POLICY FORUM: INFECTIOUS DISEASE

Medical Helminthology in the 21st Century

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Two billion people on Earth are infected by soil-transmitted helminths (such as *Ascaris lumbricoides*, hookworms, and *Trichuris trichiura*) and schistosomes (a subgroup of human helminthic infections), and the public health burden is enormous. Together with other widespread medical helminthic infections, including onchocerciasis, lymphatic filariasis, dracunculiasis (Guinea worm disease), and food-borne trematode and tapeworm infections, these infections are largely diseases of chronic morbidity and debilitation and, as such, the suffering is difficult to quantify at the population level. Nevertheless, schistosomes in Africa are responsible for some 45 million people with hematuria, 21 million with dysuria, 14 million with hydroureter, 7 million with hepatomegaly, and hookworms are now estimated to cause anemia in 33 million Africans (*1*). Overall, 300 million of the two billion infected people are estimated to have severe infections with one or more of these soil-transmitted helminths and schistosomes. Early childhood infections by soil-transmitted helminths contribute significantly to debilitation (*2*, *3*), as treatment clearly leads to increased physical and cognitive development (*4*–*7*). Although much that is good is about to happen in medical helminthology, there are also great gaps in what should be happening.

The 54th World Health Assembly recently approved resolution WHA54.19 (*8*), which calls on all member states to support a broad-based, partnership-driven assault on soil-transmitted helminths and schistosomes. The plan is to apply mass drug treatment of school-age children with albendazole, levamisole, mebendazole, or pyrantel pamoate (for nematodes) and praziquantel (for schistosomes). It is agreed, based on the prevalence of these infections in a given area, that children of school age are an appropriate target population and can safely and inexpensively be treated without prior diagnosis. The goal is regular administration of chemotherapy to at least 75% of all school-age children at risk of morbidity due to these infections by the year 2010, while ensuring access of others in the community to these drugs.

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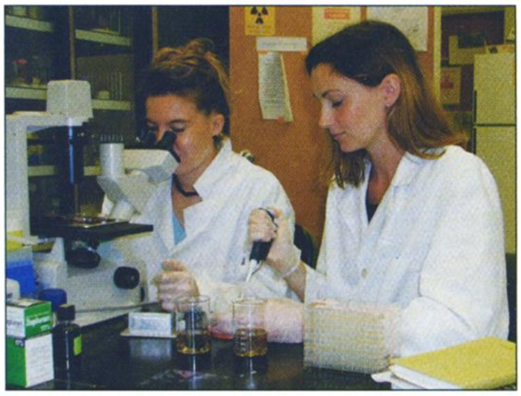
It is a good plan, and it will be implemented in some of the most affected parts of the globe. Even now, drugs are widely administered against onchocerciasis and lymphatic filariasis in global elimination programs, and the global Guinea worm eradication program is driving toward its goal. After having been largely ignored in the public health scene, this is the best of times for those concerned about human helminthic infections.



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Helminthology needs more researchers like these.

However, we must also face up to the "worst of times" aspect of the worm story in 2001. Programs against schistosomiasis and soil-transmitted helminths are control programs that will be needed for decades to centuries, until the huge challenges of economic development and improved sanitation are met in the developing world. Furthermore, there has also been a serious erosion of the support base for research in medical helminthology. This is substantiated by decreases observed between fiscal years 1985 and 2000 in the total National Institute for Allergy and Infectious Diseases, National Institutes of Health (NIAID/NIH) adjusted dollars awarded for helminth-related grants (\$18,034,207 to \$15,216,279; –16%); the number of these grants (74 to 54; –27%); and the number of helminth-related training mechanisms provided (8 to 4; –50%) (*9*).

Even graduate students who obtain their Ph.D.'s in helminth laboratories often go on to find work studying protozoans, fungi, bacteria, and viruses. Hard data on such trends are not available. However, our discussions with research and training laboratories internationally indicate that a small proportion of trainees stay in parasitology, and of those, many fewer continue to work on helminths. Why is this so? Perhaps the large-scale drug campaigns have left the impression that additional research is not needed. Yet the history of all eradication, elimination, or morbidity control programs has made the importance of parallel research programs clear (*10*, *11*).

Medical helminths are extremely challenging systems for researchers. They need to develop in a parasitized host, and sometimes this involves several disparate hosts. Helminth parasites are more complex than free-living helminths, because they have evolved mechanisms to deal with the different environments of their various hosts and living conditions. They have developed host-finding behaviors, exquisite migration patterns within each host, and the ability to evade the host immune and protective responses. There are also practical considerations such as the difficulty of culturing helminth parasites for study, whether in vitro or in animal models. In addition, the generation time for helminth parasites is usually long, and growth often requires transfers between different hosts. Genetic manipulations such as gene transfection and RNA interference have not yet been developed for parasitic worms.

There are fascinating scientific questions waiting to be answered including the following: (i) What genes and/or mechanisms are needed for parasitism? (ii) What allows a worm to evade the host immune responses? (iii) What signaling pathways are unique to the worm and are not shared by its hosts? (iv) What worm signaling pathways co-opt host molecules? (v) What worm components are vaccine and drug targets?

At this point, there is no documented human nematode resistance to drugs, [although drug resistance by nematodes is rampant in animal husbandry (*12*)], and there are only a few examples of drug resistance by schistosomes (*13*, *14*). However, it is likely that resistance will eventually develop. Now is the time for surveillance and for development of monitoring technology and alternative control measures (including drugs, vaccines, sanitation, and communication regarding behavioral modification and health). Some of the technologies that are so productive in the world of *Caenorhabditis elegans* can, with much difficulty, be moved into parasitic worms (*15*, *16*). However, among the tools that are missing are in vitro culture systems, animal models for laboratory study, appropriate cell lines, gene manipulation systems, and genome sequence information such as substantial expressed-sequence-tag databases or whole-genome sequence information. The development of these tools will be essential for helminthology questions to compete successfully in the real world of grant requests and study sections.

The situation resembles the abyss in which public health officials found themselves when Multi-Drug Resistant (MDR) tuberculosis arose in the late 1980s; there were few researchers or trained students interested in staying in the field, and no drug alternatives. The immediacy and threat of MDR TB rapidly induced funding of high-risk, technology-driven grants over a period of 4 to 8 years, which resulted in mycobacteria study becoming a vibrant, active field.

For a number of years, several philanthropic foundations have recognized the global importance and neglected nature of helminthic infections. Their efforts have been critical but not sufficient to sustain the level or focus of effort needed. We propose an "Affirmative Action for Worms" program that could attract senior and junior scientists from other fields, foster those few languishing investigators who know these systems, and entice researchers into the high-risk areas of worm-related technology development and applied usage. A 5-year, highly competitive program of $40 to $50 million, that fostered and integrated bench and field research with multiple-level training programs could lead to a real reversal in the current downward spiral of research.

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POLICY FORUM: ENERGY

Exploiting Wind Versus Coal

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Much of the recent energy debate in the United States has focused on increasing coal use. However, the cost of wind energy is now less than that of coal. Shifting from coal to wind would address health, environmental, and energy problems.

Energy costs from a new coal power plant are low [(3.5 to 4 ¢/kWh) (*1*)], but coal-mine dust kills 2000 U.S. miners yearly, and since 1973, the federal black lung–disease benefits program has cost $35 billion (*2*). Coal emissions also cause acid deposition, smog, visibility degradation, and global warming; its particles increase asthma, respiratory and cardiovascular disease, and mortality (*3*). Health and environmental costs bring the total costs to 5.5 to 8.3 ¢/kWh (*4*).

Wind is a clean energy source. We estimate its costs as follows: installing a 1500-kW turbine with a 77-m rotor diameter and design life of 20 years costs $1.5 million (*4–7*), which pays for the turbine (80%), grid connection (9%), foundation (4%), land (2%), electrical installation (2%), financing (1%), roads (1%), and consultancy (1%) (*4*, *7*). Amortizing this over 20 years at 6 to 8% interest gives $131,000 to $153,000 per year. Adding annual operation and maintenance (O&M) (*4*, *6*, *7*) leads to an estimated annual cost of $149,000 to $183,000.

A turbine's annual energy output (kilowatt-hours/year) is about $P \times 8760 \times (0.087V\text{-}P/D^2)$ (*7*), where P is rated power (in kilowatts), V is mean annual wind speed (meters/second) at rotor height ~50 m, D is rotor diameter (meters), and 8760 is hours/year. With a mean annual 50-m wind speed of 7 to 7.5 m/s [which occurs across all of North Dakota, 70% of South Dakota, and large tracts of the West, Great Plains, East, and Northeast (*8*)], the turbine energy produced is 4.7 to 5.2×10^6 kWh/year. Dividing turbine cost by energy produced and adding manufacture and scrapping costs (*7*) gives the energy cost of a large turbine as 3 to 4 ¢/kWh. Reported costs for large plus small Danish turbines are 4 ¢/kWh (*9*). These numbers suggest that the total costs of wind energy are less than those of coal energy.

Under the 1997 Kyoto Protocol, the United States proposed to reduce greenhouse gas emissions to 7% below 1990 levels. As of 1999, the target could be satisfied by replacing 59% of 1.89×10^{12} kWh/year (*10*) in coal energy with 214,000 to 236,000 turbines, thereby reducing coal-CO_2 emissions (499 Tg-C/year) (*11*) by 59%. At six turbines per square kilometer, the turbines could be spread over 194×194 km^2 of farmland or ocean.

Alternatively, every 36,000 to 40,000 turbines could displace 10% of U.S. coal at a cost of $61 to $80 billion, including O&M plus initial costs (also the present value of payments to date from the black lung–disease benefits program). This could be supported at no net federal cost by investing 3 to 4% of one year's $2.02 trillion budget in turbines and selling the electricity over 20 years. Similarly, California could provide 10% of its 1999 electricity (2.35×10^{11} kWh/year) (*12*) by buying 4500 to 5000 turbines at 7.5 to 9.9% of one year's $101 billion budget and selling the electricity over 20 years.

One concern with turbines is harm to birds This might be mitgated by siting turbines out of migration paths. Also, turbine output is unresponsive to electricity demand. This is moot when wind is one of many energy sources. Finally, remote turbines require extra transmission lines. This cost can be offset with turbine mass production. Government promotion would also catalyze private investment.

By 2000, Germany had 6113 MW of installed turbines, more than the United States (2554 MW) or Denmark (2300 MW) (*13*). Sweden and Denmark have wind parks offshore, where winds are faster than over land. Clearly, the United States has not maximized its wind potential.

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