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Parasitology in Japan

Research and control of parasitic diseases in Japan: current position and future perspectives

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Between 1950 and 1980, Japan eliminated several major parasitic diseases. In 1998, the Japanese Hashimoto Initiative was the first global programme to target parasitic diseases. Thereafter, Japan expanded its international cooperation to cover infectious diseases through integrated development programmes to improve health, to alleviate poverty and to help to achieve the Millennium Development Goals of the United Nations. Parasite control remains a major component of all subsequent operations. Opportunities to build upon past successes in order to improve the situation in the developing world – in addition to tackling emerging national threats – are promising. Substantial challenges remain and Japan has introduced major national reforms to try to overcome them.

Setting the scene

Japan occupies a unique position with respect to infectious disease research and control. Japan has been confronting problems that are faced by wealthy nations and problems that persistently threaten poor, developing countries because the Japanese islands extend from almost the Arctic north to the southern tropical Okinawa islands and because the nation recently rose quickly from relative poverty to a position among the wealthiest countries. Japan also has the invaluable experience of successfully driving the health of its citizens from a postwar low point to the elevated levels seen today. A major factor in this accomplishment was the control of parasitic diseases. Today, the country faces new challenges because the profile of parasitic diseases has shifted from the high prevalence of soil-transmitted parasitoses, seen in the 1950s, to epidemics of previously rare diseases and imported and opportunistic infections. Novel parasites, especially in immunocompromised hosts, often cause serious manifestations and present problems with diagnosis and treatment. They also necessitate individual clinical interventions rather than the mass control operations that succeeded in the past.

For a better understanding of the current position and future prospects it is important to bear past experience in mind. Stemming from Japanese advances in the 1950s, health-improvement initiatives and control programmes that involve mass screening and treatment were implemented that now enable Japanese nationals to enjoy one of the healthiest lifestyles in the world. In the space of two decades, nationwide, interdisciplinary, multisector public-health campaigns against parasitic diseases led to the control of ascariasis, trichuriasis, hookworm and other soil-transmitted parasitoses and the eradication of other major diseases such as malaria, schistosomiasis and lymphatic filariasis [1–6].

Parasite control proved to be a leading component of successful postwar development in Japan. For example, in terms of the causal factors behind the rapid declines in mortality seen between 1968 and 1978, the control and decline of parasitic diseases was second only to advances in combating diseases of the circulatory system [7]. Consequently, during the 20 to 30 years after the war, parasite research and parasite-control programmes were priorities. Parasitology departments were among the most important in universities and research institutes and there was close integration between research and field control programmes. In 1950, only ~30% of the population had a safe water supply and outbreaks of waterborne diseases were frequent [8]. Enactment of the water supply law in 1955 led to the swift introduction of proper water and sanitation systems (Figure 1), which had a rapid and notable impact (Table 1). As coverage expanded, water-borne infectious diseases declined markedly. Application of knowledge about the environment, hygiene and disease linkages, together with national advances in science, technology and medicine (i.e. vaccines, drugs and diagnostics such as the Kato–Katz thick smear test for schistosomiasis), proved crucial. The government also cooperated with numerous nongovernmental organizations (NGOs) that were established nationwide and were devoted to the control of parasitic diseases. Many researchers were also actively involved in field control programmes that operated in the vicinity of their research facilities. Collaboration

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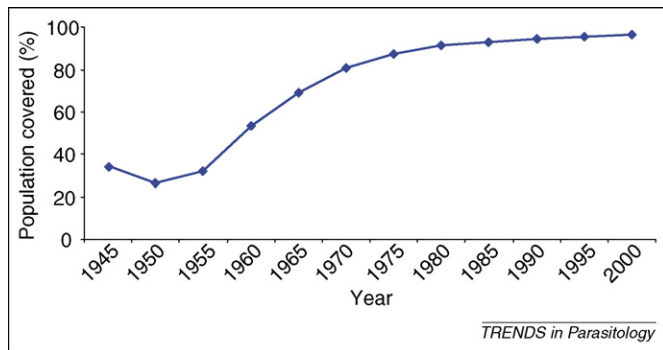


Figure 1. Water supply provision rate in Japan. A rapid increase in the provision of safe water supplies from the early-1950s helped to reduce water-borne disease.

between the education and health sectors was also pivotal. Nationwide, schools were one of the few postwar public infrastructures that remained functional. Deworming interventions in schools were combined with health education, which was provided by schoolteachers and supported by researchers. Those involved in deworming programmes recognized the invaluable nature of linking different local-level resources, especially schools and community health centres. They also experienced the impact of ‘community empowerment’ [9,10].

Exporting success

The rapid socioeconomic development in Japan, of which the traditional ‘village living’ philosophy was a driving force, saw the nation evolve from being one that received overseas development assistance (ODA) in the early-1950s to donor nation status by the late-1950s. The initial focus of Japan was to concentrate on helping neighbouring countries in Asia but in the new millennium and with globalization increasing that view has expanded to encompass a global assistance focus, with special attention currently being shown to Africa. The unique ODA philosophy in Japan, which is based on the overriding concept of self help and human security, contributes to overseas development by exporting its achievements in disease control and in shaping support for disease research and control activities (<http://www.mofa.go.jp/policy/oda/cooperation/anniv50/pamphlet/contents.html>).

The origin: the Hashimoto Initiative

Based on its successes in controlling several major parasitic diseases and its desire to help other nations achieve similar success, Japan proposed a global parasite-control initiative at the 1997 Group of Seven (G7) summit in Denver, USA, which emphasized the necessity of international cooperation to control parasitic diseases. A report entitled ‘Global Parasite Control for the 21st

Century’ submitted at the 1998 Group of Eight (G8) summit in Birmingham, UK, specified the intention by Japan to help developing countries to improve their ability to control parasitic diseases and also persuaded the G8 nations to embrace the proposal [11–13]. The so-called ‘Hashimoto Initiative’ (HI), named after its architect and the Japanese Prime Minister at the time, Hashimoto, represented an unprecedented step in Japanese ODA history. In Japan, the Prime Minister or Parliament can influence ODA policy but, usually, the bureaucracy or civil servants have been the de facto operator of ODA policy [14]. Thus, the HI was unique. Hashimoto fervently desired to contribute to the health of people in less-developed countries by transferring Japanese experience, especially in disease research and control. He envisioned support for Japanese experts who engage in such work at centres that were established abroad as a contribution not only to global health but also as a means to maintain the skills and expertise of parasitology researchers in Japan.

The evolution: Okinawa Infectious Disease Initiative

Three years after the HI was proposed, and mindful of major changes regarding the global disease-control scene, Japan expanded the scope of the target infectious diseases and announced the more expansive Okinawa Infectious Disease Initiative (IDI) in 2000 [15,16]. The IDI aimed to provide \$3 billion over a five year period. Parasitic diseases were retained as a primary target in what was planned as a comprehensive and cohesive range of measures to further social and economic development in recipient countries (http://www.mofa.go.jp/mofaj/gaiko/summit/ko_2000/outline/jp/overview.html). Actual spending exceeded expectations and totalled >\$4 billion in four years (Figure 2).

The IDI incorporated several major strategies, including promotion of research and of public-health activities. This was the first time that research was clearly defined as a matter for action in a health-related ODA policy document. It quickly became apparent, however, that the shortage of experienced personnel in parasitic-disease control was a crucial issue. As a result, plans were put in place for the development of a global network of research institutions to target infectious and parasitic diseases, to promote research on infectious and parasitic diseases in impoverished countries with a focus on benefiting the poor, and promotion of international cooperation in vaccine research and development [17]. These centres were expected to provide technical support to field control programmes using Japanese ODA and would mimic what had happened during the successful national control efforts in Japan.

Japan also had a leading role in the development of the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM: <http://www.theglobalfund.org/en/>). Spurred by the IDI, GFATM was established in 2002 after discussion at subsequent G8 summits and a United Nations (UN: <http://www.un.org>) General Assembly special session on HIV/AIDS. The then Prime Minister, Koizumi, expressed strong commitment to the global endeavour at a symposium to commemorate the fifth anniversary of the Kyushu–Okinawa Summit and announced an additional contribution of \$500 million (http://www.mofa.go.jp/policy/health_c/gfatm/address0506.html).

Table 1. Effects of small-scale water supply systems in 300 towns and villages^a

Measure	Decline (%)
Incidence of gastrointestinal diseases	88
Incidence of trachoma	49
Infant mortality	20
Cost of public health and infectious-disease control	32
Medical treatment costs	43

^aData from Ref. [41].

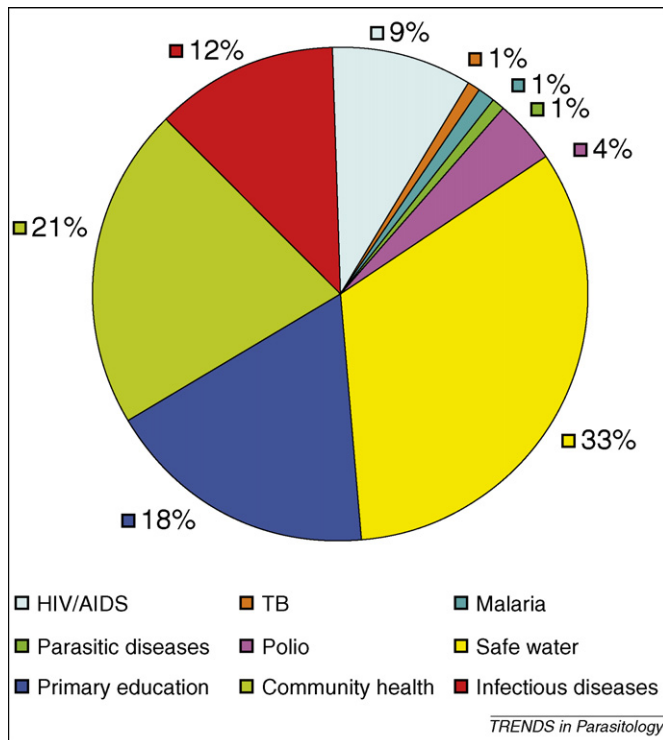


Figure 2. Japanese expenditure on the Okinawa IDI. The Okinawa IDI spending reflects the Japanese policy of using a holistic, multisector, community-driven approach to disease control and poverty alleviation. The total expenditure from 2000 to 2003 was \$4.102 billion.

New millennium initiatives

In the year 2000, all UN member states adopted the Millennium Declaration [18], which put poverty reduction at the centre of concerns and incorporated specific, measurable development goals to be achieved by 2015. These became known as the Millennium Development Goals (MDGs) [19]. The MDGs comprise eight goals, three of which refer explicitly to health. At the high-level forum on health MDGs in Asia and the Pacific, Japan stated that achieving the health MDGs is a crucial step that is necessary to attain all of the eight MDGs (<http://www.mofa.go.jp/policy/oda/category/health/state0506.html>). In response to the adoption of the MDGs, following the completion of the IDI in March 2005, Japan expanded the IDI into a comprehensive, multisectoral health and development initiative (HDI) [20], which was designed to continue and enhance active support in the health-related sector through ODA with emphasis on accomplishing the MDGs, particularly in Africa [21].

In the HI, school-based deworming of intestinal helminths was chosen as a main focus for international disease-control programmes. The direct beneficial effects of deworming are well documented and include improved nutritional status, increased weight gain [22], better micronutrient uptake, improved cognitive development of children [23], improved physical fitness and appetite [24] and increased school attendance [25]. However, the reason that school-based deworming was selected for particular attention was not only the direct effects but also the indirect socioeconomic and health benefits that would be bestowed on communities [26,27].

The concepts inherent in the HI remain major pillars of the new HDI. Japan also adopted a strong research

component within the HDI and included 'strengthening research capacity on the ground and paying due respect to local condition' as the underlying basic policy. Crucially, this reflects the Japanese self-help philosophy. The HDI emphasizes the importance of understanding local culture, traditions and norms towards ill health and seeks to strengthen research capacity at the field level, in particular those research activities that are designed to facilitate and improve project implementation.

Key national factors

In Japan, the parasitic-disease research and control community underwent some fundamental changes as a result of its success [28]. After the eradication of key parasitoses from Japan and effective control being established over many others, parasitic diseases were no longer viewed as a subject of major concern. Consequently, extensive and well-supported research groups began to lose their resources. They became divided into two groups: those that maintained their interest in disease-control programmes and applied research turned their attention to tackling parasitic diseases outside Japan, and those which kept their focus on Japan and, instead, concentrated on basic laboratory research on other diseases. This exacerbated the disconnect between research and control.

The potential threat from infectious diseases, including those that are newly emerging and some that were never eradicated from Japan (coupled with increasing international trade and travel), mean that Japan must remain continually alert and prepared. This was exemplified by the recent outbreaks of severe acute respiratory syndrome (SARS) and avian flu, which focused attention on how Japan is able to respond to infectious disease threats to its inhabitants, in addition to maintaining its responsibility to protect its less well-off neighbours. This was indicated by the creation of a regional stockpile of Tamiflu to help combat an outbreak of avian flu, should it arise [29]. Thus, the disconnect between research and control of parasitic diseases, coupled with the rapidly shrinking

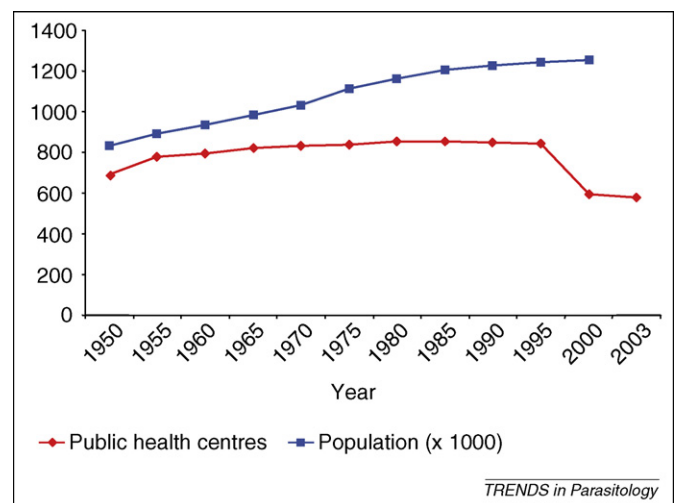


Figure 3. Trends in public-health centre number and the national population. Public-health centres were a major component of antiparasite and health-improvement programmes in Japan but began to decline post-1965 after disease control had been established and diseases such as schistosomiasis and lymphatic filariasis were substantially decreasing.

cadre of skills and expertise capable of dealing effectively with parasitic-disease matters [including the relatively sudden disappearance of community-based health centres (Figure 3)] has been a major concern in Japan. Consequently, the government has taken substantial measures to rectify the problem.

Confronting challenges

The HI conceptualized the future of Japanese parasitic-disease research and control worldwide. To remain a leader within the HDI, parasitic-disease control programmes will continuously need to work with Japanese ODA policy makers and position themselves as one of the best means of attaining the MDG targets. One major drawback is that the Japanese experience, whereby parasitic-disease control contributed substantially to overall social development, remains primarily an anecdotal record and is not documented in health-system research terms. It is, therefore, important to monitor and evaluate ongoing programmes in order to collect the data and present the results in a more scientific manner. The research agenda that is set by parasitic-disease control is not complete [30] and an additional body of knowledge and action that takes the functioning of the health system into account must complement the disease-control approach. Recognition of the importance of health-system research, in conjunction with attaining the MDGs, has been increasing [31]. The Japanese Ministry of Health, Labour and Welfare organized a symposium for health-system development in 2005 at which the importance of the linkage between the health-system research agenda and a disease-specific generated research agenda was confirmed [32]. It is reported that undernutrition is the underlying cause of a substantial proportion of all child death [33] and programmes that are aimed at controlling soil-transmitted helminths have already demonstrated their positive impact on nutrition. Therefore, it is important to maintain the integration of efforts to control parasitic diseases with all ongoing health-system activities and improvement efforts, nationally and internationally.

In Japan today, parasitoses are less of a public-health dilemma and more a problem for individuals, with the primary difficulty being one of diagnosis rather than treatment. Commonly used parasitological tests are not effective for some of the new diseases and many clinicians are untrained or inexperienced in dealing with them [34]. Moreover, the successful control of parasites has led to a vacuum of interest and attention, with parasitology departments having disappeared from medical schools and the number of staff in the departments that remain has declined substantially. In the late-1990s, of the 96 medical and veterinary schools in Japan, only 57 had either a parasitology or tropical medicine department [3]. Japan needs to solve this dearth of national experts in parasitic-disease research and control – it needs to refocus and rejuvenate its research base. The gaps between applied research, field control and basic research also need to be bridged. The Japanese research community has historically benefited enormously from working in close collaboration with control programmes to overcome parasitic diseases. Since parasitic diseases became rare and of

minor importance in Japan, the research community has been diluted and crucial experience and knowledge has been condensed, inherited by a declining number of individuals. It is important to establish collaboration and coordination between groups, in the short-term to overcome the problem of the lack of human resources and in the long-term to promote and improve parasitic-disease research and control.

It is important that Japan is able to interface and work with the international community and particularly with specialists from countries where parasitic-disease control projects take place. Research priorities for health and development in wealthy and resource-poor countries are not the same [35]. Basic research in Japan might not necessarily focus on needs that are deemed a priority elsewhere. Overall, the crucial factor is that the application of medical science in developing countries should be a joint effort between scientific institutions in countries from the South (i.e. resource-poor) and the North (i.e. wealthy) [36]. Irrespective of a national or global focus, there must also be an underlying principle of engaging affected communities themselves and of them having a pivotal role in developing interventions jointly with NGOs, industry and local and central health departments. Furthermore, it is imperative to ensure that research is cohesively and continually integrated into control initiatives, as was the case in Japan and elsewhere. An example is the community-directed treatment system being used by the African Programme for Onchocerciasis Control (<http://www.apoc.bf>) to combat onchocerciasis in Africa [37].

Japan is facing the (re)emergence of several water- and food-borne parasitic diseases and parasitic zoonoses. This is because of increasing international trade, faster transport, demographic changes and increasing immigration and tourism [6]. In addition, there are now cases of imported diseases such as malaria and cysticercosis [38] and the northernmost Hokkaido island prefecture is experiencing an epidemic of alveolar echinococcus [39]. As part of a major rejuvenation of research and development work in science and technology, which began in 1996, the government has been taking active steps to boost national capacity in all aspects of disease research and control. The fundamental reforms and almost complete restructuring of the science and technology system in Japan has caused a paradigm shift from 'science, technology and society' to 'science and technology for society' [40]. There has also been an increase in funding that is devoted to parasitic and infectious diseases. Between 1998 and 2000, \$3–4 million annually was being devoted to parasitology research from the Ministry of Education, Culture, Sports, Science and Technology (MEXT). Overseas collaboration is also expanding, with the National Institute for Science and Technology Policy reporting that 20% of all scientific publications in 2001 arose from international collaborations, compared with only 5% in 1981. In 2003, MEXT allocated \$23 million to inaugurate a new programme to intensify research into measures for coping with infectious diseases and to create centres of excellence (COE) nationally and internationally. So far, at least three COE have been created overseas and four in Japan, all coordinated through the newly established Center of

Research Network for Infectious Diseases (<http://www.riken.go.jp/engn/index.html>).

The third Japanese Science and Technology Basic Plan (2006–2010) is designed to promote science and technology that provides an immediate, exact solution to socially essential issues, including international bioterrorism and emerging or re-emerging infectious diseases, such as SARS and avian flu, that threaten global safety and security. In addition, human resources will be developed in order to respond to new needs and to contribute towards combating infectious diseases and bioterrorism, natural sciences, humanities and social science and the burgeoning bioinformatics and technology disciplines (<http://www8.cao.go.jp/cstp/english/basic/index.html>). These activities should promote ongoing international collaboration in basic research, including genomics work. In addition, the activities should facilitate the participation of Japan-based basic research groups in field control and applied-research programmes in developing countries that are supported by Japanese ODA and technical cooperation.

Concluding remarks

Despite the challenges, the opportunities for further advancements in parasitic research and control are good, with renewed interest and entrepreneurship, the development of new techniques, tools and delivery systems and deployment of substantial amounts of funding. Knowledge drives productivity, economic growth and health; however, unless all stakeholders put a concerted effort into resolving the challenges, the opportunities might fade and the unique and privileged acquired knowledge and experiences of Japan could be lost.

Disclaimer

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Some Parasitology Meetings in 2007

10–14 June 2007

A combined meeting of the Livestock Insect Workers Conference and the International Symposium on Ectoparasites of Pets

Lexington, KY, USA

http://www.pestmanagement.info/ISEP_LIWC/

14–16 June 2007

1st Three Countries Joint Meeting

Living Together: Physiopathology of intracellular parasitic diseases

Strasbourg, France

French Society of Parasitology. Ermanno Candolfi: candolfi@medecine.u-strasbg.fr

German Society of Parasitology. Uwe Gross: ugross@gwdg.de

Swiss Society of Parasitology. Andrew Hemphill: andrew.hemphill@ipa.unibe.ch

17–21 June 2007

XIII International Congress in Animal Hygiene

Tartu, Estonia

Online registration form: http://www.frens.info/site/tmpl/reg9_54.php

<http://www.emu.ee/isah2007>

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Washington DC, USA

<http://www.aavp.org>

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Microbial Pathogenesis: Mechanisms of Infectious Disease

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The 21st International Conference of the World Association for the Advancement of Veterinary Parasitology

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Malaria Vaccines for the World

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**Dormy House II. Immunology, molecular cell biology and genetics of leishmaniasis:
integrated functional genomics on the road to leishmaniasis control**

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Paul M. Kaye: pmk2@york.ac.uk

9 November 2007

**British Society of Parasitology Autumn Symposium
Parasite species and speciation – tackling a host of problems**

Linnean Society, London, UK

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Organizers: Mark Viney: mark.viney@bristol.ac.uk,

Mark Booth: mb350@cam.ac.uk and Andrea Graham: andrea.graham@ed.ac.uk