, and to sustain these parameters at low levels. The need for innovation and a sufficiently flexible control approach to adapt interventions in response to the changing nature and challenges of schistosomiasis control from the initial phase of morbidity control to the final state of elimination is emphasised. The aim of the presentation and the analyses is to inspire researchers and disease control managers elsewhere in Asia, Africa, and the Americas to harness the experiences gained and the lessons presented here to improve the control and eventual elimination of schistosomiasis and parasitic diseases.

6.1. INTRODUCTION

Approximately, 12% of all people on Earth are at risk for schistosomiasis, a disease widely spread access the tropical belt where a third of the global population lives. More than 200 million people are infected by schistosomiasis and close to 800 million are daily at risk (Steinmann et al., 2006). There is a great variation in prevalence estimates, which results from the focal character of this disease (Brooker et al., 2009; Engels et al., 2002; Utzinger et al., 2009). The distribution is not easy to pin down in detail and most overviews therefore express countries as either endemic or not. However, this is a spurious way of viewing the situation, as the endemic areas in most cases, including Africa, are limited to particular places suitable for transmission such as natural water bodies (ponds, lakes, and rivers) and man-made constructions such as multi-purpose small dams, large dams for hydropower production, feeding irrigation systems, and large-scale irrigation schemes (Steinmann et al., 2006). Thus, most countries are characterised by large stretches of safe land punctuated by numerous small areas of high transmission. Schistosomiasis can be controlled where the public health importance of the disease has been recognised, political will and commitment prevail, and financial and technical resources exist (Engels et al., 2002; Wang et al., 2008a). However, elimination has proved difficult in many places, particularly in sub-Saharan Africa (Stothard et al., 2009).

6.1.1. Life cycle of *Schistosoma japonicum*

Schistosomes are parasitic, trematode worms with a complicated life cycle (Gryseels et al., 2006; Ross et al., 2002). Mammals act as the definitive host in which large amounts of eggs, the cause of almost all symptoms, are produced by the adult female worm. Humans have been implicated in the transmission of five species of *Schistosoma*, but more than 90% of all infections are caused by just three: *S. mansoni* (mainly in Africa and South America) and *S. japonicum* (predominantly in the People's Republic of China (P.R. China), the Philippines, and Indonesia) produce intestinal disease, while *Schistosoma haematobium* (common in Africa and some countries in the Middle East) causes urinary schistosomiasis. The two less common species with human involvement are *S. intercalatum* in Western and Central Africa, and *S. mekongi* in Cambodia and Lao People's Democratic Republic (Lao PDR). *S. malyayensis*, a species only reported in Malaysia, is known to cause natural infections in humans, but sustained transmission through human populations has not been confirmed.

In most cases (in four of the five species involved in human transmission), the adult worms live in the capillary network around the intestines where they release hundreds or thousands of eggs daily, many of which end up in the liver, and remaining eggs move to the membrane layer of intestine, thereby causing intestinal schistosomiasis. *S. haematobium*, being the exception, causes the urinary form of the disease due to its location around the bladder, where the inflammatory reaction to the eggs not only affects the bladder but also the urethra, ureters, and kidneys. Up to 50% of all eggs become sequestered in the final host, but the life cycle requires that at least some eggs work themselves through the tissues to eventually become excreted with the faeces or, in the case of *S. haematobium* infection, the urine. Those eggs that are deposited in water hatch and release the miracidium, an intermediate form capable of infecting snail intermediate hosts in which several generations of asexual sporocyst stages develop. The life cycle is completed when cercariae from the snails return to the final host, penetrate the skin and rapidly develop into schistosomula upon skin penetration, which finally mature into millimeter-long adult worms as shown in Fig. 6.1.

6.1.2. Morbidity of schistosomiasis japonica

The human symptoms caused by schistosomiasis vary from hardly detectable to very serious. The majority of all infected people might not even know that they are infected, far from all develop clinical symptoms and only a minority become seriously affected. In principle, three clinical stages of schistosomiasis are recognised, the first or acute phase, the second or ''silent'' phase, and the third or chronic phase. These clinical

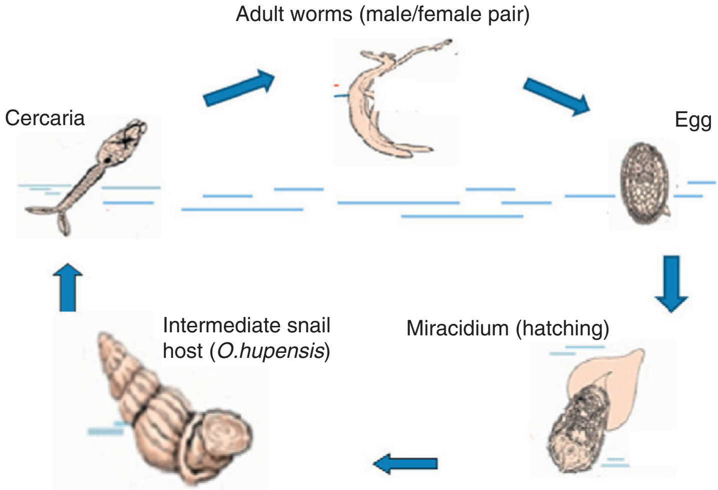

FIGURE 6.1 Simplified *Schistosoma japonicum* life cycle.

stages are similar in all forms of the disease with some exceptions, that is, the *S. haematobium* infection presents differently due it its focus in the bladder and the acute form seems to be more pronounced in schistosomiasis japonica compared to the other forms of intestinal schistosomiasis.

Mortality due to schistosomiasis is comparatively low, but the chronic character of the disease causes widespread human suffering. The social impact resulting from the fact that most people in the endemic areas are more or less continuously infected has yet to be fully appreciated. In our opinion, and that of others (King, 2010; King et al., 2005; Li et al., 2005), the full impact of schistosomiasis on a global level is not far less than that caused by malaria and tuberculosis. This may appear counterintuitive considering the success of praziquantel, the safe and effective treatment, which has contributed to the remarkable reduction of morbidity due to schistosomiasis worldwide (Chen, 2005; Doenhoff et al., 2008; Fenwick et al., 2003; Xiao et al., 2010).

In spite of the major public health impact of schistosomiasis in endemic countries, research on this parasite has not received the levels of funding required to make sustained progress. The current situation in Southeast Asia is summarised in Table 6.1. Even if vigilance is high in some countries, for example, P.R. China and in private initiatives such as the Schistosomiasis Control Initiative (SCI) in Africa (Fenwick et al., 2009), the overall problem caused by this disease remains large. However, since transmission is only marginally affected by treatment of the human host, rapid reinfection limits the success of drug-based control due to the need for indefinitely continued treatment (Utzinger et al., 2009). This disease

TABLE 6.1 Current status of schistosomiasis in Southeast Asia

Country	Prevalence (%)	No. of cases[a]	No. at risk[a]	Disease distribution	Risk and problems	Country goals
P.R. China	2.5	720	56,000	In seven provinces. New endemic foci found in the lake region	Three Gorges Dam, water-development projects, animal reservoirs, global warming	Infection rate <5% by 2008, <1% by 2015
Indonesia	0.17–1.7	0.269	30.5	Two foci (the Lindu and Napu valleys). New endemic area found in Bada valley	Mobile populations, domestic and wild animal reservoirs	Elimination by the year 2010
Philippines	3	100	1900	Three regions (Luzon, Visayas, Mindanao). New endemic foci found in the northern part and central parts of the country	Environmental changes, changes of land cover, animal reservoirs	Lowered to <1% by 2010
Total		820.3	57,930	Three countries in Asia	Natural, social, and economic factors	

[a] $\times 1000$.

thus remains a hurdle for economic development, posing a threat that can be kept at bay only by regular re-treatment; therefore only a strong research initiative resulting in new approaches can make a decisive impact (Utzinger et al., 2005).

Regardless of the angle from which morbidity due to schistosomiasis is viewed, it is beyond doubt that the widespread use of praziquantel is the main reason for the global, dramatic drop of morbidity due to this disease. Prevalence, on the other hand, is more difficult to pin down. Stool examination, using the Kato-Katz thick smear technique (Katz et al., 1972), recommended by the World Health Organization (WHO) for the diagnosis of intestinal schistosomiasis, is useful when the intensity of disease is generally high. However, it is less well suited for application in controlled areas since many low-level infections are missed when the number of parasites in the host falls below the threshold needed to produce above 100 eggs per gram (EPG) of stool (Bergquist et al., 2009; de Vlas and Gryseels, 1992; de Vlas et al., 1997; Utzinger et al., 2001). *S. japonicum* may also be more difficult to diagnose due to the pronounced propensity of the eggs of this species to aggregate (Pesigan et al., 1958; Yu et al., 1998). Indeed, based on three Kato-Katz thick smears from two separate stool samples as the diagnostic ''gold'' standard, Lin et al. (2008a, b) found the rate of underestimation in a well-controlled area in P.R. China to be as high as 36% when compared to records based on two Kato-Katz thick smear readings.

6.2. SCHISTOSOMIASIS JAPONICA IN ASIA

6.2.1. Regional status of schistosomiasis japonica

6.2.1.1. Historical records

S. japonicum was first discovered in Japan (Katsurada, 1904) and its life cycle was established by Fujinami and Nakamura (1909). At the beginning of the 1900s, *S. japonicum* was also found in P.R. China (Logan, 1905) and in the Philippines (Wooley, 1906). The eggs of this parasite have been found in ancient corpses (Mao and Shao, 1982), which serves as a reminder that the parasite has been a human companion for millennia and probably much longer than that. In 1906, human infections were found in the Philippines and later (in 1937) also in Indonesia (Tanaka and Tsuji, 1997). Schistosomiasis was thus established in four countries of the region. Transmission of *S. japonicum* has been interrupted in Japan and, although animal reservoirs still remain, no more new human cases have been discovered there since 1978 (Tanaka and Tsuji, 1997; WHO, 2001). Therefore at present, *S. japonicum* only exists in three Asian countries, namely P.R. China, the Philippines, and Indonesia.

6.2.1.2. Current status

Although transmission intensity has been reduced significantly during the past 50 years, a total of 820,300 human cases are currently reported from P.R. China, Indonesia, and the Philippines (Coutinho et al., 2005; Garjito et al., 2008; Zhou et al., 2007). However, there are great differences in the distribution and impact of schistosomiasis as it affects large areas and large numbers of people in some areas, while it is limited to a few foci in other places. Table 6.1 gives an overview of the situation based on estimates from 2005.

6.2.2. Schistosomiasis in P.R. China

6.2.2.1. Historical background and geographical distribution

P.R. China has been spectacularly successful in managing to reduce the extent of the endemic areas. The hard work aimed at elimination of schistosomiasis in all feasible and eradicable areas bore fruit relatively early on, but the lower reaches of the Yangtze River valley and some high-altitude areas in the Sichuan and Yunnan provinces remain severely affected to this day. The endemic areas were traditionally stratified into three types, that is, (i) ''plains and waterways'', (ii) ''marshlands and lakes'', and (iii) ''mountainous regions'', an ecosystem stratification which is still in use. The main thrust was snail control through environmental engineering (Mao and Shao, 1982), but the strategy also offered free diagnosis and treatment, including health education to everyone living in an area at risk (Maegraith, 1958). Irrigation ditches were reconstructed by turning over the soil in a scheme to destroy the snail intermediate host using an environmental approach that also involved lowering of the water level of canals and the building of dykes along the lake shores (Mao and Shao, 1982). This course of action was effective and rapidly reduced the endemic areas by more than two-thirds, leading to disappearance of the disease; first in Shanghai and Guangdong (1985) and later in Fujian (1987), Guangxi (1989), and Zhejiang (1995) (Wu et al., 2005; Zhou et al., 2005). After these achievements, the pace slowed as the problems in the seven remaining endemic provinces were more difficult to deal with (Utzinger et al., 2005; Zhou et al., 2005). Nevertheless, national prevalence has continued its downward trend. The most severely affected areas were, and still are, the Yangtze River valley, the marshlands around the Dongting and Poyang lakes, and certain mountainous areas in the West (Fig. 6.2) (Hao et al., 2007).

6.2.2.2. Control programme

Compared with the 1989 baseline data, the final 2002 evaluation of the impact of the World Bank Loan Project (WBLP) revealed that most of the objectives had been met, that is, the total number of infected people had

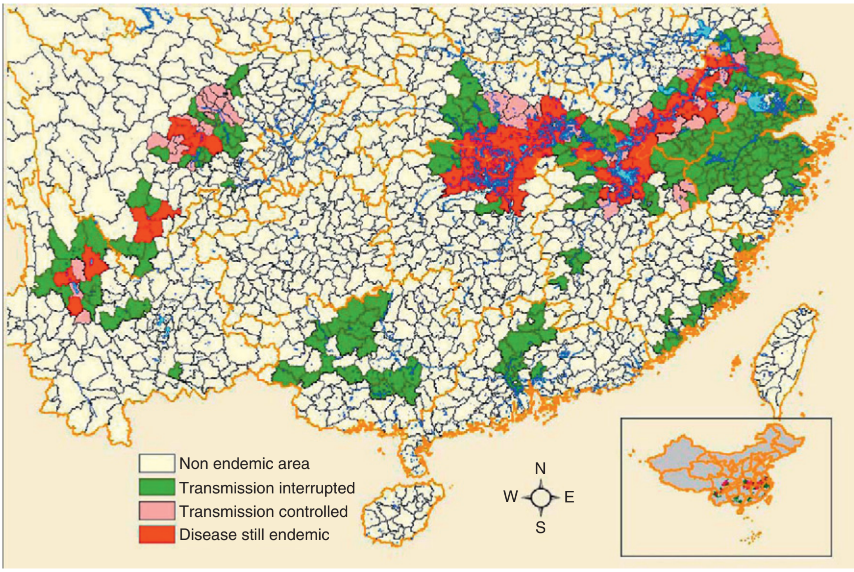

FIGURE 6.2 The epidemiological status of schistosomiasis in P.R. China in 2006.

dropped to somewhere between 700,000 and 800,000, the prevalence in the remaining endemic areas had been halved in both humans and bovines, and the snail-infested areas had been reduced by three-quarters (Chen et al., 2005). However, there were also problems, for example, the diminishing trend of snail infection had stalled with rates fluctuating at a low level rather than disappearing completely (Chen et al., 2005). Indeed, although the infection rate and density of infected snails had decreased by 69% and 45%, respectively, the areas affected had again increased by the end of the project (Zhang and Wong, 2003). The control of schistosomiasis japonica became a priority after a survey carried out in the 1950s. The national control programme was initiated soon after that and has now continued uninterrupted for more than 50 years (Utzinger et al., 2005; Zhou et al., 2005). By employing vast resources and diverse approaches, the national control programme led to the elimination of the disease from a large area involving 260 counties and transmission has been controlled in another 63 counties. Substantial progress has also been made in most of the remaining endemic areas and, as can be seen in Fig. 6.3 (Wu et al., 2006), the total number of infected people has been reduced by over 90% since 1950 (Wang et al., 2008a). A recent nationwide sampling survey provided a detailed picture of the contemporary epidemiological situation (Fig. 6.3). According to this survey, the number of infected people in 2005 was estimated at 725,000 (Zhou et al., 2007).

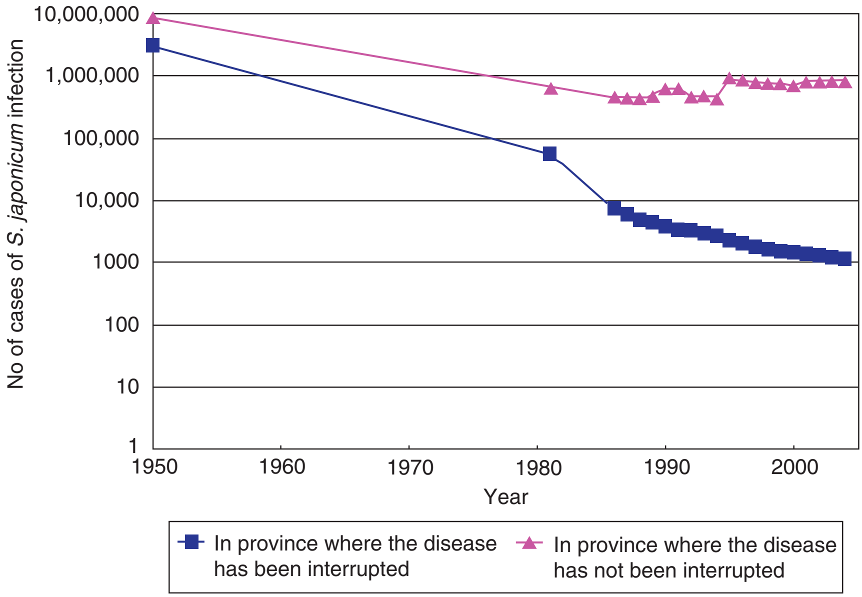

FIGURE 6.3 Reduction of schistosomiasis cases in P.R. China in the period 1950–2000.

6.2.2.3. Experience and lessons from the control programme

Although the fact that the overall epidemiological situation has much improved since the national control programme was initiated in the early 1950s, recent survey results confirm that progress is now less vigorous. In fact, there has been only little progress since the end of the 10-year WBLP that lasted from 1992 to 2001 (Chen et al., 2005; Utzinger et al., 2005). Schistosomiasis japonica even re-emerged in at least 38 counties where transmission control and interruption had been declared previously (Liang et al., 2006). There has also been a resurgence of schistosomiasis in terms of the total number of infected cases, also following the termination of the WBLP (Fig. 6.4) (Utzinger et al., 2005). In addition, foci of intensive transmission and high prevalence rates in humans and cattle are still found in the areas mentioned earlier. The ongoing transmission in other endemic areas, albeit at a lower level, is also of considerable concern, as the situation is likely to deteriorate as soon as control efforts are scaled down (Utzinger et al., 2005; Wang et al., 2008a). It is therefore crucial for continued success to maintain and sustain the current efforts to further reduce transmission.

As a consequence, the Government of P.R. China has renewed its commitment by assigning equal priority to schistosomiasis, tuberculosis, HIV/AIDS, and hepatitis B (Engels et al., 2005). New and ambitious targets for control have been set: infection control (prevalence $<5\%$) for

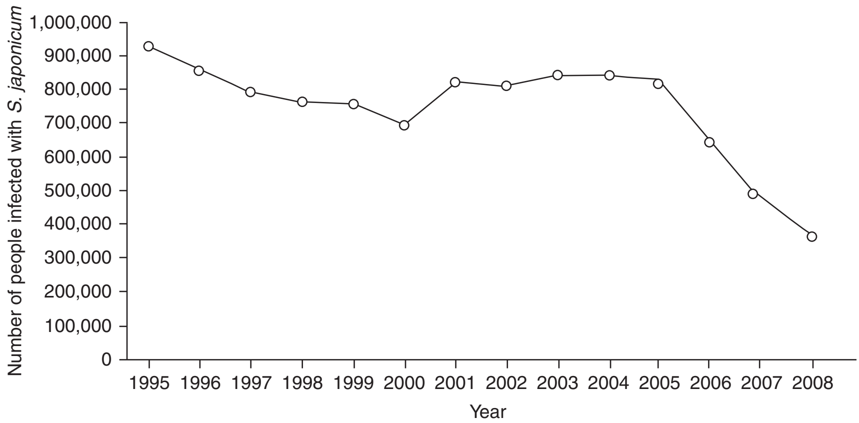

FIGURE 6.4 People infected with *S. japonicum* in P.R. China between 1995 and 2008.

the whole country by 2008 and transmission control (prevalence $<1\%$) by 2015 (Wang et al., 2008a, 2009a).

6.2.2.4. Contribution of research to the control programme

The main research achievements related to schistosomiasis in P.R. China during the last five decades have contributed to the improvement of the national control programme; these improvements are reflected in three main fields. Firstly, new tools of diagnostics and intervention have been developed, secondly, epidemiological knowledge has been gained from field settings and, thirdly, new control approaches have been developed and field-tested (Liu et al., 2008).

The discovery and development of antischistosomal drugs and diagnostic assays related to schistosomiasis has provided good tools for the detection and treatment of infected cases, and has reduced the disease burden through preventive chemotherapy. For example, the local production of praziquantel, in collaboration with several Chinese institutions since 1982, facilitated widespread use of the drug at low cost for individual treatment and large-scale community-based morbidity control. Numerous reports on the clinical use of praziquantel in P.R. China have been published since the late 1970s (Chen, 2005; Chen et al., 2007; Wu, 2002; Xiao, 2005a,b; Xiao et al., 2000; Yang et al., 2009b; Zhu, 2005).

More than 50 million treatment courses have been administered in P.R. China, and several studies on the optimisation of praziquantel at the individual patient level and within community-based control programmes have been described (Chen, 2005; Song et al., 1998; Wu, 2002; Xiao, 2005a,b; Xiao et al., 2000; Zhu, 2005). Large-scale use of praziquantel was particularly widespread during WBLP, with a significant reduction in morbidity due to *S. japonicum* by more than 30% (Chen et al., 2005).

In 1980, Chinese scientists discovered that artemisinin and its derivatives (e.g. artemether and artesunate) could kill the early developmental stages of *S. japonicum*, which makes it possible to prevent the development of egg-laying adult worms, and hence prevent morbidity associated with the immunological reactions to schistosome eggs trapped in the host tissue (Xiao, 2005a,b; Xiao et al., 2000, 2002, 2010).

Based on the finding that the artemisinins exhibited highest activity against juvenile *S. japonicum* worms, these drugs have been used as a ''chemoprophylactic'' agent against schistosomiasis. Nowadays, artemisinin is used to prevent patent infections in high-risk populations, for example, flood relief workers, who are exposed to schistosome-infested water for a short period of time (Song et al., 1998).

With regard to diagnostic assays, in P.R. China, more than 20 serologic assays have been developed during the last 30 years in different institutions (Wu, 2002). These immunodiagnostic kits, often in combination with stool examination among those individuals who showed a positive immunodiagnostic test result, have improved the screening of cases, especially in communities with low prevalence and low intensity infection, resulting in more cost-effective control programmes (Zhu, 2005).

Epidemiological studies on schistosomiasis have improved the understanding of schistosomiasis transmission in natural field settings, leading to the classification of endemic areas into specific ecosystem types (Wang et al., 2008a; Zhou et al., 2005). Classification based on ecological characteristics helped greatly in the development of both short-term and long-term goals and monitoring and evaluation (M&E) indicators in the national control programme. Model-based epidemiological findings have also improved control strategy adaptation at the base-level or community-level in different environmental settings (Chen et al., 2007; Yang et al., 2009b).

In terms of control approaches, numerous investigations focused on environmental management for enhancing the national schistosomiasis control programme. In particular, approaches that integrated with other sectors improved the efficiency of the control programme significantly (Wang et al., 2009a). In the last 30 years, control was integrated with (i) agricultural activities, for example, alteration of crops planted, reclamation of land and plantations to eliminate snail habitats (Gao, 2002); (ii) water resources development projects, for example, cement lining of irrigation canals, installation of sinks to obstruct snail dispersal, and construction of flood gates in the connection areas of main irrigation canals or rivers(Li et al., 2007; Wang et al., 2002); (iii) forestry projects, for example, planting trees in the marshlands to change the ecology of snail habitats and to discourage buffaloes from grazing on the marshland, and establishing new forests in the mountainous areas (Zhang et al., 2003; Zuo et al., 1999); and (iv) agricultural projects, for example, construction of fish ponds, rearrangement of irrigation systems and establishment of drainage systems (Zhang et al., 2003). These approaches have contributed to the gradual elimination of transmission of *S. japonicum* in vast endemic areas of P.R. China (Zhou et al., 2005).

6.2.3. Schistosomiasis in the Philippines

6.2.3.1. Historical background

As elsewhere, snail control dominated schistosomiasis-related activities in the Philippines before the 1980s (Pesigan and Hairston, 1961). Drainage, stream canalization and pond management were tried in combination with molluscicides, but the Chinese success could not be duplicated due to ecological differences (Blas, 1976). Health education and environmental hygiene were essential components of the control programme, but efforts to enforce sanitation were not successful as only a third of the population had satisfactory latrines. In the end, it was not possible to mount an initiative capable of reducing the national prevalence of *S. japonicum* infection until chemotherapy was introduced as the main control approach (Santos et al., 1979).

The first case, a Filipino male who had never been out of the country, was reported in 1906 (Crowell and Hammack, 1913). Subsequently, schistosome ova were found in several cases among 500 autopsies reported in 1908 and in the faeces of some prisoners admitted to the Bilibid Prison, City of Manila in 1914 (Ramos, 1928). Several years later, in 1928, a case of Katayama disease presenting as chronic appendicitis was reported (Tubangui, 1932). However, in spite of all these human cases, attempts to identify the intermediate host of the parasite were not successful until the discovery of the small, amphibious *Oncomelania hupensis quadrasi* freshwater snail in Palo, Leyte in 1932 (Garcia, 1976). The life cycle and the multi-host characteristics of the parasite were confirmed when the infection could be transferred to mice, rabbits, and monkeys by cercariae obtained from the *Oncomelania* snails. Since then, the distribution of *O. h. quadrasi* has been well characterised and shown to correspond to the major endemic areas for human schistosomiasis.

6.2.3.2. Epidemiology and distribution

Following the identification of the intermediate host snail, *Onchomelania quadrasi*, research on the basic biology of the parasite was overtaken by field surveys delineating the schistosomiasis-endemic areas and by studies on the clinical and pathological aspects of schistosomiasis japonica. Research activities were disrupted in the 1940s during World War II but revived when an outbreak of schistosomiasis occurred in the Americans and Allied Armed Forces landing on the island of Leyte in 1945 (Santos, 1984). In 1953, schistosomiasis was recognised as a public health problem in the Philippines and from the early 1960s to the latter part of the 1970s, extensive research activities were conducted, ranging from parasite biology and transmission and control to clinical and pathological aspects of the disease. By 1975, the endemic areas of *S. japonicum* infection in the Philippines had been delineated (Hernandez, 2003) and indicated that approximately 5 million people lived in schistosomiasis-endemic areas. It was estimated that over 700,000 individuals were infected. The major foci of schistosomiasis japonica were, and still are, the islands of Leyte, Samar, and Mindanao covering 24 provinces of eight regions of the country as shown in Fig. 6.5.

These regions are predominantly rice-growing areas as there are no distinct dry seasons, a fact which maximizes contact between humans and freshwater snails. In 2006, it was estimated that the population in the endemic areas had grown to 12 million. However, thanks to the implementation of extensive preventive chemotherapy programmes, the number of individuals with active infection had been reduced from the mid-1970s estimate to around 150,000 in the new millennium (Olveda, 2006). The current endemic areas in the Philippines cover 11 regions and 28

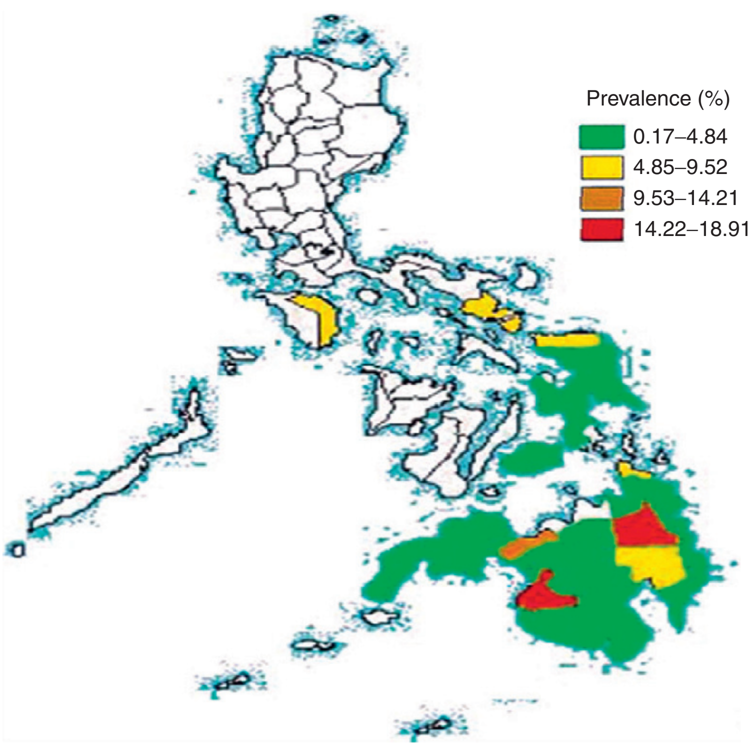

FIGURE 6.5 Provinces endemic for schistosomiasis in the Philippines in 1997.

provinces, affecting 189 municipalities, and 2222 barangays (villages). The total population at risk is 12 million people, 2.5 million of which are directly exposed to the disease. The 3391 positive snail colonies in the endemic barangays cover approximately 11,250 ha.

In the period 1981–1985, prevalence in the endemic areas first declined to an average 10%, in 1987, it reached 7%, and then stabilised at a level thereabouts until eventually dropping to near 4% in 1992 (Blas et al., 2004). In 1997, a report from the Department of Health (DoH) put the prevalence of schistosomiasis at 4.7% (DoH, unpublished). The same report classified three provinces as endemic with a prevalence rate of 18.9%, two provinces as moderately affected and 19 provinces with low endemicity, that is, less than 2% prevalence. This progress first gave the impression that the schistosomiasis problem was manageable and that it should be possible to eliminate the disease by community-based mass treatment. However, prevalence increased to 5.4% in 1994 as the looming termination of the PHDP led to less regular prevalence surveys, which had to be concentrated on highly endemic areas with sampling limited to 10–20% of the population (Bergquist and Tanner, 2010). Indeed, with 10 out of 16 regions in the country affected by schistosomiasis japonica in 2002 (Leonardo et al., 2002), the disease remained a public health problem.

6.2.3.3. Research activities

The early 1980s saw the beginning of a multi-disciplinary approach in the study of the disease. This was made possible with inputs from WHO, the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) and the Rockefeller Foundation, followed by a Tropical Medicine Research Center (TMRC) grant from U.S. National Institutes of Health (NIH) in the United States.

In addition to direct control approaches, the University of the Philippines, College of Public Health (UP-CPH) Schistosomiasis Research Group (UP-CPH SRG) focused on vaccine development as a long-term solution. That work led to the identification of several candidate vaccine molecules such as Sj 26, glutathione-*S*-transferase (GST), Sj 23, and several promising proteases from egg and adult stages of the parasite (Olveda, 2006). A strong supporting factor for pursuing vaccine development was that vaccines would also be effective against transmission by reducing the excretion of mature eggs in the faeces of infected humans and animals (Santiago et al., 1998).

Based on its immunological expertise, the Research Institute for Tropical Medicine (RITM) Schistosomiasis Study Group (RITM SSG), which also contributed greatly to the vaccine approach through the WHO/TDR vaccine initiative programme, also carried out a study of human immune responses as correlates of protection to specific *S. japonicum* recombinant antigens. Immune responses of individuals identified as resistant or susceptible to *S. japonicum* infection to the different antigens were analysed (Acosta et al., 2002). Studies were also conducted to measure the impact of *S. japonicum* infection on childhood growth and development of Filipino children (McGarvey et al., 1992).

6.2.3.4. Control efforts

Before the advent of effective chemotherapy, the Government focused on health education, limiting human exposure to the infective form of the parasite, and efforts to break the parasite life cycle through control of the intermediate host snail using agro-engineering methods and environmental modification. Then, as now, the constraint was mainly financial, that is, the prohibitive cost of agro-engineering methods and the protracted effect of environmental sanitation and health education. Hence, pilot projects were conducted with assistance from WHO and UNICEF and other foreign agencies. Control programmes evolved from these projects became integrated with existing health structures or functioned as independent bodies solely aimed at disease control. Foreign aid in the form of technical assistance, supplies and equipment, and funds sustained many of the components of the early control programme activities. There were significant achievements but none sufficiently effective to significantly reduce the national prevalence of *S. japonicum* infection. For example, environmental manipulations such as drainage, stream canalization, and pond management in combination with molluscicides were used but found to be too expensive. In addition, pilot studies have shown that this approach does not have a significant impact on transmission. Improved environmental hygiene was an essential component of the control programme but was difficult to sustain in a population no more than one-third of which had satisfactory latrines. The successful snail control approach used in P.R. China was not implemented due to differences in ecology and habitat of the snails found in the Philippines, while chemotherapy was not possible because the drugs available at the time showed unsatisfactory safety profiles and had significant side effects (Antimony potassium tartrate trihydrate).

A dramatic decrease in national prevalence of *S. japonicum* infection was noted after the introduction in 1978 of praziquantel in the Philippines. The most impressive effect was in the first half of the 1990s and was attributed to the implementation of the Philippine Health Development Plan. With support from the World Bank, the National Schistosomiasis Control Service of the DoH was able to intensify case finding and treatment in all endemic areas in the country and managed to reduce national prevalence from more than 10% before 1990 to less than 5% after 1995. The significant drop in the national prevalence of *S. japonicum*, which was sustained at less than 5% from 1996 to 2006, gave the impression that schistosomiasis was in retreat and that elimination could be achieved with the next few years. However, longitudinal studies, carried out by the RITM SSG showed that chemotherapy alone would only lower morbidity and prevalence but not eliminate schistosomiasis due to continuous transmission supported by animal reservoirs. In addition, interruption of treatment for more than 2 years was shown to produce rebound morbidity and increased intensity of *S. japonicum* infection (Leonardo et al., 2002; Olveda et al., 1983, 1996). These findings, and the decreasing compliance encountered by the control programme, strongly suggest that chemotherapy-based control programmes must be sustained with high compliance and in combination with other control measures until a more effective alternative approach has been developed (e.g. vaccination).

It is, in this connection, important to realize that the national prevalence data in the Philippines for the last 5 years may be significantly underestimated because only around 10–20% of all individuals in the endemic areas were examined. In addition, it is known that examination of a single stool sample from each individual using the Kato-Katz technique considerably underestimates the prevalence of infection (Lin et al., 2008a; Zhang et al., 2009; Zhou et al., 2008a,c).

The discovery of praziquantel brought about a shift of focus from the highly expensive snail control approach to a more manageable strategy involving case detection and treatment. This significant development renewed hopes of eventually gaining control of the disease with the limited resources available. From a four-pronged approach that included treatment of cases, environmental sanitation, snail control, and health education intended to control transmission or eliminate schistosomiasis, the government adopted the more feasible objective of morbidity control through praziquantel-based chemotherapy supplemented by environmental sanitation, health education, and mollusciciding.

Figure 6.6 shows the dramatic drop in disease prevalence in the 1980s. This trend continued up to the early 1990s. This period marks the intensification of the control programme, which was sustained for several years by influx of external funds, particularly by loans from the World Bank. In 1990, the Philippine Health Development Project (PHDP) provided the push to expand the target to 95% case detection and 100% treatment coverage. However, in 1994, prevalence increased to 5.4% from a low of 4.0%, coinciding with the end of PHDP support (Fig. 6.6). Thereafter, prevalence surveys became irregular and limited mostly to the highly endemic areas and in those provinces where research was being undertaken.

RITM contributed greatly in terms of policy formulation, which brought about a significant drop in prevalence and morbidity in many areas. In some municipalities, prevalence was sharply reduced in just 3 years, that is, from a high of 42–50% prevalence to a plateau level of 10%, a level that has been maintained for 6 years, but the fear of resurgence is still there. A 1997 report from the DoH puts the overall prevalence of

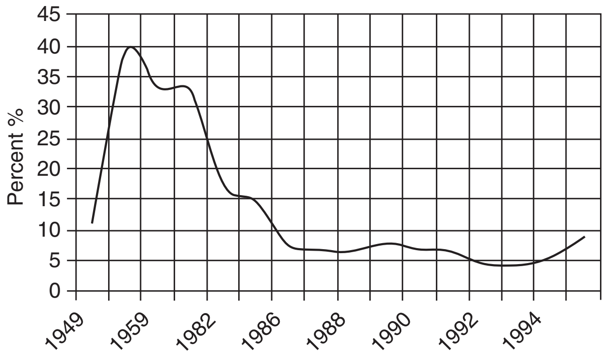

FIGURE 6.6 Mean schistosomiasis prevalence in the Philippines from 1953 to 1997.

schistosomiasis in the country at 4.7%. The same report classified three provinces as endemic with a prevalence rate of 18.9%, two provinces as moderately endemic and 19 provinces with low endemicity. One province is reported to have reached the point of elimination as the prevalence rate had reached a very low value (0.17%). In the National Objectives for Health, which is a statement of the national goals for health of the Philippine Government, schistosomiasis was targeted for elimination as a public health problem in endemic areas over the next 4 years (Fig. 6.7).

Although problems in the control of schistosomiasis have recently been aggravated by the diminishing attention given to it as a result of the growing problems posed by other diseases such as tuberculosis, malaria, and HIV/AIDS, the government hopes to achieve the goal of elimination of the disease by embarking on a multi-sectoral and more vigorous approach; this approach will continue to involve interventions in treatment, environmental sanitation, snail control, and other preventive actions (Leonardo et al., 2008).

A WHO-assisted project, initiated in order to determine the baseline prevalence of schistosomiasis in the country from 2005 to 2007, marked the first time that a stratified two-step systematic cluster design was used for sampling in a prevalence study. Of the three largest islands, Luzon, Visayas, and Mindanao, the latter showed the widest coverage of the disease at 60% compared with 45% in the Visayas and 37.5% in Luzon. Figure 6.8 shows the distribution and intensity of schistosomiasis in the three island groups. The highest prevalence is along the southeastern part of the Visayas and Mindanao. The lower coverage in Luzon and the Visayas could be due to the geographical separation of the regions into islands deterring easy transport of the disease into other regions. Considering the situation by region: Region 13 or Caraga in Mindanao, which includes the provinces of Surigao del Norte, Agusan del Norte, Surigao del Sur, and Agusan del Sur, ranked first in prevalence at 1.6%, followed

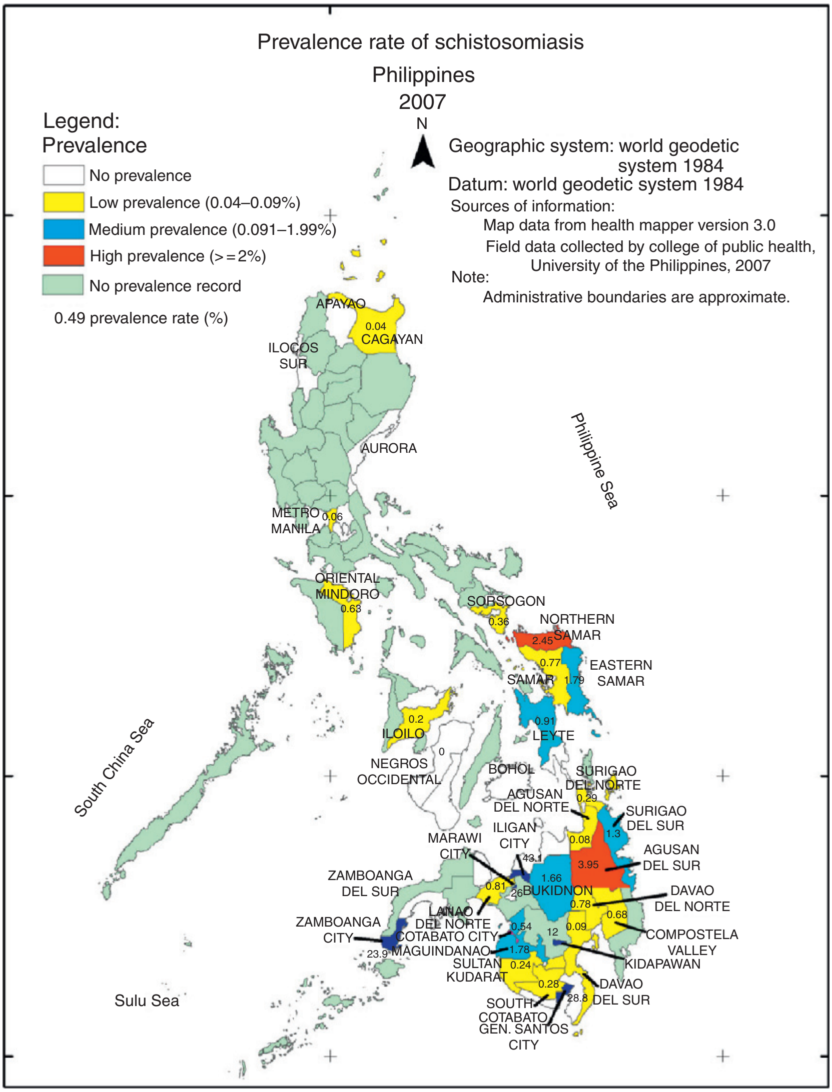

FIGURE 6.7 The distribution and intensity of *S. japonicum* infection in the Luzon, Visayas, and Mindanao regions.

by Region 8 in Visayas, which is composed of Northern Samar, Eastern Samar, Leyte, Southern Leyte, and Biliran at 1.5%. By province, Agusan del Sur, as in previous records, showed the highest prevalence at 4.0%, followed by Northern Samar at 2.5% and Eastern Samar at 1.8%. Overall, the prevalence rate among males was higher than that of females suggesting occupational hazards related to farming and fishing. The higher

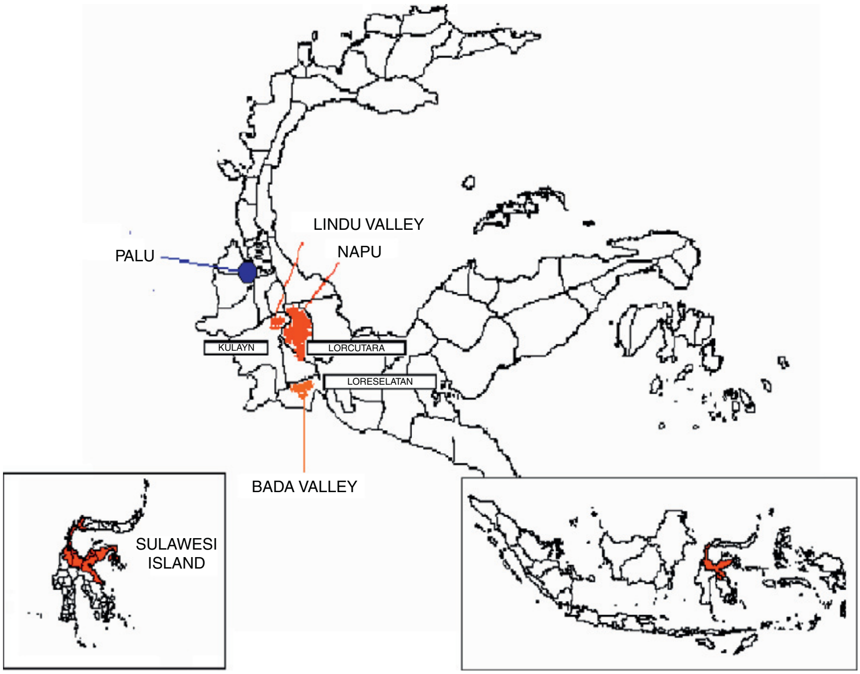

FIGURE 6.8 Schistosomiasis prevalence in humans between 1984 and 2006 in Napu and Lindu Valleys, Central Sulawesi Province, Indonesia.

occupational exposure is also borne out by the age distribution, which showed the prevalence to be consistently high among the adults compared with the younger age groups in all the regions.

New endemic foci have been discovered in the last 7 years. These new endemic areas are found in Gonzaga, a municipality in Cagayan Valley located in the northernmost part of Luzon and in the municipality of Calatrava in Negros Occidental in the Visayas region. WHO-funded research showed the presence of indigenous cases, infected snails and infected animals in several villages in the new endemic municipalities. It is proposed that *Oncomelania* snails must have been there even before the discovery of the disease and that population movement due to job opportunities must have brought cases into the new endemic sites.

The national survey showed that schistosomiasis occurs together with other helminthic infections, most importantly, soil-transmitted helminthiasis and also heterophyidiasis, taeniasis, and echinostomiasis, demonstrating that inadequate environmental sanitation facilitates transmission of schistosomiasis, soil-transmitted helminthiasis, and other coinfections. The wisdom of an integrated approach to helminth control that could effectively target as many helminths as possible is supported by the survey results and underscores recent recommendations for integrated control of helminths and other neglected diseases (Steinmann et al., 2010; Utzinger et al., 2009; Wang et al., 2009b).

6.2.4. Schistosomiasis in Indonesia

6.2.4.1. Historical background and geographical distribution

The unusually limited distribution of schistosomiasis to only two very isolated regions of central Sulawesi, that is, the marshes around Lake Lindu and an area in the Napu Valley, illustrates the strong focal character of human schistosomiasis (Fig. 6.8). As in P.R. China and the Philippines, the disease is caused by *S. japonicum*, with the first case in Indonesia discovered in 1937 by Müller and Tesch in a male patient who later died in a hospital (Garjito et al., 2008; Hadidjaja, 1985; Hadidjaja and Sudomo, 1976). Later, in the same year, Brug and Tesch traced the infection to the patient's home village, which was recognised as a schistosomiasis-endemic area (Garjito et al., 2008; Leonardo et al., 2008). A large-scale study of schistosomiasis in the area was initiated in 1940 when the prevalence of infection was reported to be 56% in this village (Leonardo et al., 2008). The reservoir of infection seemed to be important, comprising mammals other than humans, notably deer and dogs. However, the intermediate host snail was not identified until 1971 when an oncomelanid snail was found under the grass of abandoned rice fields in the Paku subvillage of Anca in Lindu valley. It was named *O. hupensis lindoensis* Davis & Carney 1973 (Hadidjaja and Sudomo, 1976).

Napu valley is located about 30 km southeast from Lindu and was recognised as an endemic area in 1972 and first reported by Carney et al. (1974). As a pilot to a comprehensive control programme, a study in the Napu area was conducted in 1974, which reported an extraordinarily high prevalence among the local population, which numbered about 4000 people, for example, as high as 72% in Winowanga village. Data for the same year also reported that *S. japonicum* was infecting 13 mammalian species, nine of them wild animals, in the region (Carney et al., 1974). Schistosomiasis surveillance and control are a public health priority of the province of central Sulawesi. The Directorate General of Communicable Diseases Control of Indonesia estimated that more than 10,000 people were at risk of infection in both areas. Further coordinated surveys focused on Lindu valley in 1975 and found schistosomiasis in seven villages in the upper valley of Lindu where the highest prevalences observed were 70.6%, 56.3%, and 56.0% in Anca, Langko, and Tomado, respectively. The intermediate host snails were also found to be focally distributed around Lindu Lake.

6.2.4.2. The control programme

Over the past six decades, schistosomiasis has been successfully controlled through five phases, and the average infection rate is currently much lower than prior to initiation of the control programme. The average prevalence was 0.49% in seven villages in Lindu valley during 2005 and 2006. In Napu valley, the average prevalence among 17 villages was 0.79% (2005) and 1.08% (2006). In the same period, the infection rate among snails ranged from 0% to 13.4% and 0–9.1% in Napu and Lindu valleys, respectively. The prevalence in the main reservoir host (*Rattus* spp.) ranged from 0% to 20%. The highest prevalences in both humans and reservoir hosts were found in Dodolo village.

Even though the endemic areas are very limited, schistosomiasis control in Indonesia has faced many difficulties. Diminishing funding after the termination of the Central Sulawesi Integrated Area Development Project (CSIADC-P), funded by the Asian Development Bank (ADB) in 2005, resulted in staff reductions in schistosomiasis control stations in both endemic regions, and in inconsistent surveillance and control. A relatively stable level of very low prevalence has been achieved, but additional efforts are needed to eliminate the disease. The full participation of the health sector and intersectoral collaboration has been identified as key factors in the struggle to eliminate schistosomiasis in Indonesia. Unfortunately, a lack of coordination and collaboration between the Ministry of Health and other departments repeatedly occurred, which possibly led to increased reinfection rates and control failures. Increasing awareness among the local community is essential to support the environmental management programme, as this approach has proved to be the best one in Napu and Lindu valleys.

6.3. REGIONAL RESEARCH NEEDS

Basic research on schistosomiasis has a long tradition and operational research has always been an important component of the national control programmes in Southeast Asia (Liu et al., 2008; Utzinger et al., 2005). Both have contributed much to the past successes in control, now paving the road towards elimination. For instance, research was an integral part of the WBLP on schistosomiasis control in P.R. China; about 2% of the total loan was used for this purpose (Bergquist and Tanner, 2010; Chen et al., 2005).

The identification of research needs and determination of priorities are always important to a control programme, particularly in the initial stages of a new control initiative, so as to ensure the quality and progress of the control activities in coordination with new technological developments (Hotez and Ehrenberg, 2010; WHO, 1993). Therefore, considering the current status of schistosomiasis in Asia, it is important to define weak points in current control programmes and thereby identify areas that would benefit from further research. This goal has already been approached through the annual workshops organised by the Regional Network of Asian Schistosomiasis and Other Helminth Zoonoses ($RNAS^+$) that have taken place during the last 10 years. These meetings have proved to be a good basis for setting research priorities (McGarvey et al., 1990; Zhou et al., 2005, 2008a).

6.3.1. Research needs orientated by control goal

Based on an overview of all the national schistosomiasis control programmes in all endemic countries in the region, a general goal seems to be to reduce the prevalence to a sustainable, low level. As prevalence approaches levels as low as around 1%, it becomes increasingly difficult to find the remaining cases (Leonardo et al., 2008; Li et al., 2009a). At this stage, it is also essential to know how to maintain the control efforts and to move decidedly forward on several fronts, such as the control of snail intermediate hosts and animal infection reservoirs (WHO, 2007).

6.3.1.1. Tackling the challenges faced by the control programme

Evaluation of the present epidemiological situation and development of the new control strategy have revealed that some critical tools for completing the task of national schistosomiasis control and elimination are lacking (King, 2009). Shortcomings in presently available knowledge and control approaches are among the reasons for the persistence of pockets of uncontrolled snail propagation, parasite transmission, and faecal contamination of the environment by the many species of infected definitive hosts. The problem of re-emergence has also made it obvious that not all measures employed thus far are sustainable in the long term. The envisaged intersectoral collaboration is also considered crucial for the success of the control programme, yet there are many unsolved questions with reference to this issue (Zhou et al., 2008a).

Research should be done proactively and planned with a consideration of future challenges, for example, the effects of global warming and large-scale water resource development projects (Yang et al., 2007, 2010; Zhou et al., 2008b). Finally, the profound socio-economic changes taking place in all realms of society require constant readaptation of control programmes. Therefore, new efforts in operational as well as institutional and basic research are needed to develop improved tools and strategies for schistosomiasis control and to make them available to the control programme (Utzinger et al., 2005; Wang et al., 2009b).

6.3.1.2. Improvement of the quality of the control programme and surveillance

6.3.1.2.1. Development of improved tools and strategies The current set of control tools and guiding strategies is not sufficient to cope with the challenges in hyper-endemic areas and in places where endemicity is low, but stable. Detailed study of the local conditions is required to guide the development of new strategies to overcome the deadlock of the control programmes. Some of the issues which have to be investigated are the failure of traditional methods to permanently reduce endemicity in hyper-endemic areas, the decreased compliance rates for stool sample collection in residents after massive morbidity reductions by repeated rounds of praziquantel administered to at-risk populations, and the low sensitivity of the Kato-Katz method that results in failure to detect light infections (Lin et al., 2008b). Another factor compromising further progress in schistosomiasis control is the high cost and environmental toxicity of niclosamide, the only commercially available molluscicide.

The multitude of serological diagnostic tests for case detection and surveillance has made it difficult to come up with reliable national data and to analyse trends (Bergquist et al., 2009; Lin et al., 2008b). Standardisation of serological tests and rapid diagnostic reagents is therefore of utmost importance. In P.R. China, the adaptation of the control programme to the rapid changes in socio-economic and environmental conditions triggered by the ongoing market reforms and the major ecological transformations brought along with these changes in society and economy are further crucial areas which must be investigated. Finally, the development of a vaccine and a strategy for its use in areas with persisting high prevalence levels could be the much-needed additional tool to achieve sustained control by breaking the transmission cycle even in areas that have proved resistant to control attempts so far (Da'dara et al., 2008; McManus and Loukas, 2008).

6.3.1.2.2. Efficient management structures The transformation from a planned to a market-oriented economy system and the process of decentralisation in P.R. China has made it increasingly difficult to maintain the old system of administration in schistosomiasis control. Collaboration with other sectors such as agriculture, water resources, forestry, and infrastructure development becomes ever more important (Utzinger et al., 2005; Zhou et al., 2005). The present system of reporting cases and surveillance data for central evaluation and epidemiological trend analysis has to be improved, and there are pressing needs to design control strategies which are adapted to the local eco-epidemiological conditions and versatile enough to respond to changing needs while maintaining comparability for evaluation (Chen et al., 2007; Wang et al., 2008b, 2009a).

6.3.1.3. Requirements for locally tailored control strategies

The rapid pace at which enormous water resources development projects such as the Three Gorges dam, anti-flood measures, and the South–North water transfer project are implemented in P.R. China makes it imperative to closely evaluate their effects in all endemic or at-risk areas and to develop predictive models allowing a more reliable evaluation of the potential effects of future projects (Yang et al., 2006; Zhu et al., 2008). The effects of flooding events on snail dispersal into previously snail-free areas and especially of climate change are further topics where research is urgently needed into the possible impact on the epidemiology of schistosomiasis (Yang et al., 2007, 2009a; Zhou et al., 2008b).

The mobilisation of people has become more difficult for research and control efforts, the increased mobility of the population, especially of migrant workers, has made surveillance less comprehensive, and there is an increased risk of schistosomiasis cases moving to non-endemic areas where they are not recognised (Leonardo et al., 2002). Such migrations could also spread the parasite to new locations, establishing new foci of transmission. Economic development can mean that more people have access to safe infrastructure such as running water but this is not always reflected in the individual risk behaviour. Economic hardship can also force people to take greater risks and it is conceivable that high infection risks are increasingly concentrated in a fraction of the society, possibly leading to a dilution effect which makes it more difficult to identify them. Last but not least, the livestock numbers have vastly increased, partly without adaptation to the production system and thus enlarging the pool of definitive hosts (Zhou et al., 2007a,b).

6.3.2. Areas in need of further research

Further progress in schistosomiasis control critically depends on the diversification of the tools and strategies available to the national control programme. More research is needed in a wide range of fields, covering operational, institutional, and basic biological aspects. Emphasis should be laid on operational research and capacity building and on the close collaboration between research and control; and priority should be assigned to those areas to be able to directly improve the control activities.

6.3.2.1. Operational research relevant to control

The emphasis of operational research should be on new strategies and tools, technical standardization, investigation of eco-epidemiological determinants, and social justice. The ultimate goal is to further focus the control programme on crucial issues so as to make it more sustainable and cost-effective.

6.3.2.1.1. New technologies The effectiveness of the national control programme could be boosted by the development of new tools and techniques to broaden the available selection and to better respond to local as well as future requirements. New tools should be developed in the following fields: (i) assessment of treatment effectiveness, (ii) rapid epidemiological assessment of community prevalence, (iii) detection of infected snails, and (iv) surveillance of existing and suspected snail habitats.

6.3.2.1.2. Eco-epidemiological determinants The epidemiology of schistosomiasis japonica is not yet fully understood in all settings and current rapid socio-economic development as well as shifts in environmental conditions make it imperative to study further the contextual determinants of schistosomiasis japonica, the optimal allocation of health-care resources, and to evaluate the true morbidity associated with different infection intensities (Jia et al., 2007). The following priorities are proposed: (i) interaction between ecosystem and schistosomiasis transmission, (ii) burden of disease estimates, (iii) animal schistosomiasis in different settings, (iv) new animal management strategies, (v) environmental changes and their epidemiological impact, and (vi) socio-economic context and impact on control approaches, including the impact of climate changes and socio-economic changes.

6.3.2.1.3. Technical standardization The technical standardization of policies and procedures, which can nevertheless be readily adapted to changing local socio-economic and eco-epidemiological conditions, is of utmost importance to ensure that data can be compared across endemic areas, and thereby to facilitate quality assurance and communication between all parties (Steinmann et al., 2006; Wu et al., 2008). Uniform standards are required in strategy adjustment, surveillance, and responses to outbreaks.

6.3.2.1.4. Novel products The development of new, standardized products to be used in the control programme is important as this will allow a certain technical harmonization of the programme, thereby broadening its range of activities and enhancing its ability to respond to specific requirements. New products are required as drugs and treatment procedures, diagnostic kits, molluscicides, and vaccines.

6.3.2.2. Innovative approaches to control

Sustained research on basic questions of the biology of *S. japonicum* and its epidemiology will produce new insights into this complex parasite, its life cycle, and the determining factors for transmission and infection (Zhou et al., 2009). This could result in new concepts and innovative methods for control, most welcome additions to the current arsenal of tools and approaches. Research should focus on the following domains:

6.3.2.2.1. Biology of S. japonicum Reinfections in different settings cause resurgence of the diseases. The genetic and immunological background for human reinfection with *S. japonicum* should be elucidated to better understand human reinfection in hyper-endemic areas. At the same time, bioinformatics, genome and proteome research is suitable for application to *S. japonicum* and their reservoir hosts in an effort to find specific molecular and immunological markers characteristic of different stages and to elucidate the molecular interplay between the parasite and its host (Liu et al., 2009). This information could inform the development of novel diagnostic tools, drugs, and vaccines to improve the control programme.

6.3.2.2.2. Biology of snail intermediate hosts Studies of the biological interactions between *S. japonicum* and *O. hupensis* could help improve our understanding of the genetic co-evolution among *S. japonicum* and its snail intermediate host. The genetic basis and immunological mechanisms governing the infection susceptibility of *O. hupensis* and variations therein should be further studied. Genome and proteome studies are, in principle, able to identify the functional genes of *O. hupensis* conferring resistance against *S. japonicum* infection (Li et al., 2009b).

6.3.2.2.3. Epidemiology and immunology of schistosomiasis Transmission models employing environmental, demographic, and socio-economic variables should be developed in order to provide the theoretical basis for transmission estimations and forecasting, a valuable tool for the management of the control programme (Spear et al., 2004; Wang et al., 2006).

The immunological events following an infection in end hosts should be further investigated to provide detailed information for the development and field evaluation of diagnostic kits and vaccines (Da'dara et al., 2008; Hotez et al., 2007). Defining the immunological factors causing this type of morbidity and study of the factors leading to the increased vulnerability should be investigated. This would allow the creation of specific control programmes focusing on acute infections in hyper-endemic areas (Bergquist et al., 2009; Hafalla et al., 1999; Planas, 2008).

6.3.2.3. Capacity building and construction of a research platform

Closer collaboration between all involved scientists and institutions will considerably strengthen research by sharing limited resources, information, and experience (Zhou et al., 2008a). It will also facilitate the development of standardized products and foster the education of the next generation of scientists. The following steps and structures are proposed:

6.3.2.3.1. Networking between laboratories in the region Networks connecting laboratories and institutions could combine their respective potential and special experiences, resulting in superior performance of research and control. Networking is also crucial to standardize the quality of control approaches and diagnostic products and to unify reporting. The following networks should be set up: (i) a network of laboratories working on the development of diagnostic kits to standardize existing ones and develop a generally accepted standard kit which is available to the whole control programme; (ii) a network of laboratories involved in drug screening will enable them to share the work and to engage in large-scale projects (allocation of specific tasks to the most suitable laboratory will also be much easier); and (iii) a similarly designated network for the development of novel vaccine candidates.

Easy access to standardized reference samples of *S. japonicum*, *O. hupensis*, and human serum will improve and facilitate research in many fields. Therefore, it is proposed to set up a serum bank containing blood samples from well-characterised infected humans, a gene bank of *S. japonicum* and *O. hupensis*, and a collection of standardized strains of the parasite and its intermediate host.

6.3.2.3.2. Information databases The establishment of comprehensive computerized databases containing epidemiological and snail distribution data, and of a geographical information system (GIS) database on schistosomiasis and intermediate host snail distribution will grant rapid access to information and facilitate the exchange between all involved parties. Easy and fast access to information is crucial for the management of the control programme, for surveillance and outbreak response and the ready detection of epidemiological trends (Chen et al., 2007; Leonardo et al. 2005; Yang et al., 2006, 2009b; Zhou et al., 2008a,b,c). A specific research database could improve the exchange and knowledge sharing among the scientific community.

6.4. CONCLUSIONS

It is essential to attract more funds for the neglected areas. Support of local government units, non-government organizations, other government organizations, and the community is expected to sustain regular control activities, for example, clearing of vegetation, drainage, provision of safe source of water supply and water-sealed toilets, construction of footbridges, and agro-engineering measures that will cut disease transmission. In addition to these, research activities, for example, basic research, implementation research, and product development, also have a role to play in reaching the goal of eliminating schistosomiasis in Asia as a public health problem, and to save lives among those vulnerable populations, for example, children, women, and workers in affected water-bodies.

More attention has recently been focused on research activities related to the elimination of schistosomiasis japonica in Asia, after the prevalence is reduced to the 1% level. However, global research activities related to elimination of the disease are still neglected with respect to tools for the assessment of progress towards elimination, with respect to the scheme of surveillance to consolidate the achievement of low prevalence, and with respect to the alerting system to detect and combat resurgence of the disease. Therefore, the schistosomiasis control programmes in Asia are facing the problem of sustainability. There is a great need to approach the declining transmission intensity and scale with an integrated strategy that would include agricultural development programmes, modernization programmes in water/irrigation projects, and local socio-economic development programmes.

Both research and control will benefit from international collaboration. Such cooperation will enhance the exchange of information and expertise in research, surveillance and control, and encourage the training of the next generation of researchers and control staff. The existing RNAS^{+} is an excellent platform for this purpose and should be further strengthened in the fields of training, risk mapping, and advocacy of integrated control to broaden the focus from schistosomiasis to other parasitic diseases such as food-borne trematodiases and soil-transmitted helminthiases. It should also encourage information exchange in spite of language barriers and the publication of research findings in internationally accessible journals.

ACKNOWLEDGEMENTS

X.N. Zhou received financial support from the National Natural Science Foundation of China (grant no. 30590373), the National S & T Mayor Project (grant no. 2008ZX10004-011), and UNICEF/UNDP/World Bank/WHO Special Programme on Research and Training in Tropical Diseases (grant no. 200020548). Thanks to Dr. Peter Steinmann for his help on manuscript improvement.

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