



Multi-disciplinary integration of networking through the RNAS⁺: Research on other target diseases

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Abstract

In 2005, the network decided to increase its number of target diseases to include other helminthic zoonoses such as fascioliasis, clonorchiasis, opisthorchiasis, paragonimiasis and cysticercosis and in the process expanding membership to include South Korea, Vietnam, Thailand and Japan. NTDs were eventually included as awareness is heightened on these diseases affecting poor and developing countries. Researches on clonorchiasis and opisthorchiasis unravel the mechanism by which these diseases eventually predispose to cholangiocarcinoma. The liver cancer associated with these liver fluke infections necessitate the need to clarify the global burden of disease of these infections. The magnitude of these liver fluke diseases in endemic countries like China, Vietnam, Laos, Cambodia and Thailand is described. Success in elimination of lymphatic filariasis in PR China and Cambodia is highlighted to show how intensified multisectoral collaboration and strong political become strong ingredients in elimination of parasitic diseases like LF. New advances are presented that clarify species and strain differences in *Fasciola* spp., *Paragonimus* spp., *Taenia* spp. and *Echinococcus* spp. Conventional diagnostic techniques are compared with new serologic techniques that are being developed. New control strategies such as the Lawa model are presented.



1. Introduction

When the network, at its fifth meeting held in Bali, Indonesia August 8–10, 2005, decided to include fascioliasis, clonorchiasis, cysticercosis, opisthorchiasis and paragonimiasis, besides schistosomiasis, it paved the way for adding Japan, South Korea, Thailand, and Vietnam and a change of name to the Regional Network on Asian Schistosomiasis and other Helminthic Zoonoses or RNAS⁺. At its ninth meeting in Vientiane, Lao PDR October 19–20, 2009, the target diseases were further increased to include any NTD endemic in a member country. At this meeting, RNAS⁺ also drafted a programme to fit WPRO's Research Strategic Plan, identifying issues and operational research priorities, reassessing its role, defining strategies and future plans in contributing to the development of functional research on neglected tropical diseases (NTDs) in Asia. This chapter presents advances made with respect to target diseases, in particular those contributing to a better understanding of the epidemiology, pathogenesis, diagnosis, treatment and prevention and control of target diseases, mainly food-borne trematodiasis (FBTs), echinococcosis, cysticercosis, but also other NTDs.



2. Neglected tropical diseases under the network

Zhou et al. (2009) reported the results of the 1st International Symposium on Geospatial Health which was held in Lijiang, Yunnan province, People's Republic of China from 8 to 9 September 2007. The aim of the conference was to review progress made with the application of spatial techniques on zoonotic parasitic diseases, particularly in Southeast Asia. There were 71 presentations delivered on various parasitic diseases such as soil-transmitted and waterborne helminth infections and arthropod-borne diseases such as leishmaniasis, malaria and lymphatic filariasis. Various approaches in the study of these diseases were highlighted such as geographical information systems (GIS), global positioning systems (GPS) and remote sensing (RS), including spatial statistics, web-based GIS and map visualization of field investigations.

Tambo et al. (2014) presented the results of the “First Forum on Surveillance-Response System Leading to Tropical Diseases Elimination” which was held in Shanghai in June 2012 for the purpose of identifying and prioritizing strategic research on elimination of tropical diseases. Following a review of the current strategies and the NTD roadmap, identification and critical examination of the prevailing challenges and opportunities that include inter-sectoral collaboration and approaches for elimination of several infectious, tropical diseases, a priority research agenda was developed that involved a “One Health-One World” framework of global health. This research agenda included (i) the establishment of a platform for resource-sharing and effective surveillance-response systems for Asia Pacific and Africa with an initial focus on elimination of lymphatic filariasis, malaria and schistosomiasis; (ii) development of new strategies, tools and approaches, such as improved diagnostics and antimalarial therapies; and (iii) rigorous validation of surveillance-response systems; and (iv) designing pilot studies to transfer Chinese experiences of successful surveillance-response systems to endemic countries with limited resources.

Yang et al. (2015) made a review of emerging and re-emerging diseases like schistosomiasis, dengue, avian influenza, angiostrongyliasis and soil-transmitted helminthiasis that have affected China as a result of environmental and agricultural change. The association between poverty and infectious diseases is further influenced by environmental changes, agricultural practices

and social status affecting emerging and re-emerging diseases such as schistosomiasis, dengue, avian influenza, and angiostrongyliasis. The group underscored research priorities and response strategies especially those involving mitigation and adaptation to eliminate re-emergence of these infectious diseases.



3. Food-borne trematodiasis

Food-borne diseases (FBTs), transmitted through contaminated food, are important worldwide because of the significant mortality and morbidity especially in low and middle income countries where they contribute to high burdens of disease. A study of [Torgerson et al. \(2010\)](#) estimates the global and regional human disease burden of 10 helminth diseases and toxoplasmosis acquired by contaminated food. The results could pave the way to understanding the impact of FBTs globally and regionally. The study also indicates that the disease burden from most these parasites is highly focal but can lead to significant morbidity and mortality among vulnerable populations.

Human liver fluke infections caused by *Opisthorchis viverrini*, *O. felineus* and *C. sinensis* persist as significant public health problems in many countries world-wide especially in Asia. *C. sinensis* can be found in the southern part of PR China, South Korea and northern Vietnam, while *O. viverrini* is confined to the lower Mekong Basin, including Thailand, Lao PDR, Cambodia and central Vietnam. *O. felineus* is endemic in the former Soviet (USSR) and in Central-Eastern Europe. Recent estimates put a total of 700 million people at risk of clonorchiasis and opisthorchiasis. [Qian et al. \(2013c\)](#) compare clonorchiasis with hepatitis B which infects 23 million in China. Both diseases show higher prevalence among adult males compared to females and children. Both cause liver disease and impaired biliary conditions and produce similar symptoms such as fatigue, loss of appetite, fever, nausea, abdominal pain, jaundice and hepatomegaly. Both lead to liver cancer.

[Qian et al. \(2019\)](#) pointed out the importance of cooperation between PR China and Association of Southeast Asian Nations (ASEAN) in fight against human liver flukes. It is argued that RNAS⁺ significantly provides important platform for further cooperation.

The first case of *C. sinensis* infection was found in 1874, which was completely documented in the Lancet in 1875. Thus, in the 140 years' anniversary of the discovery of the fluke, [Qian et al. \(2015\)](#) carried out a complete review on clonorchiasis in the Lancet. The seminar held for this purpose summarized the advance in clinical manifestations and complications, pathogenesis and carcinogenesis, epidemiology, environmental

determinants and social-ecological systems, diagnosis, treatment and control of clonorchiasis. This disease is a common FBT in Southeast Asia including China, South Korea and Viet Nam where the estimates amount to 15 million infected people with populations at risk exceeding 600 million. However, the disease which is acquired by consumption of raw infected fish can also be found in countries where immigrants from endemic countries live. Chronic infections result in mild to serious sequelae leading to modification of the liver parenchyma with thickening and expansion of ducts including the gallbladder wall. However, this infection eventually develops into cholangiocarcinoma. Based on results of several studies on the association between *C. sinensis* infection and this type of cancer, this liver fluke was in 2009 considered as “carcinogenic to humans” (Group 1) by the International Agency for Research on Cancer (IARC). Still, clonorchiasis remains a NTD due to lack of paucity of information about the true disease burden, in particular the lack of a reliable disability-adjusted life year (DALY) score.

The study by [Qian et al. \(2013c\)](#) was the first attempt to calculate this showing that *C. sinensis* infection causes apparent disability. A positive correlation between disability and infection intensity was found and the overall score for the male is higher than that for the female. It is hoped that the disability determined in this study would pave the way for further studies facilitating a final estimation of disease burden to be used as basis for promoting health awareness and implementation of intervention. [Qian and Zhou \(2017\)](#) recently concluded that inadequate studies, incomplete data including the complex and chronic characteristics of cancers have not been helpful in determining an accurate estimate of the number of cholangiocarcinoma cases that can be attributed to liver flukes. Thus, it is important that more research be conducted in this field so as to raise awareness of the importance of these flukes in east Asia that will eventually lead to promotion of their control and elimination.

In PR China, where clonorchiasis is an important public health problem, comprehensive intervention strategies based on chemotherapy using praziquantel were implemented in the two endemic counties with the highest prevalence rates in 2006. The study of ([Qian et al., 2013b](#)) in one county in Guangdong showed differences in knowledge, behaviour and infection intensity among different populations necessitating the adoption of different intervention measurements for these different population groups. The group proposed that chemotherapy be prioritized among the adults especially adult males. Health education targeting children is seen to have a crucial role in the long term. Immigrants similarly should also be involved as well as

restaurants that serve raw fish dish. Given the serious sequelae resulting from chronic infections with *C. sinensis*, early case management and treatment depend crucially on accurate and rapid diagnosis. Qian et al. (2013a) evaluated the diagnostic performance of Kato-Katz method and Formalin-ether concentration technique (FECT) in a clinical trial demonstrating that the Kato-Katz method is more sensitive in a setting of low infection intensity after drug treatment. However, the sensitivity of conventional stool examination techniques is inadequate and compliance has also decreased. Li et al. (2018) conducted a parallel and systematic evaluation of the performance of available immunodiagnostic kits detecting clonorchiasis in China. Their results showed good performance of three immunodiagnosis kits targeting IgG antibody in detecting chronic *C. sinensis* infection. But the kits detecting IgM antibody did not perform well.

Although praziquantel developed in later 1970s shows good efficacy against *C. sinensis* infection, new drugs are needed. Tribendimidine, a new drug against soil-transmitted helminths (STH) approved by the Chinese administration department in 2004, has been shown, both in vivo and in vitro efficacy against *C. sinensis*. Two clinical trials were conducted in PR China, one carried out by Qian et al. (2013a) in Guangxi in 2012, the other in Hunan province. Particularly, the side effect was less in tribendimidine group. In the former, the cure rate of a single dose of tribendimidine (400 mg) was a slightly inferior to praziquantel (25 mg/kg, t.i.d), but the egg reduction rates were comparable. On the other hand, the side effects were lower in tribendimidine group. The latter trial showed an efficacy of a single dose of tribendimidine (400 mg) comparable to praziquantel (75 mg/kg divided into four doses over 2 days), and the efficacy increased significantly by the second praziquantel treatment. The results of the two trials agreed with regard to the lower side effect of tribendimidine. In addition, Qian et al. (2019) demonstrated the effectiveness of school-based behavioural intervention against the practice of consuming raw freshwater fish. It was demonstrated that through comprehensive education, the knowledge on control of clonorchiasis increased and the practice of raw freshwater fish consumption decreased significantly.

Sithithaworn et al. (2012) describe the present status and control of *O. viverrini* and *C. sinensis* infections in the Mekong Basin countries. Presentations from the session “96 Years of Opisthorchiasis” during the International Congress of Liver Flukes (2018) provided up-to-date data on prevalence and distribution. It was concluded that high endemicity persists in all endemic countries of the lower Mekong Basin including high levels of cholangiocarcinoma incidence in spite of decades of treatment and control efforts. The review by Sithithaworn et al. (2012) noted that

lowlands have significantly higher prevalence of *O. viverrini* compared with highlands. The higher prevalence was associated with wetlands, flooding patterns and human movement and settlement prevailing in the lowlands. The group recommended a more collaborative effort among all related government sectors.

Like *C. sinensis*, *O. viverrini* infection is classified by the International Agency for Research on Cancer as a Group 1 carcinogen: definitely carcinogenic in humans. [Sripa et al. \(2017\)](#) reviewed latest results that try to explain the role of liver fluke associated *Helicobacter pylori* in hepatobiliary disease and malignancy. Previous studies show cholangiocarcinoma cases with concurrent *H. pylori* infection to manifest higher portal inflammation and biliary cell proliferation as determined by PCNA immunohistochemistry. Further studies have shown the presence of *H. pylori* in the gut epithelium of *O. viverrini* leading to the conclusion that this liver fluke possibly serves as a reservoir of *H. pylori* within the biliary system. [Sripa et al. \(2017\)](#) have further brought up the possibility of co-infection with *O. viverrini* and *H. pylori* being at the core of the liver fluke infection associated cholangiocarcinoma.

Poor prognosis and limited efficacy of chemotherapy characterize this disease. [Chng et al. \(2016\)](#) report findings that show how the unique microbial communities found in the bile duct, parasitic infections and the tissue micro-environment can interact with each other to eventually lead to development of cancer. The group found that a specific bacterial family Bifidobacteriaceae dominated other bacterial families like Enterobacteriaceae and Enterococcaceae in tumours associated with *O. viverrini* infections which provides a mechanistic link to the parasite. Further functional analysis and comparison of cholangiocarcinoma microbiomes (for example, in tumours associated with *O. viverrini* and in tumours not associated with parasitic infection) showed higher possibility to produce bile acids and ammonia in tumours associated with *O. viverrini* thus providing the link between the changed microbiota to carcinogenesis.

Opisthorchiasis is endemic in Thailand and Lao PDR where it is considered an important public health problem throughout the Mekong Basin. [Miyamoto et al. \(2013\)](#) clarified the status of this liver fluke infection in Cambodia by documenting the extent and distribution of *O. viverrini* infection there. An extensive survey of 55 villages revealed the presence of this infection in four Cambodian provinces. This research group recommends careful planning in the field surveys because of the influence of complex environmental factors in the distribution of the disease. A nationwide baseline survey is further recommended to clarify the status of the disease in the country.

O. felineus is one of the three species belonging to the family Opisthorchiidae that causes liver disease. While *O. viverrini* and *C. sinensis* are classified as group 1 agents and a major risk factor for cholangiocarcinoma by the International Agency for Research on Cancer, while the potential of *O. felineus* to cause cancer is not that clear. *O. felineus* used to be endemic only within the territory of the Russian Federation, especially in Western Siberia, the Ukraine, Byelorussia, Kazakhstan and the Baltic countries but has recently been observed to be increasing in European regions, including Italy where reports of outbreaks of acute cases have been made lately. This fluke causes 1 in 10 cases of opisthorchiasis worldwide.

Pakharukova et al. (2015) conducted the first functional study of the cytochrome P450 (CYP) enzyme of flatworms using *O. felineus*, which causes biliary tract diseases in Russia, Kazakhstan and central Europe. Only one CYP450 enzyme was identified in *O. felineus*. This enzyme belongs to a group of proteins that are specifically involved in the synthesis of physiologically active compounds, in drug metabolism, and in biotransformation of xenobiotics. These researchers concluded that this could be a promising drug target but should be further investigated especially in understanding the physiology of this liver fluke.

Gouveia et al. (2017) support the inclusion of *O. felineus* in the Group 1 list of biological carcinogens. First, novel oxysterol-like metabolites, markedly similar to oxysterol-like molecules known from *O. viverrini*, both in egg and adult developmental stages of *O. felineus* by liquid chromatography-mass spectroscopy. These metabolites were also found in the bile, sera, and urine of liver fluke-infected hamsters. Second, portal area enlargement, inflammation with severe periductal fibrosis and changes in the epithelium of the biliary tract characterized as biliary intraepithelial neoplasia were validated by histological analysis of liver sections from hamsters infected with *O. felineus*. These biochemical and histopathological evidences seen in *O. felineus* infection in the rodent model suggest induction of precancerous lesions conducive to malignancy.

In spite of Thailand's protracted history of FBT control with corresponding nationwide reduction in prevalence of opisthorchiasis, the northeastern provinces in Thailand continue to harbour high prevalence of the infection. Sripa et al. (2015) reported the introduction of a new strategy using the EcoHealth/One Health approach in the Lawa Lake area in Khon Kaen Province where most of the endemic areas are found. The programme entitled the "Lawa model" uses anthelmintic treatment, novel intensive health education methods both in the communities and in schools, ecosystem monitoring

and active community participation. Results show significant decline to one-third of the 50% baseline in the infection rate in more than 10 villages surrounding the lake. Infection rate in the fish intermediate host decreased also considerably to less than 1% from a baseline of 70%. At present, the Lawa model has been recognized not only nationally but also internationally and being extended to neighbouring countries of the Mekong Basin.

Paragonimiasis (flukes encapsulated in the lungs) is not well understood from the point of view on disabilities caused and the DALY score fluctuates in different global burden of disease (GBD) estimates. [Feng et al. \(2018\)](#), in a systematic review of clinical paragonimiasis cases, recomputed the disability weight of human paragonimiasis and conclude that this DALY needs to be reconsidered in the light of the availability of morbidity data and species variation. However, determining the disease burden from paragonimiasis requires further modification with significant implications for public health prioritization in research, monitoring, and control. [Chen et al. \(2004\)](#) concluded that populations of *P. skrjabini* from five provinces of China are different strains of this species. *P. szechuanensis* is not a separate species but may be a geographical strain of *P. skrjabini* and *P. miyazaki* may be synonymous with *P. skrjabini*.

FBT infections due to *C. sinensis* constitute a major public health problem in Vietnam with transmission by consumption of raw fish or fish products. [Hung et al. \(2015\)](#) report that results from an extensive cross-sectional study reveal that there are FBT hotspots that remain in spite of the awareness of people on the risks of eating raw fish. These researchers recommend that any strategy to control FBT should stress the serious consequence of these infections and the critical need to stop the habit of eating raw fish.

Fascioliasis caused by either *Fasciola hepatica* or *F. gigantica* is the most common helminth infection in ruminants all over the world. This disease commonly causes death among cattle and goats. Human fascioliasis however is rarely reported, except in some countries. [Chen et al. \(2013\)](#) report that, while fascioliasis is common among livestock in PR China, human cases however are rarely reported. An outbreak of human fascioliasis was however reported in Yunnan Province in 2011. Symptoms observed among the cases were intermittent fever, epigastric tenderness, and hepatalgia. Blood tests showed eosinophilia and ultrasound revealed tunnel-like lesions in the liver. Administration of triclabendazole, the drug of choice for fascioliasis, significantly improved the patients' condition. Animal surveys yielded prevalence of 28.6% in cattle and 26.0% in goats. Molecular analysis confirmed

co-existence of *F. hepatica* and *F. gigantica*. It was proposed that the herb *Houttuynia cordata* was most likely the source of infections. [Chen et al. \(2013\)](#) recommend distribution of triclabendazole for treatment of fascioliasis.



4. Echinococcosis and cysticercosis

Echinococcosis and cysticercosis are parasitic zoonoses of global concern. Although they do not cause high mortality, they result in significant impairment of human health and also agricultural production resulting in poor quality of life. There are key socioeconomic and environmental factors that influence transmission of both diseases that include poorly developed public health programmes, low hygiene and education standards, inefficient medical and veterinary services; climatic and environmental situations that perpetuate the zoonotic life-cycles. Several international meetings and workshops, held in PR China from 1998 to 2001, have led to an understanding of the seriousness of these diseases resulting in the development of a strategy to control echinococcosis and cysticercosis. [Ito et al. \(2003\)](#) report that this strategy involves an inclusive method that relies on a systematic analysis of the local settings especially concerning differences in the cycle, ecology and ethology with regard to the animal hosts, and behavioural characteristics of the population at risk. In addition, the use of newly developed tools, such as immunodiagnostics, molecular tools and imaging techniques and the convergence of traditional control measures (slaughter control, anti-parasitic treatment and control of the definitive hosts and health education) and more recent developments such as vaccination of the intermediate hosts.

Neurocysticercosis caused by *Taenia solium* metacestode or cysticercus larvae is one of the most common parasitic diseases in the central nervous system. Increased immigration rates and frequency of travel to endemic areas have resulted in the re-emergence of this disease in many communities. Symptoms depend on the size, number of cysticercus larvae and their location in the brain including the stage of infection. [Chung et al. \(2005\)](#) in the first seroepidemiological study of cysticercosis in the Nabo, Guangxi Zhuang Autonomous Region, report results that imply that cysticercosis is only relatively endemic in this area, with behavioural and environmental practices of the community responsible for the continued transmission of this parasitic infection. [Chung et al. \(2005\)](#) suggest that control and prevention of this disease should consider cultural traditions including human behaviour and promote the use of dedicated latrines.

[Qian and Zhou \(2018\)](#) report on the “Belt and Road Network for the Elimination and Control of Echinococcosis and Cysticercosis” that was set up in Chengdu, PR China in latter part of 2017. The primary objective of the network is to establish capacity for the research and development necessary to reach the control targets for echinococcosis, as well as those for cysticercosis by 2030. This will be based on the commitment, coordination, and cooperation of all endemic countries and the international community. The Chengdu Declaration to combat echinococcosis and cysticercosis was signed by experts representing 13 countries. The network invites participation of more countries in Europe and Asia to fight echinococcosis together.

Following the increased awareness from Chinese government on control of echinococcosis, more tools are developed to combat this zoonotic helminth. [Yu et al. \(2017, 2018\)](#) report the application of the technique of bait delivery with praziquantel using unmanned aerial vehicle for canine deworming, which could save manpower, time and overall cost in areas highly endemic for echinococcosis. [Jiang et al. \(2017\)](#) developed an in situ slow-release formulation of praziquantel by subcutaneous injection, which should be capable of resisting new *Echinococcus* infections for at least 6 months. [Li et al. \(2007\)](#) point out that echinococcosis has been put on high priority with the western endemic areas being the focus of substantial control activities.

In 2004, Jiang et al. reported the presence of potential antigenic proteins specific for alveolar echinococcosis or cystic echinococcosis from among different antigens shared by the two species of *Echinococcus*. Results could pave the way for further identifying specific antigens for immunodiagnosis. Now, [Jiang et al. \(2004a\)](#) have cloned, expressed and serologically evaluated the Em 18 antigen gene of *Echinococcus multilocularis* for diagnostic purpose. Their results are promising showing specificity of Re Em 18 antigens for alveolar echinococcosis with serum antibody level showing good correlation with the course of the disease at the early stage. Similar results were shown by evaluation of the ReEm 18-1 and ReEm18-2 antigens.



5. Lymphatic filariasis, soil-transmitted helminthiases and other helminthiases

Lymphatic filariasis (LF), one of the NTDs and a major public health problem in many tropical and sub-tropical countries, was targeted by the World Health Organization (WHO) for elimination as a public health problem by 2020. There are three species of nematode filarial worms

(*Wuchereria bancrofti*, *Brugia malayi*, and *B. timor*) that are transmitted by different species of mosquitoes. LF was confirmed to be endemic in Cambodia in 1956 when infected mosquitoes were found in Kratie province. An extensive study in 2001 further confirmed the endemicity of both *Brugia malayi* and *Wuchereria bancrofti*. A national task force to set up policies and work out strategies for controlling and eliminating NTDs was organized in 2015 with the goal of eliminating LF by 2015. [Khieu et al. \(2018\)](#) gave an account of the work done to eliminate LF as a public health problem in Cambodia. This involved successful MDAs, development of health center capacity for patient care, including the gains from socioeconomic progress and other measures against vector-borne diseases and NTDs. In 2016, WHO declared Cambodia as having achieved LF elimination as a public health problem. In China, LF was eliminated much earlier in 2006 after decades of sustained efforts focused on multisectoral collaboration involving various departments of the government, intensified control, prevention and elimination programme for LF and continued and massive cooperation from endemic populations ([De-jian et al., 2013](#)).

[Qian et al. \(2015\)](#) discuss the possibility of interrupting transmission of STH in China. Rapid economic development and intensified helminth control activities have reduced greatly the prevalence of STH in China from 536 million infected in 1988–1992 to 129 million in 2001–2004. National surveillance data also indicate continuing decline hence the shift to a higher goal of interruption transmission of STH in China which is expected not only to benefit China but the whole world as well. The group recommend the implementation of an expanded surveillance system for STH to provide real time data needed to assess transmission interruption process and make necessary adjustments. [Tarafder et al. \(2011\)](#), using Kato-Katz technique in an epidemiological study, show how mistakes in misclassification can affect the association between soil-transmitted helminth infection and schistosomiasis in humans. Using a statistical technique to compute for epidemiological measures of association after correcting for the inaccuracy of the test, results indicate a major difference between epidemiological measures of association before and after the correction of the inaccuracy of the test. Following correction of the error in the test, STH infection was shown to have an association with an increase in the risk of infection with schistosomiasis. The public health implications of this finding may be significant since this means that the effective control of one helminth can result in the decrease in the occurrence of another and therefore bring about a reduction in the overall burden of worm infections in affected regions.

Ezeamama et al. (2005) quantified the effect of polyparasite infections, including multiple concurrent low intensity infections on anaemia and found that low-intensity polyparasite infections were correlated with increased odds of anaemia. Often, the frequency of concurrent infection with multiple parasite species is higher than single-species infections. Results of the study indicate that concurrent low-intensity infections with more than one parasite species can eventually lead to clinically significant morbidity. Ezeamama et al. (2005) also estimate the synergistic effect caused by helminth species in their combined effects on anaemia. For example, concurrent infections of hookworm and either *S. japonicum* or *T. trichiura* were correlated with increased levels of anaemia than would be expected if the effects of these species had only independent effects on this. These findings indicate that an integrated anti-helminth treatment programmes synchronized with deworming for *S. japonicum* and STHs could result in a bigger effect than additive benefit for reducing anaemia in helminth-endemic regions.

McManus et al. (2014) report on the development and successful trial of a health education package to prevent STH infections among students of Han Chinese primary school in Hunan province, PR China. Results of the trial showed the direct effect of health education in improving knowledge and awareness, and in changing hygiene behaviour. Additionally, it could further improve the understanding of the public health outcomes of a multi-component integrated control programme especially where health education can result in prevention of re-infection while periodic drug treatment brings down prevalence and morbidity.

Qian and Zhou (2018) systematically evaluated the education products aiming at control and prevention of helminthiasis in China. It is demonstrated that massive education products have been established for helminthiasis in China. Most the products came from Centers for Disease Control and Prevention and Institutes of Parasitic Diseases at provincial and county levels. High number of products targeted schistosomiasis and echinococcosis, which also showed high quality, while those aiming other helminthiasis were limited and inadequate.

Angiostrongyliasis is a food-borne nematode acquired by ingestion of molluscan intermediate host infected by the third stage larvae of *Angiostrongylus cantonensis*. Rodents are the regular definitive hosts with molluscs as intermediate hosts. Hu et al. (2018) investigated the infection status and spatial distribution of the hosts which can be used as basis for developing strategy for the prevention and control of angiostrongyliasis. The group report the existence of spatial correlation and spatial clusters in the distribution of

infected *Pomacea canaliculata* snails and rats. The maximum radius of spatial cluster areas of infected rats also coincided with the rats' sphere of activity. A geographically weighted regression (GWR) model was found more advantageous than the ordinary least squares regression (OLS) model in the spatial analysis of hosts of *A. cantonensis*. The results point out that the risk of angiostrongyliasis is clearly present in Nanao Island, PR China and that large-scale monitoring should be undertaken without delay.

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