REVIEW



History of schistosomiasis epidemiology, current status, and challenges in China: on the road to schistosomiasis elimination

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Abstract Schistosomiasis is a snail-borne disease caused by worms of the genus Schistosoma. Worldwide, human schistosomiasis remains a serious public health problem, threatening \sim 800 million people in 78 countries with a loss of 70 million disability-adjusted life years. Schistosoma japonicum is the only human blood fluke that occurs in China. As one of the countries suffering greatly from schistosomiasis, over the past 65 years, China has made great strides in controlling schistosomiasis, blocking the transmission of S. japonicum in five provinces, remarkably reducing transmission intensities in the other seven endemic provinces, and China is currently preparing to move toward the elimination of this disease before 2025. However, while on the road to schistosomiasis elimination, emerging challenges merit attention, including severe advanced cases, increased movements of population and livestock, large-area distribution of intermediate host snails, limitations of new drug developments and no vaccine available, as well as imported schistosomiasis and its potential risk.

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Keywords *Schistosoma japonicum* · Elimination of schistosomiasis · Emerging challenges · P. R. China

Introduction

Human schistosomiasis, as one of the most prevalent neglected tropical diseases, is a snail-borne disease caused by parasitic blood-dwelling flukes, leading to serious socioeconomic consequences, only second to malaria, and ~250 million people acquire infection by cercaria-contaminated water contact in 78 countries and ~800 million at risk of this infection, with a loss of 70 million disability-adjusted life years (WHO 2016; The Carter Center 2014; Gray et al. 2010). There are five main species of schistosomes that are able to infect humans, including Schistosoma japonicum (Katsurada, 1904), Schistosoma mansoni (Sambon, 1907), Schistosoma haematobium (Bilharz, 1852), Schistosoma intercalatum (Fischer, 1934), and Schistosoma mekongi (Voge Bruckner, and Bruce, 1978), among which, S. japonicum is the only human blood fluke that occurs in China (WHO 2016). As one of the countries suffering greatly from schistosomiasis, China has made tremendous achievements in schistosomiasis control after six decades of grueling work, despite the extremely severe epidemiologic situation at the start (Utzinger et al. 2005; Xu et al. 2016). Now, China is currently preparing to move toward the elimination of this disease before 2025 (Xu et al. 2016). Here, we summarized the history of schistosomiasis epidemiology in China, the current status of schistosomiasis, and the emerging challenges, including severe advanced patients, increased movements of population and livestock, large-area distribution of intermediate host snails, limitations of new drug developments and no vaccine available, as well as imported schistosomiasis and its potential risk.

Discovery, epidemiology, and history of schistosomiasis in China

In January 1972, a female corpse named Xinzhui of the Xi Han Dynasty (186 BC), in Mawangdui, Changsha, Hunan, was unearthed, and *S. japonicum* eggs were discovered in her liver and rectum tissues by autopsy, which confirms that schistosomiasis has existed in China since 2100 years ago (Chen and Feng 1999). However, due to limitations of the scientific and technological condition at that time, little was known of this disease, and only some records regarding schistosomiasis-associated symptoms could be found in old volumes of traditional Chinese medicine, which can be traced back to 400 BC (Mao and Shao 1982).

In November 1905, Longan confirmed the first case of schistosomiasis in Changde, Hunan, China, in an 18-yearold fisherman who presented with abdominal pain, hemafecia, hepatosplenomegaly, and varicosity, and typical S. japonicum eggs were observed by microscopy (Logan 1905). Subsequently, schistosomiasis cases were constantly emerging in other provinces like Anhui (1907), Hubei, Jiangxi, Shanghai and Zhejiang (1910), Guangdong (1911), Jiangsu (1913), Fujian (1924), and Guangxi and Sichuan (1938), followed by Yunnan (1940) (Zhou et al. 2005). In 1924, Tootell conducted a preliminary survey of schistosomiasis infection in Changde, Hunan. He found a positive rate of 60.3 % (38/63), reflecting the severe situation at that time in China (Tootell 1924). During that time, the first systemic study on schistosomiasis japonica in China was carried out in Suzhou and Jiaxing, Jiangsu, by both Faust and Meleney (1924), illustrating the etiology, pathology, and clinical manifestations. In the early 1930s, an epidemiological investigation launched

by Chen and Li in the southern region of the Yangtze River showed that the distribution of Oncomelania hupensis snails and schistosomiasis cases were highly prevalent, which provides a perspective for schistosomiasis control in China (Guo and Zheng 2000). However, during this period, China was at civil war, and thus, little attention was paid to schistosomiasis, the pathogenesis of which was poorly understood, let alone the prevention and control of this disease. As a long-neglected disease, the epidemiologic situation of schistosomiasis at that time was extremely severe, with 11.6 million schistosomiasis patients, 1.2 million infected cattle, 14.3 billion square meters of O. hupensis snail areas, and over 100 million people at risk, which posed a great threat to people's health and economic development (Zhou et al. 2007; Ross et al. 2001). The impact of this disease has been vividly described in the poem "Farewell, God of Plague" composed by Chairman Mao Zedong, as well as the call for action to eliminate schistosomiasis (Fig. 1).

After the founding of the People's Republic of China, the central government embarked on schistosomiasis control to promote health and ease the disease burden resulting from schistosome infection. By census, 380 counties (cities) of 12 provinces in southern China (Hunan, Hubei, Jiangxi, Fujian, Guangdong, Anhui, Jiangsu, Zhejiang, Yunnan, Sichuan, Shanghai, and Guangxi) were proven to be endemic for schistosomiasis. The geographical distribution of this disease was broad, north to Baoying county in Jiangsu (33°25' N latitude), south to Yulin county in Guangxi (22°42' N latitude), west to the Yunlong county in Shanghai (121°45' E longitude; Fig. 2), and the range of altitude was also wide, from 0 m (Shanghai) to 3000 m (Yunnan), indicating complex environmental

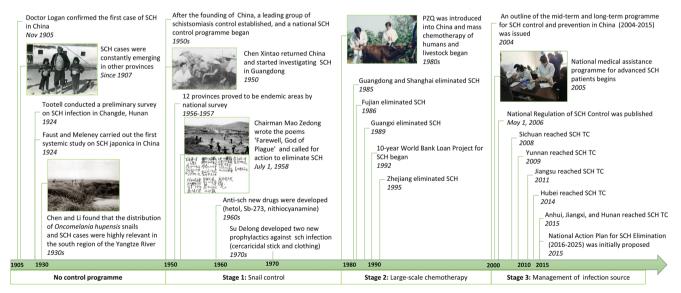


Fig. 1 Key events in the history of schistosomiasis in China. *Below the timeline* are the three major stages of schistosomiasis control in China and the main strategy at each stage. Five photographs (*left*) were reproduced

by the permission of Prof. Chen Xintao Memorial Hall and the other two photos (*right*) were from the author's collections. *SCH* schistosomiasis, *sch* schistosome, *TC* transmission control, *PZQ* praziquantel

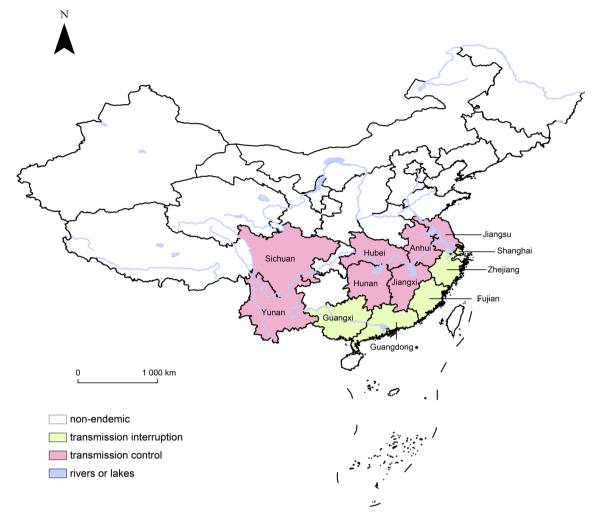


Fig. 2 Geographical distribution and epidemic status of schistosomiasis in China in 2015. Twelve provinces in southern China (Hunan, Hubei, Jiangxi, Fujian, Guangdong, Anhui, Jiangsu, Zhejiang, Yunnan, Sichuan, Shanghai, and Guangxi) were endemic areas of schistosomiasis, among

factors of snail habitats. Areas along the bank of the Yangtze River or around limnetic areas such as Dongting Lake and Poyang Lake were highly epidemic (Mao and Shao 1982; Zhou et al. 2005; Ross et al. 2001; Zou and Ruan 2015).

At the very beginning of the campaign, China was at the exploration stage due to poor knowledge and limitations in economic and technical conditions. As experience accumulated and the economy and technology advanced, the strategy for schistosomiasis control developed and changed with the times and can be divided into three stages (Wang et al. 2014; Zhou et al. 2012; Hipgrave 2011): (1) the first stage (from the mid-1950s to the mid-1980s) focused on intermediate snail control, including farmland water conservancy capital construction project and mollusciciding, complemented with improving access to clean water and sanitary facilities, individual protection, and health education; (2) the second stage (from the mid-1980s to the early 2000s) paid attention to large-scale chemotherapy of both humans and livestock due to the introduction

which, five (Guangdong, Shanghai, Guangxi, Fujian, and Zhejiang) have reached schistosomiasis interruption and the other seven (Sichuan, Yunnan, Jiangsu, Hubei, Anhui, Jiangxi, and Hunan) have achieved schistosomiasis transmission. This map was made by ArcGIS 10.2

of praziquantel (PZQ), mainly including mass screening and treatment, which was supplemented by snail control in foci areas; and (3) the third stage (from the early 2000s up to now), the stage of integrated control, emphasizes the control and management of infection sources, namely, grazing prohibition, using machines instead of cattle, improving drinking water and lavatories, perfecting living environment, etc. Due to the unremitting efforts put into schistosomiasis control, the five provinces of Guangdong (1985), Shanghai (1985), Fujian (1987), Guangxi (1989), and Zhejiang (1995) had achieved transmission interruption (no local case of schistosomiasis; Table S1), and the other seven endemic provinces of Sichuan (2008), Yunnan (2009), Jiangsu (2011), Hubei (2014), Anhui (2015), Jiangxi (2015), and Hunan (2015) had reached transmission control (the prevalence of human and livestock <1 %; Tables S1 and S2 and Fig. 2; Xu et al. 2016; Zhou et al. 2005; HFPCA 2015; HFPCJ 2015; HFPCH 2015).

Current status of schistosomiasis japonica in China

According to the latest report of the endemic status of schistosomiasis in China (2014), there were 453 counties (cities) endemic for schistosomiasis, with 251 million total residents, among which, 69.09 % (313/453) had achieved transmission interruption and 29.80 % (135/453) had reached transmission control; the other 1.10 % (5/453) were still at morbidity control. About 115,614 patients were estimated to have schistosomiasis. *O. hupensis* snails were found in an area of 364,324.42 hm² within an area of 576,505.37 hm² investigated, and only 666 of 494,620 heads of cattle were found stoolpositive (Lei et al. 2015; Fig. 3).

Despite many achievements having been made, great effort has to be done in order to reach the goal of schistosomiasis elimination in China before 2025. The issues to be considered are as follows: (1) *S. japonicum* can infect over 40 species, which represents a huge number of reservoir hosts (e.g., bovines, pigs, dogs, cats, goats/sheep, rats, etc.; He et al. 2001; McManus et al. 2010, 2011), and thus, zoonotic transmission plays a crucial role for this parasite, but these non-human mammalian animals are relatively harder to control; (2) clean water supply, health education, reduced high-risk behaviors (such as swimming, bathing, and washing in infected water) can dramatically contribute to morbidity management. However, many residents make a living by farming or fishing and thus inevitably have contact with contaminated water because of their occupations, making them still at high risk of acquiring infection and reinfection (WHO 2016); and (3) the ecological environment of areas infested with snails is highly complex, and the distribution area of snails is particularly wide (Lei et al. 2015). Additionally, measures of snail control are limited by cost and environmental protection.

In the seven provinces (Sichuan, Yunnan, Jiangsu, Hubei, Anhui, Jiangxi, and Hunan) that had achieved transmission control, despite the fact that the epidemiologic situation of schistosomiasis is at a low level in general (the prevalence rate of humans and livestock is <1 %; HFPCA 2015; HFPCJ 2015; HFPCH 2015; Lei et al. 2015), it is relatively unstable and has a tendency to rebound. Management and control of infection sources is of significance, as well as surveillance and forecasting. Cattle are considered as the main source of infection, accounting for 75 % of all infection sources (Williams et al. 2002), and thus, large-scale chemotherapy of livestock, especially the cattle, is still strongly recommended to combat schistosomiasis.

In the five provinces (Guangdong, Shanghai, Fujian, Guangxi, and Zhejiang) that have achieved transmission interruption, imported cases (from other provinces or countries) are repeatedly observed (Wang et al. 2014; Zhou et al. 2012) because increases in personal mobility and worldwide trade make it possible for

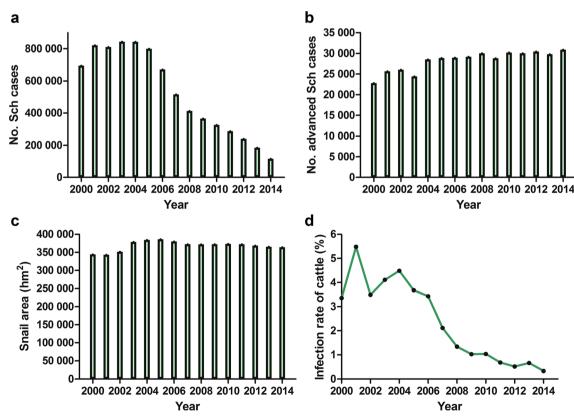


Fig. 3 Epidemic status of schistosomiasis in China from 2002 to 2014. a Estimated total number of patients with schistosomiasis. b Estimated total number of patients with advanced schistosomiasis. c Estimated size of

area infested with *Oncomelania hupensis* snails. **d** Estimated infection rate of cattle. *Sch* schistosomiasis. All the data above were collected from official reports (China CDC) and visualized by GraphPad Prism 5

infection to spread to people in other provinces or countries from a single source (Zhou et al. 2012). Population movement plays a significant role in the epidemiology of many infectious diseases; for example, some infectious diseases such as lymphatic filariasis, Chagas disease, leishmaniasis, and Zika virus infection have emerged or reemerged in urban areas or previously controlled regions, which are intimately associated with population movements (Zhou et al. 2012; Alirol et al. 2011; Shuaib et al. 2016). After years of diligent efforts, it seems a vain attempt to eliminate the snails, which means surveillance should not relax or cease due to transmission interruption since the intermediate host snails still exist. Otherwise, it is possible to experience a reoccurrence of schistosomiasis and even an outbreak and thus result in huge economic losses. Therefore, we should focus on the surveillance of the floating population from endemic areas as well as snail status and consolidate the achievements which have been obtained.

Emerging challenges and responses (Table 1)

Advanced schistosomiasis is becoming a national concern

Advanced schistosomiasis is the most severe form of schistosomiasis japonica. The eggs of *S. japonicum* deposited in the intestine and liver tissues elicit a granulomatous response,

 Table 1
 Emerging challenges and responses of schistosomiasis control in China

Category	Emerging challenges	Responses	
Advanced schistosomi- asis japonica	High morbidity, disability, and fatality; lack of early and precise diagnosis method	Raise the national medical assistance program	
Livestock and population movements	Reoccurrence of schistosomiasis japonica in transmission- interrupted area	Manage the infection sources of schistosomiasis japonica	
<i>Oncomelania</i> <i>hupensis</i> snail control	Expansion of snail distribution due to climate change, leading to transmission risk	Develop novel methods of snail control	
Drug and vaccine develop- ment	Limitations of drugs; no effective vaccine available	Accelerate the pace of the development of drug and vaccine	
Imported African schistosomi- asis	Potential transmission risk of schistosomiasis mansoni in China (<i>Biomphalaria</i> invaded China; the potential sources of infection increase sharply)	Monitor in snail <i>Biomphalaria</i> and high- risk population (re- turnees and internation- al visitors from endemic countries)	

which leads to continuous fibrosis of the periportal tissue and then develops a pipestem fibrosis. Afterwards, the granulomatous response is downregulated in order to prevent excessive inflammatory response. Egg-induced periportal fibrosis may progress to induce obstruction of the portal vessels and then damage to the liver parenchyma, causing the development of advanced schistosomiasis. This debilitating condition is associated with liver fibrosis/cirrhosis, portal hypertension, ascites, splenomegaly, and gastroesophageal varices (Fig. 4; Colley et al. 2014), causing varying degrees of workforce loss, the ability to live alone, or death (Lewis and Tucker 2014). Therefore, patients require long-term health care, but many cannot afford it due to illness-related poverty, and thus, the disability and fatality rate remains high. In China, advanced schistosomiasis japonica still represents a severe health burden. It was estimated that the number of advanced schistosomiasis patients took up 5-10 % of all schistosomiasis morbidities, but the precise mechanism of the pathological progress remains obscure. And intriguingly, some clinically cured patients may also re-progress into advanced schistosomiasis without known history of re-exposure to S. japonicum (Hua et al. 2015).

There are four clinical subtypes of advanced schistosomiasis according to the Chinese Diagnostic Criteria for Schistosomiasis (WS 261-2006; Ministry of Health of the People's Republic of China 2006): (1) megalosplenia, referring to the enlargement of the spleen; (2) ascites, usually induced by upper gastrointestinal bleeding, co-infection, strain and use of medication, and frequent relapse; (3) colonic tumoroid proliferation, mainly manifesting as abdominal pain, diarrhea, and alternate episodes of diarrhea and constipation; and (4) dwarfism, referring to patients who have repeated infections of schistosomes during their childhood and often suffer from developmental retardation and short stature. Megalosplenia and ascites types are clinically common, accounting for more than 80 % of all advanced cases, while cases of dwarfism and colonic tumoroid proliferation are less often seen in the clinic, which may have association with mass chemotherapy.

The total number of schistosomiasis cases documented dropped from 694,788 in 2000 to 115,614 in 2014, displaying a rapid decline tendency. Nevertheless, there are 30,880 advanced schistosomiasis cases documented in 2014, while 22,786 were documented in 2000 (Lei et al. 2015; Chen et al. 2001; Fig. 3), indicating that the overall number of advanced schistosomiasis cases is even on a small upward trend. Possible reasons include: (1) a complete healing is hardly seen among advanced patients and relapse is not rare (Lewis and Tucker 2014). It was reported that the recurrence rate was up to 44.5 % (Mao et al. 2012); (2) in the past, the government paid less attention to advanced patients compared to those with a better prognosis (acute/chronic infection), and thus the false negative rate was high, but large-scale screening is

Fig. 4 Clinical features of advanced schistosomiasis. a Abdominal sign: subcutaneous varicose vein of the abdominal wall and abdominal distension (ascites/splenomegaly). b Ultrasonography of the liver: fibrosis and increased diameter of the portal vein (portal hypertension). c CT image of the liver: fibrosis. Photographs were from Jingzhou City No. 3 People Hospital, with permission of the patients



carried out in recent years, so a rise in the prevalence is observed; (3) the pathological process of advanced schistosomiasis generally takes a long time (Colley et al. 2014). For example, elimination of schistosomiasis was declared in 1995 in Zhejiang, but by 2014 there were still 1142 advanced patients (Lei et al. 2015), and thus the overall number of advanced cases will remain at a certain level for a period of time in the future; and (4) genetic susceptibility might play a role according to our research (data not published), and the sustained high morbidity of advanced schistosomiasis may be partially attributed to this reason.

In 2005, China raised a national medical assistance program with a clinical guideline intended to help those patients in desperate need of health care (Song et al. 2016). In brief, for patients with splenomegaly, if the condition is stable, splenectomy is recommended to improve hypersplenism and portal hypertension and thus prevent upper gastrointestinal bleeding and ascites; for patients with ascites, supportive and symptomatic treatment such as diuresis and correcting effective circulating blood volume deficiency are of a priority; for patients with colon proliferation, controlling infection is the first step to prevent malignant transformation, and pathogen treatment and regular follow-up are needed to avoid consequences such as intestinal perforation, intestinal obstruction, or cancer; and for patients with dwarfism, deworming treatment is essential, supported by hormone therapy, with the purpose of improving their growth and development.

Now, this program is reaching more patients and providing more aid, with support from both central and local governments. Medical assistance for advanced schistosomiasis has become an increasingly important component of schistosomiasis control in China, especially on the road to schistosomiasis elimination.

Management of livestock and population movements is needed

With China's rapid economic development and urbanization over the past decades, it has witnessed its largest human movement (Zhou et al. 2012). The floating population moving from rural areas to coastal cities is approximately 120 million. Meanwhile, population movements are also occurring between cities, especially from small ones to big ones (Alirol et al. 2011). For transmission-interrupted areas with residual snails, such as Shanghai, Zhejiang, and Fujian, migrant workers from endemic areas might bring sources of infection, which may lead to local infection and even outbreaks. Besides, with the continuous development of tourism, an increasing number of urban tourists travel to endemic areas and thus might lead to a steady rise of acute infection, which also becomes an important source of infection. In addition to population movement, livestock movement (e.g., through livestock trade or movement to new grazing fields) occurs frequently in endemic areas in China as well (Kloos et al. 2010), which raises another concern for the goal of elimination.

Therefore, management and control of the infection source is of importance, and regular examination and treatment is required. Occupational populations at high risk (e.g., fishermen, boatmen, etc.) and migrant workers (from endemic regions) should be monitored regularly for early diagnosis and intervention. Public awareness on schistosomiasis transmission should be raised, especially those leaving for schistosomiasis endemic areas.

Lack of effective tools for *Oncomelania hupensis* snail control

As the only molluscicide recommended by the World Health Organization, niclosamide is widely used in China to kill Oncomelania for years, and resistance against niclosamide might be induced after long-time use in the field (WHO Expert Committee 2002; Jiang and Li 2015). There is still a large distribution of O. hupensis snails in China despite continued and intensified control efforts, and the vector ecological system is very complex (Zheng et al. 2013). Climate change has been proven to be a driver of the transmission of vectorborne diseases, and schistosomiasis seems to be influenced by climate change. For example, global warming might lead to snail survival and reproduction in currently non-breeding areas (Mas-Coma et al. 2009; McCreesh and Booth 2013). Newly discovered or reemerging snail areas are repeatedly reported, and sometimes the size is even bigger than the area already under control (Wang et al. 2014; Lei et al. 2015). Under the current technical conditions and economic situation, it seems a daunting task to control the intermediate snails. Environmental modifications such as the cementing canal construction proved to be a success in Japan (Minai et al. 2003), but it seems not realistic in China given the size and number of lakes. Chemical-based mollusciciding has been studied in China for a long time, and over 2000 compounds were screened, but only a few were applied for snail control due to safety concerns and severe problems of environmental pollution (Yang et al. 2010). As is evident by several studies, restoring prawns (predators of snails) might be a novel contribution to snail control and, thus, schistosomiasis elimination (Sokolow et al. 2015).

Little breakthrough in drug and vaccine development

Since the introduction of PZQ in the 1980s, this broad-spectrum, highly effective, low-toxicity, easy-to-use, and cheap drug has been widely applied in schistosomiasis chemotherapy and became the first-choice drug recommended by WHO in the past 30 years (WHO 2013). In the 1990s, Fallon and Doenhoff (1994) successfully induced a PZQ-resistant *S. mansoni* strain under experimental drug pressure. Furthermore, though PZQ is effective against adult stage of schistosomes, it has little effect against juvenile worms, which may be related to poor PZQ cure rates and treatment failures that have been reported to occur in Egypt, Zimbabwe, and Cameroon (Midzi et al. 2008; Barakat and EI Morshedy 2011; Tchuenté et al. 2004). Also, it is ineffective in alleviating the pathological damage caused by granulomas induced by the deposition of eggs, which may progress to liver fibrosis and even liver cancer (Song and Wu 2015). Artemisinin drugs (a front-line drug against malaria) also exhibit effectiveness against *Schistosoma* spp., and they are effective against immature worms, despite less activity on adult worms (in contrast to PZQ), making them promising drug candidates for use as prophylaxis in high-transmission areas (Doenhoff et al. 2008). Apart from drug resistance surveillance of PZQ, we should speed up the pace of novel drug development.

Reinfection is still a common phenomenon in highly endemic areas due to the lack of enough immune protection. This is an obstacle on the road to schistosomiasis elimination. Moreover, long-term single-drug use may lead to drug resistance, which in turn would worsen the situation of schistosomiasis control. Thus, a long-acting vaccine is likely to be an essential component of effective control and elimination of schistosomiasis. Though numerous candidate molecules have been identified against S. japonicum, the protection effect induced by these molecules is far from satisfactory. Until now, no effective vaccine for the disease appears on the market, though two candidates (Sm-TSP-2, Sm14 and Sh28GST) have reached the level of clinical trials (Merrifield et al. 2016). Given that the genome sequencing of S. japonicum has been completed and its genome sequences have been deciphered, we should actively seek promising candidate vaccine antigens and then accelerate the pace of the development of multivalent and combined vaccines in order to achieve better immune protection.

Overseas imported cases might lead to local infection of *S. mansoni*

S. japonicum, S. mansoni, and S. haematobium are the three most important species of the genus Schistosoma that might cause severe human schistosomiasis (Colley et al. 2014). Though S. japonicum is the only human blood fluke that occurs in China for now, it does not mean the other species of the genus Schistosoma could be ignored, which are highly prevalent in Africa, especially in Nigeria (~121.2 million infections), United Republic of Tanzania (~33.2 million infections), and Congo (~2.6 million infections; WHO 2008, 2010a, b). It was estimated by WHO that approximately 258 million schistosomiasis patients are in need of preventive treatment worldwide in 2014, at least 90 % of which are from Africa (WHO 2016). Since globalization greatly promotes the movement of population as well as the close cooperation and friendship between China and Africa (Xu et al. 2016), travelers from Africa are likely to be potential sources of infection to native Chinese. Furthermore, the intermediate host of S. mansoni, Biomphalaria, has been found in Hong Kong since 1974 and Shenzhen in 1981 (Meier-Brook 1974; Liu et al. 1982), and its distribution has expanded to nearby cities such as Dongguan and Huizhou, Guangdong Province,

according to the 2013 survey by Guangdong Provincial Centre for Diseases Control and Prevention (Fig. S1; Huang et al. 2014), indicating the parasite's life cycle could be set up once the patient's feces dropped into water with distribution of suitable snails, which might lead to an outbreak of schistosomiasis mansoni (Lu et al. 2014). Though the intermediate host of S. haematobium, Bulinus, has not been found in China yet, it might be introduced to China via shipping, like Biomphalaria. Due to China's aid projects, especially on infrastructure construction, the number of migrant workers moving to Africa has risen sharply since the 1970s, and in the past 10 years, more and more Chinese companies, particularly communications industries such as Huawei and ZTE, have established overseas subsidiaries in order to capitalize on the market in Africa. According to the recent estimates, there is approximately 1 million Chinese living in Africa (Zhou

2014). Imported cases of schistosomiasis mansoni or haematobium have been repeatedly reported among these returnees (Table 2; Liu and Gan 2001; Xu et al. 1979; Lu and Xu 1980; Feng et al. 1984; Wu et al. 1988; Zeng and Cai 1991; Jin et al. 1992a, b; Hao 1992; Huang 1992; Qian et al. 2005; Lei et al. 2007; Zou et al. 2011; Yi et al. 2011; Xie et al. 2013; Chai et al. 2014; Zheng et al. 2013; Gao et al. 2015; Jiang et al. 2015). Once these people enter the regions with the intermediate host Biomphalaria, they could give rise to schistosomiasis mansoni in China. Additionally, more and more Africans are coming to China for trade, study, travel, etc. Certainly, most of them enter legally, but there is still a substantial proportion via illegal entry, which means it is a great challenge for the public health personnel to know their infection status, let alone to institute interventions. For example, Guangzhou, one of the biggest cities in China, is now faced with an

Year	No. of reported cases	No. of literature ^a - based cases	No. of NNIDRS ^b - based cases	Species	Provinces	References
1974	75	75	_	Sm	Unreported	Liu and Gan (2001)
1979	67	67	_	Sm	Beijing	Xu et al. (1979)
1980	15	15	_	Sh	Beijing	Lu and Xu (1980)
1984	2	2	_	Sh	Shanxi	Feng et al. (1984)
1988	22	22	_	Sh	Beijing	Wu et al. (1988)
1991	2	2	-	Sh	Hubei, Jilin	Zeng and Cai (1991); Jin et al. (1992a)
1992	24	24	_	Sh	Fujian, Beijing, Hubei	Jin et al. (1992b); Hao (1992); Huang (1992)
2005	1	1	0	Sh	Jiangsu	Qian et al. (2005)
2007	1	1	0	Sh	Shanxi	Lei et al. (2007)
2008	2	0	2	Sm, Sx	Beijing, Guangdong	
2009	8	2	8	Sm, Sx	Beijing, Guangdong, Shanxi	Zou et al. (2011)
2010	32	28	4	Sh	Hunan, Shanxi	Zou et al. (2011)
2011	184	184	0	Sh	Hunan	Yi et al. (2011)
2012	3	2	3	Sh	Shanxi, Fujian, Hubei	Xie et al. (2013)
2013	3	2	2	Sh, Sm, Sx	Jiangsu, Zhejiang, Shanxi	Chai et al. (2014); Zheng et al. (2013)
2014	1	1	1	Sh	Shangdong	Gao et al. (2015)
2015	5	1	5	Sh, Sm, Sx	Beijing, Shanxi, Guangxi, Zhejiang	Jiang et al. (2015)
Total	447	429	25	—	_	

Sm Schistosoma mansoni, Sh Schistosoma haematobium, Sx species of Schistosoma not mentioned

^a Literature-based: using keywords such as "imported schistosomiasis mansoni" or "schistosomiasis haematobia" and searching in the three main Chinese databases (*CNKI*: http://cnki.net/; *Wangfang*: www.wanfangdata.com. cn/; and *VIP*: http://www.cqvip.com/)

^b NNIDRS: National Notifiable Infectious Disease Reporting System, established in April 2004

Table 2Overall number ofdocumented imported cases ofschistosomiasis mansoni/haematobia from 1979 to 2014 inChina

increasingly large number of African people, and they even set up their own communities. According to the data from Guangzhou Public Security Bureau in 2014, the total number of African residents (with a residence permit) in Guangzhou is approximately 16,000 (GPPSD 2014), and certainly the number is largely underestimated due to numerous reasons, such as illegal entry and cumbersome procedures in obtaining a residence permit. Additionally, China Import and Export Fair, also known as the Canton Fair, is held biannually in Guangzhou every spring and autumn, with the largest scale and the broadest distribution of overseas buyers in China (China Import and Export Fair 2012).

Investigations on *Biomphalaria* snail distribution, susceptibility to *S. mansoni*, and the relevant environment factors for breeding and spreading are essential. However, for now, only surveys on snail distribution have been conducted in Guangdong Province, and no information is available concerning the condition in other provinces, which is of great public health concern. Meanwhile, management (e.g., screening, treatment, follow-up, etc.) of returnees and international travelers from high-risk areas should be conducted and strengthened regardless of difficulties. Importantly, evaluation on the transmission risk of schistosomiasis mansoni/ haematobium in China should be put on the agenda, as well as the development of serological screening methods and diagnostic techniques.

Global implications

Since the first case of schistosomiasis was confirmed by Logan in Hunan Province in 1905 (Logan 1905), little attention was paid to this parasitic disease until the 1950s (the founding of China). As a long-neglected disease, the epidemiologic situation of schistosomiasis in China at that time was extremely severe, posing a great threat to people's health and economic development (Chen and Feng 1999; Zhou et al. 2007), but remarkable achievements had been made during the past 65 years, as is evident by the total number of human schistosomiasis cases dropping from 12 million in the 1950s to 115,614 in 2014 (Guo and Zheng 2000; Lei et al. 2015). China's experience in rapid screening, detection, and treatments is now tested in Zanzibar, Africa, to control schistosomiasis transmission there (WHO 2014). More and more African countries now have established intimate collaborations with the Chinese government in the fight against schistosomiasis (Xu et al. 2016). China-Africa cooperation will make a tremendous contribution to schistosomiasis control or elimination.

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References

- Alirol E, Getaz L, Stoll B, Chappuis F, Loutan L (2011) Urbanisation and infectious diseases in a globalised world. Lancet Infect Dis 11(2): 131–141
- Barakat R, El Morshedy H (2011) Efficacy of two praziquantel treatments among primary school children in an area of high *Schistosoma mansoni* endemicity, Nile Delta, Egypt. Parasitology 138:440–446
- Chai ZW, Xu QH, Xu CM (2014) Schistosomiasis haematobia misdiagnosed as urinary tract infection: one case report. Chin J Schisto Control 26(1):I (in Chinese)
- Chen MG, Feng Z (1999) Schistosomiasis control in China. Parasitol Int 48(1):11–19
- Chen XY, Jiang QW, Zhao GM, Hao Y, Wang LY, Zheng J (2001) Endemic status of schistosomiasis in People's Republic of China in 2000. Chin J Schisto Control 13(3):129–131 (in Chinese)
- Colley DG, Bustinduy AL, Secor WE, King CH (2014) Human schistosomiasis. Lancet 383(9936):2253–2264
- Doenhoff MJ, Cioli D, Utzinger J (2008) Praziquantel: mechanisms of action, resistance and new derivatives for schistosomiasis. Curr Opin Infect Dis 21(6):659–667
- WHO Expert Committee (2002) Prevention and control of schistosomiasis and soil-transmitted helminthiasis. World Health Organ Tech Rep Ser 912:7–17
- China Import and Export Fair (2012) http://www.cantonfair.org. cn/html/cantonfair/en/about/2012-09/130.shtml. Accessed September 2012
- Fallon PG, Doenhoff MJ (1994) Drug-resistant schistosomiasis: resistance to praziquantel and oxamniquine induced in *Schistosoma mansoni* in mice is drug specific. Am J Trop Med Hyg 51(1):83–88
- Faust EC, Meleney HE (1924) Studies on schistosomiasis japonica. Am J Hyg 3:331–339
- Feng B, Liu YL, Han XZ (1984) 2 case reports of schistosomiasis haematobia. Shanxi Med J 13(2):38–39 (in Chinese)
- Gao JX, Yao Y, Zhao YY, Zhang JY (2015) A case of imported schistosomiasis haematobia first reported in Linyi City, Shandong Province. Int J Med Parasit Dis 42(5):294–301 (in Chinese)
- Gray DJ, McManus DP, Li Y, Williams GM, Bergquist R, Ross AG (2010) Schistosomiasis elimination: lessons from the past guide the future. Lancet Infect Dis 10(10):733–736
- GPPSD (Guangdong Provincial Public Security Department, the People's Republic of China) (2014) The number of African people in Guangzhou. http://www.gdga.gov.cn/jwzx/gdjx/gzsj/201412 /t20141217_725697.html. Accessed 18 December 2014 (in Chinese)
- Guo JG, Zheng J (2000) Schistosomiasis epidemic and control in China. Chin J Dis Control Prev 4(4):289–293 (in Chinese)
- Hao XH (1992) 2 cases of imported schistosomiasis haematobia in returned migrant workers. Chin J Frontier Health Quarantine 13(6):340–341 (in Chinese)
- He YX, Salafsky B, Ramaswamy K (2001) Host–parasite relationships of Schistosoma japonicum in mammalian hosts. Trends Parasitol 17(7):320–324

- HFPCA (Health and Family Planning Commission of Anhui Province, the People's Republic of China) (2015) Anhui Province reached transmission control of schistosomiasis. http://www.ahwjw.gov. cn/dbfzc/gzdt/201504/1f689197fc154b598e74fc690d34e682.html. Accessed 3 April 2015 (in Chinese)
- HFPCH (Health and Family Planning Commission of Hunan Province, the People's Republic of China) (2015) Hunan Province reached transmission control of schistosomiasis. http://www.hunanwst.gov. cn/gzdt/jswsyw/201512/t20151230_47122.html. Accessed 30 December 2015 (in Chinese)
- HFPCJ (Health and Family Planning Commission of Jiangxi Province, the People's Republic of China) (2015) Jiangxi Province reached transmission control of schistosomiasis. http://www.jxwst.gov. cn/wsyw/201504/t20150415_364662.htm. Accessed 15 April 2015 (in Chinese)
- Hipgrave D (2011) Communicable disease control in China: from Mao to now. J Glob Health 1(2):224–238
- Hua H, Yin A, Xu M, Zhou Z, You L, Guo H (2015) Advanced schistosomiasis reappeared after curing seemingly being cured for over 20 years and without known history of reexposure to *Schistosoma japonicum*. Parasitol Res 114(9):3535–3538
- Huang LS (1992) Schistosomiasis haematobia in returned migrant workers (report of 21 cases). Chin J Schisto Control 3(6):355 (in Chinese)
- Huang SY, Zhang QM, Li XH, Deng ZH (2014) Distribution and schistosomiasis transmission risks of *Biomphalaria straminea* in inland China. Chin J Schisto Control 26(3):235–237 (in Chinese)
- Jiang DZ, Li HM (2015) Molluscicidal mechanism of combining use of extract of *Glycyrrhiza uralensis* and niclosamide. Chin J Schisto Control 27(6):608–611
- Jiang ZH, Tang WQ, Lin Y, Yang YC (2015) First report of one imported case of schistosomiasis haematobia in Guangxi Zhuang Autonomous Region. Chin J Schisto Control 27(5):560–561 (in Chinese)
- Jin LQ, Yi SH, Liu Z, Chang XH, Na WL, Wang PX (1992a) A case report of schistosomiasis haematobia. Chin J Parasit Dis Control 5(3):243–245 (in Chinese)
- Jin LQ, Yi SH, Liu Z, Chang XH, Na WL, Wang PX (1992b) A case of schistosomiasis haematobia. J Pathogen Biol 5:III (in Chinese)
- Kloos H, Correa-Oliveira R, dos Reis DC, Rodrigues EW, Monteiro LA, Gazzinelli A (2010) The role of population movement in the epidemiology and control of schistosomiasis in Brazil: a preliminary typology of population movement. Mem Inst Oswaldo Cruz 105(4): 578–586
- Lei JC, Liu ZX, Huang YX (2007) An imported case of *Schistosoma haematobium* infection in Angola. Chin J Parasitol Parasitic Dis 25(1):I (in Chinese)
- Lei ZL, Zhang LJ, Xu ZM, Dang H, Xu J, Lv S et al (2015) Endemic status of schistosomiasis in People's Republic of China in 2014. Chin J Schisto Control 27(6):563–569 (in Chinese)
- Lewis FA, Tucker MS (2014) Schistosomiasis. Adv Exp Med Biol 766:47–75
- Liu J, Gan SB (2001) Long-term follow-up observation on patients with schistosomiasis mansoni. Chin J Zoonoses 17(2):69 (in Chinese)
- Liu YY, Wang YX, Zhang WZ (1982) The discovery of *Biomphalaria* straminea (Dunker), an intermediate host of *Schistosoma mansoni*, from China. Acta Zootaxonomica Sin 7:256 (in Chinese)
- Logan OT (1905) A case of dysentery in Hunan Province, caused by the Trematoda, *Schistosomum japonicum*. Chin Med Missionnary J 19: 243–245
- Lu QS, Xu ZB (1980) Summary on 15 cases of schistosomiasis haematobia. J Peking Univ Health Sci 22(3):215–216 (in Chinese)
- Lu P, Wang W, Dai J, Liang Y (2014) Imported African schistosomiasis: is it an emerging public health concern in China? J Travel Med 21(1):72–73 (in Chinese)

- Mao SP, Shao BR (1982) Schistosomiasis control in the People's Republic of China. Am J Trop Med Hyg 31(1):92–99
- Mao YH, Hu WC, Tu J, Chen FJ, Wang RF, Ning A et al (2012) Advanced schistosomiasis chemotherapy and assistance in Xinjian County, 2005–2009. Chin J Schisto Control 24(02):203–204 (in Chinese)
- Mas-Coma S, Valero MA, Bargues MD (2009) Climate change effects on trematodiases, with emphasis on zoonotic fascioliasis and schistosomiasis. Vet Parasitol 163(4):264–280
- McCreesh N, Booth M (2013) Challenges in predicting the effects of climate change on *Schistosoma mansoni* and *Schistosoma haematobium* transmission potential. Trends Parasitol 29(11):548–555
- McManus DP, Gray DJ, Li Y, Feng Z, Williams GM, Stewart D et al (2010) Schistosomiasis in the People's Republic of China: the era of the Three Gorges Dam. Clin Microbiol Rev 23(2):442–466
- McManus DP, Gray DJ, Ross AG, Williams GM, He HB, Li YS (2011) Schistosomiasis research in the Dongting Lake region and its impact on local and national treatment and control in China. PLoS Negl Trop Dis 5(8):e1053
- Meier-Brook C (1974) A snail intermediate host of *Schistosoma mansoni* introduced into Hong Kong. Bull World Health Organ 51(6):661
- Merrifield M, Hotez PJ, Beaumier CM, Gillespie P, Strych U, Hayward T, Bottazzi ME (2016) Advancing a vaccine to prevent human schistosomiasis. Vaccine 34(26):2988–2991. doi:10.1016/j. vaccine.2016.03.079
- Midzi N, Sangweme D, Zinyowera S, Mapingure MP, Brouwer KC, Kumar N, Mutapi F, Woelk G, Mduluza T (2008) Efficacy and side effects of praziquantel treatment against *Schistosoma haematobium* infection among primary school children in Zimbabwe. Trans R Soc Trop Med Hyg 102:759–766
- Minai M, Hosaka Y, Ohta N (2003) Historical view of schistosomiasis japonica in Japan: implementation and evaluation of disease-control strategies in Yamanashi Prefecture. Parasitol Int 52(4):321–326
- Ministry of Health of the People's Republic of China (2006) Chinese diagnostic criteria for schistosomiasis (WS 261-2006). http://www. nhfpc.gov.cn/ewebeditor/uploadfile/2014/12/20141208170326851. pdf. Accessed 7 April 2006 (in Chinese)
- Qian GY, Li YZ, Xu GQ (2005) Quantitative observation on *Schistosoma haematobium* eggs in urine sample treated with praziquantel. Chin J Schisto Control 17(6):466–467 (487, in Chinese)
- Ross AG, Sleigh AC, Li Y, Davis GM, Jiang Z, Feng Z et al (2001) Schistosomiasis in the People's Republic of China: prospects and challenges for the 21st century. Clin Microbiol Rev 14(2):270–295
- Shuaib W, Stanazai H, Abazid AG, Mattar AA (2016) Re-emergence of Zika virus: a review on pathogenesis, clinical manifestations, diagnosis, treatment, and prevention. Am J Med. doi:10.1016/j. amjmed.2016.02.027
- Sokolow SH, Huttinger E, Jouanard N, Hsieh MH, Lafferty KD, Kuris AM et al (2015) Reduced transmission of human schistosomiasis after restoration of a native river prawn that preys on the snail intermediate host. Proc Natl Acad Sci U S A 112(31):9650–9655
- Song LG, Wu ZD (2015) Pathology and pathogenesis of liver fibrosis induced by *Schistosoma japonicum*. Chin J Schisto Control 27(2): 213–216 (220, in Chinese)
- Song L, Wu X, Ren J, Gao Z, Xu Y, Xie H, Li D, Gong Z, Hu F, Liu H et al (2016) Assessment of the effect of treatment and assistance programme on advanced patients with schistosomiasis japonica in China from 2009 to 2014. Parasitol Res. doi:10.1007/s00436-016-5207-y
- Tchuenté L-AT, Shaw DJ, Polla L, Cioli D, Vercruysse J (2004) Efficacy of praziquantel against *Schistosoma haematobium* infection in children. Am J Trop Med Hyg 71:778–782
- The Carter Center (2014) Schistosomiasis control program. http://www. cartercenter.org/health/schistosomiasis/index.html. Accessed March 2014

- Utzinger J, Zhou XN, Chen MG, Bergquist R (2005) Conquering schistosomiasis in China: the long march. Acta Trop 96(2–3):69–96
- Wang W, Dai JR, Liang YS (2014) Apropos: factors impacting on progress towards elimination of transmission of schistosomiasis japonica in China. Parasit Vectors 7:408
- WHO (2008) Nigeria. http://www.who.int/neglected_ diseases/preventive_chemotherapy/databank/CP_2008_Nigeria. pdf?ua=1. Accessed 2008
- WHO (2010a) United Republic of Tanzania (the). http://www.who. int/neglected_diseases/preventive_chemotherapy/databank/CP_2008_ UR_Tanzania.pdf?ua=1. Accessed 2008
- WHO (2010b) Congo (the) http://www.who.int/neglected_ diseases/preventive_chemotherapy/databank/CP_Congo.pdf?ua=1. Accessed 2010
- WHO (2013) Schistosomiasis: control and preventive chemotherapy. http://www.who.int/schistosomiasis/strategy/en. Accessed 7 Mar 2013 (in Chinese)
- WHO (2014) WHO signs Memorandum of Understanding with China and Zanzibar for collaboration on schistosomiasis elimination in Zanzibar. http://www.who.int/neglected_diseases/schistosomiasis_ china_zanzibar/en/. Accessed 21 May 2014
- WHO (2016) Schistosomiasis. http://www.who. int/mediacentre/factsheets/fs115/en/. Accessed February 2016
- Williams GM, Sleigh AC, Li Y, Feng Z, Davis GM, Chen H et al (2002) Mathematical modelling of schistosomiasis japonica: comparison of control strategies in the People's Republic of China. Acta Trop 82(2):253–262
- Wu ZT, XJ E, Wang AX (1988) Schistosomiasis haematobia (report of 22 cases). Acta Acad Med Sine 10(4):306–307 (in Chinese)
- Xie HG, Lin CX, Jiang DW (2013) A case of imported schistosomiasis haematobia first reported in Fujian Province. Chin J Schisto Control 25(3):329 (in Chinese)

- Xu ZP, Chen MG, Wang H, Song GY, Chen RY, Yu SH et al (1979) A clinical study of 67 cases of schistosomiasis mansoni. Acta Acad Med Sin 1(2):127–130 (in Chinese)
- Xu J, Yu Q, Tchuente LA, Bergquist R, Sacko M, Utzinger J et al (2016) Enhancing collaboration between China and African countries for schistosomiasis control. Lancet Infect Dis 16(3):376–383
- Yang GJ, Li W, Sun LP, Wu F, Yang K, Huang YX et al (2010) Molluscicidal efficacies of different formulations of niclosamide: result of meta-analysis of Chinese literature. Parasit Vectors 3:84
- Yi P, Yuan LP, Wang ZH (2011) Retrospective survey of 184 patients infected with *Schistosoma haematobium* from African countries. Chin J Schisto Control 23(4):441–442 (in Chinese)
- Zeng TY, Cai YH (1991) A case report of urinary schistosomiasis haematobia. Railway Med J 28(6):382–383 (395, in Chinese)
- Zheng Q, Vanderslott S, Jiang B et al (2013) Research gaps for three main tropical diseases in the People's Republic of China. Infect Dis Poverty 2(1):15
- Zhou HJ (2014) The living condition of overseas Chinese in Africa and their relation with the local ethnicities. Southeast Asian Stud 01:79– 84 (in Chinese)
- Zhou XN, Wang LY, Chen MG, Wu XH, Jiang QW, Zheng J et al (2005) The public health significance and control of schistosomiasis in China—then and now. Acta Trop 96(2–3):97–105
- Zhou XN, Guo JG, Wu XH, Jiang QW, Zheng J, Dang H et al (2007) Epidemiology of schistosomiasis in the People's Republic of China, 2004. Emerg Infect Dis 13(10):1470–1476
- Zhou YB, Liang S, Jiang QW (2012) Factors impacting on progress towards elimination of transmission of schistosomiasis japonica in China. Parasit Vectors 5:275
- Zou L, Ruan S (2015) Schistosomiasis transmission and control in China. Acta Trop 143:51–57
- Zou Y, Qi ZQ, Feng ML, Wang F, Li W, Su SG et al (2011) Clinical analysis of imported *Schistosoma mansoni* infections: a report of two cases and review of the literature. Chin Trop Med 11(2):250– 252 (in Chinese)