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Current Comments®

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Schistosomiasis: The Scourge of the Third World. Part 2. Diagnosis and Treatment

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In Part 1 we discussed the life cycle of the schistosome and the etiology of schistosomiasis in Third World countries as well as the need for increased awareness of this problem in industrialized nations.[1] As a result of the widespread occurrence of schistosomiasis, many organizations, including those listed in Table 1, are concerned with learning more about this debilitating disease. This part of the essay will focus on the diagnosis and treatment of schistosomiasis. A review of relevant ISI® research fronts follows affording us a more precise view of the methods of prevention currently being researched.

Diagnosis

Definitive diagnosis of schistosomiasis is generally made by detecting eggs in the stool or urine. Two standard methods for stool egg identification are the formalin-ether technique and the quick Kato smear. Larry W. Laughlin, director, US Naval Medical Research Unit No. 2, Jakarta Detachment, Indonesia, notes that the formalin-ether technique requires reagents and a centrifuge and is highly sensitive in that it is able to detect low egg concentrations.[2] (p. 730) The quick Kato smear uses fewer supplies and only a simple microscope, and results are ready within the hour.[3] Once eggs are identified, the severity of the infection can be estimated from the number of eggs present in the stool sample.

In cases of light or chronic infection, eggs may not be found, and serological tests may be useful. According to Laughlin, these tests are most useful for epidemiological surveys and in assessing individual response to treatment.[2] (p. 730) A.M. Deelder and D. Kornelis, Laboratory for Parasitology, Medical Faculty, State University of Leiden, The Netherlands, compared the sensitivity of various serological methods for diagnosing recent schistosome infections.[4] They found that the immunofluorescent antibody technique and the enzyme-linked immunosorbent assay (ELISA) were the most sensitive techniques in detecting antibodies in *Schistosoma mansoni*-infected patients who were not passing eggs. In the immunofluorescent technique, smears are stained with preparations of an egg-specific antibody labeled with fluorescent compounds and are examined for parasites with a fluorescent microscope. The ELISA test is similar to the immunofluorescent test except that the smear is labeled with peroxidase and is quantified by microscopy.[4]

Urinary schistosomiasis, caused by *Schistosoma haematobium*, is generally detected by finding eggs in the urine. However, Kenneth E. Mott, Parasitic Diseases Programme, World Health Organization (WHO), Geneva, and colleagues compared reagent strip urine tests for hematuria (blood in the urine), an associated symptom of *S. haematobium* infection, with egg counts for detecting *S. haematobium* infection. They found that reagent strips for hematuria identify a high proportion of infected individuals. The use of reagent strips to di-

agnose infection in the field allows rapid surveys of products in the urine.[5] However, since there is a geographic difference in the incidence of hematuria, the authors suggest that preliminary evaluation at a broader level is necessary before the reagent strips are used for diagnostic purposes.

Control

Once a diagnosis of schistosomiasis has been made, the decision regarding the best treatment strategy depends on the goals of that therapy. A.M. Polderman, Laboratory for Parasitology, State University of Leiden, notes that controlling the disease involves interrupting the life cycle of the schistosome.[6] The snail, as the intermediate host, is considered the weakest link in the disease cycle. The most popular means of reducing the snail population is with molluscicides, chemicals that kill snails. Peter Jordan, then at the Medical Research Council, London, and colleagues found that reduction of snail colonies reduced the incidence of schistosomiasis from 22 to 4.3 percent.[7]

Laughlin notes that while snail control is a rapid and effective method of schistosomiasis control, it requires a prolonged effort.[2](p. 736) In addition, Kenneth S. Warren, director for health sciences, Rockefeller Foundation, New York, warns that molluscicides are potentially toxic chemicals. They are absorbed into the soil and water, causing damage to the environment, fish, and other aquatic life forms.[8] Connie Weil and Katherine M. Kvale, Departments of Geography, University of Minnesota, Minneapolis, and University of Wisconsin, Eau Claire, note that in the past 20 years there has been growing concern over the environmental effects of these molluscicides, and their widespread application has decreased.[9]

Molluscicides of plant origin supposedly cause less environmental damage than those of synthetic origin. Aklilu Lemma, then director, Institute of Pathobiology, Haile Selassi I University, Addis Ababa, Ethiopia, noted that the highly potent saponins, a group of plant glycosides in the berries of *Phytolacca dodecandra*, appear to be the most promising chemicals of plant origin for snail control.[10] The successful use of plants as molluscicides depends on abundant growth of the plant in the endemic area as well as easy extraction of the plant chemical.

F.S. McCullough, Division of Vector Biology and Control, WHO, Geneva,

Table 1: A selected list of organizations that are concerned with schistosomiasis research and control.

American Society of Parasitologists
1041 New Hampshire Street
Lawrence, KS 66044

American Society of Tropical Medicine and Hygiene
P.O. Box 29837
San Antonio, TX 78229

British Society for Parasitology
62 London Road
Reading RG1 5AS, UK

Centers for Disease Control
1600 Clifton Road NE
Atlanta, GA 30333

Commonwealth Institute of Parasitology
395A Hatfield Road
St. Albans, Hertfordshire AL4 0XQ, UK

Edna McConnell Clark Foundation
250 Park Avenue
Room 900
New York, NY 10017

Infectious Diseases Society of America
1728 Freeman Bldg.
6431 Fannin
Houston, TX 77030

National Council for International Health
2100 Pennsylvania Avenue NW
Suite 740
Washington, DC 20037

National Institutes of Health
National Institute of Allergy and Infectious Diseases
Laboratory of Parasitic Diseases
Bethesda, MD 20205

Pan American Health Organization
525 23rd Street NW
Washington, DC 20037

World Health Organization
Parasitic Diseases Programme
Avenue Appia
1211 Geneva 27
Switzerland

and colleagues report that various species of *Phytolacca* grow in Africa, Asia, and South America.[11] Although the potency of this plant-derived molluscicide is lost in a few days and the frequency of application is double that of the synthetic molluscicides, Lemma states that crushed *P. dodecandra* berries in water kill snails within 24 hours.[10] In addition, McCullough and colleagues report that repeated applications show no apparent harmful environmental effects.[11]

Although controlling snail populations would prevent schistosome reproduction, Warren indicates that snails are impossible to completely eradicate, even with the most potent molluscicides.[8] To be effective, applications must be repeated indefinitely, since snails from other locations can become established in a previously snail-free environment.

An alternative to the use of molluscicides is the biological control of snails by using various natural predators, such as other snails, ducks, and turtles. (In the near future, we will discuss turtles in more detail.) A recent study by Asim A. Daffalla and colleagues, Schistosomiasis Research Project, Institute for Tropical Medicine, Khartoum, Sudan, suggests that *Protopterus annectans*, a snail-eating lungfish, could successfully reduce the snail population in areas where molluscicides cannot be used.[12] However, the authors warn that the introduction of this fish for snail control requires further study of the ecological implications.

Chemotherapy

A recent *Lancet* editorial[13] noted that the emphasis in schistosomiasis control has been shifting from control of the snail intermediate host toward a direct attack on the parasite by chemotherapy. Chemotherapy is an effective form of control that reduces both the number of eggs in the excreta and the number of eggs released within the body. Chemist Sydney Archer, Rensselaer Polytechnic Institute, Troy, New York, indicates that in the past 15 years major advances have been made in chemotherapy for schistosomiasis. He recently reviewed the literature in the *Annual Review of Pharmacology and Toxicology*.[14]

One of the newer compounds used in chemotherapy is praziquantel, a schistosomicide that has the advantage of being effective in a single dose against the three major schistosome species. Archer reports that praziquantel is effective for all schistosome species tested, is well tolerated by the patient, and so far has not produced any cases of drug resistance in the parasite.[14] Laughlin confirms that praziquantel is currently the most important drug for treating schistosomiasis.[2] (p. 732) However, *Science* writer Gina Kolata notes that praziquantel is costly for poorer nations, especially since the chance of reinfection is high.[15] In fact, a 1985 paper by Mohamad W. Kardaman, Gezira Schistosomiasis Project, Khartoum, and colleagues reports that 12 months after praziquantel treatment, 73 percent of the treated children were again passing *S. mansoni* eggs due to reinfection.[16]

While praziquantel is the drug of choice, species-specific drugs are also effective. For example, metrifonate is effective against *S. haematobium* infection. S.A. Tswana and P.R. Mason, Department of Medical Microbiology, University of Zimbabwe Medical School, Harare, found that a single dose of metrifonate can significantly reduce the fluke burden in patients with urinary schistosomiasis.[17] Similarly, a recent study by Aziz El Kholy, Biomedical Research Center for Infectious Diseases, Cairo, Egypt, and colleagues found that single-dose metrifonate-treated children had a 90 percent reduction in urine egg counts 30 weeks after treatment.[18] Warren, who also worked on this study, notes that metrifonate is relatively inexpensive, at approximately $0.25 per treatment, and is an excellent drug for treating urinary schistosomiasis.[19]

The drug oxamniquine is specific for *S. mansoni*. H.C. Richards, administration manager of human drug research, Pfizer Central Research, Kent, UK, notes that after extensive tests in Brazil and Africa, this drug has proven safe, effective, and suitable for mass administration. In Brazil, more than seven million doses have been given since 1975. Adults are cured with a single oral dose and children with two doses, taken a few hours apart.[20]

Chemotherapy is also useful for targeted mass treatment. This involves treatment of the most heavily infected segments of a population to reduce the egg burden in the environment. According to T.K. Arap Siongok and colleagues, Division of Vector Borne Diseases, Ministry of Health, Nairobi, Kenya, lowering egg counts not only prevents the severe effects of schistosomiasis, but also decreases the number of eggs excreted into the environment, thereby offering some measure of control.[21] However, in a study of the effectiveness of targeted mass treatment, Polderman and J.P. Manshande, Mining Society of Kivu, Kalima, Zaire, found that schistosome reinfection is very rapid. Only one year after using chemotherapy to treat a population infected with *S. mansoni*, egg counts were at about two-thirds of the original level.[22]

Chemicals such as chlorine, added to water for disinfection, may also kill the schistosome in the cercarial stage. Warren indicates that chlorine at the level used in swimming pools is effective.[23] We recently discussed chlorination as a means of purifying drinking water.[24]

Education

Control of schistosomiasis is based on understanding the ecology of the snail, the schistosome life cycle, and the epidemiology and clinical aspects of the disease. Health education can also play an important role in schistosomiasis control. A recent study by Abu El Gasim and Ali Murda, Community Participation and Health Education Unit, Blue Nile Project, Wad Medani, Sudan, suggests that schistosomiasis control can be improved by teaching village women about the transmission of the disease and the various means of avoiding infection.[25] In fact, in 1977 Jordan, then with the Research and Control Department, Ministry of Health, St. Lucia, West Indies, found that instituting a health-education program in five settlements in the Riche Fond Valley area of St. Lucia caused a significant decline in water contact and lowered the incidence of schistosomiasis.[26]

This study was part of an intensive 15-year research program designed to examine three approaches to schistosomiasis control using three distinct geographical areas in St. Lucia. The effects of snail control, chemotherapy, and protected water supplies were compared with an area where no control measures were used. In his recently published book *Schistosomiasis—The St. Lucia Project*, Jordan explains that this study showed that, of the three, chemotherapy was the most inexpensive method and resulted in the most rapid reduction of infection. Controlling snail populations or reducing exposure to infected water resulted in slower declines in infection prevalence and intensity that only slowly affected the disease. Jordan warns, however, that no endemic area of schistosomiasis can be considered a typical area since ecology, transmission patterns, and population vary. But principles of control can be common to all areas where the requirements for schistosomiasis transmission are present—a low level of sanitation and a snail intermediate host in water used by the population.[27]

Schistosome Vaccine

Most major control projects use a combination of chemotherapy, molluscicides, and education of the population

at risk to lower the incidence of schistosomiasis. Presumably, however, the ultimate control will be a vaccine to prevent the disease. There is much evidence that schistosomes are able to suppress their host's immune system. However, investigators believe that a vaccine will be developed in the near future that will trigger the immune system to combat the disease. This belief is based on recent studies in which researchers have induced partial immunity to schistosomiasis in experimental animals. In addition, there is some indication that certain people become immune to the disease. A.E. Butterworth, Department of Pathology, University of Cambridge, UK, and colleagues found that some individuals within a restricted age range (9-15 years) are not reinfected with schistosomes despite reexposure to the parasite.[28] This demonstration of possible immunity in some individuals may help to identify the immune responses that an effective vaccine will need to elicit.

Monoclonal antibodies (discussed in an earlier essay on the 1984 Nobel Prize winners[29]) are being used to develop vaccines. Researchers are making monoclonal antibodies to schistosomes and then trying to determine whether these antibodies can confer immunity. Donald A. Harn, Department of Medicine, Harvard Medical School, and colleagues have isolated the antigen (the structure of foreign invaders that spark an immune response) recognized by the monoclonal antibody developed. They are testing this antigen as an immunizing agent.[30] Unfortunately, monoclonal antibody studies have so far produced inconsistent results and low levels of protection.

Although vaccine development is still in its infancy, it is a highly active area of research and investigators are confident that a vaccine will provide the best protection against schistosomiasis. Alan Sher, National Institute of Allergy and Infectious Diseases, noted in an interview with Kolata that "schistosomes don't divide in their host, so if you knock off 60 to 70 percent of them you will reduce the worm burden, so [that] the disease [becomes] negligible."[15]

Schistosomiasis Literature

Table 2 lists the major journals in which research articles on schistosomiasis occur most frequently, along with their 1983 impact factors. This table was derived using a series of rigid criteria. Initially, keywords, concepts, and prominent authors from the schistosomiasis field were used in an online and manual literature search to develop a

Table 2: Journals that publish research on schistosomiasis with the year each began publication. A = title. B = 1983 impact factor. This is calculated by dividing the 1983 citations to 1981 and 1982 articles in the journal by the number of articles that the journal published in those two years.

A	B
Advances in Parasitology (1963)	1.9
American Journal of Tropical Medicine and Hygiene (1921)	1.6
Annales de Parasitologie Humaine et Comparee (1923)	0.2
Annals of Internal Medicine (1922)	7.0
Annals of Tropical Medicine and Parasitology (1907)	0.8
Bulletin of the World Health Organization (1947/8)	1.8
Experimental Parasitology (1951)	1.7
Folia Parasitologica (1966)	0.5
Infection and Immunity (1970)	3.1
International Journal for Parasitology (1971)	0.9
Journal of Helminthology (1923)	0.6
Journal of Immunology (1916)	6.4
Journal of Infectious Diseases (1904)	4.0
Journal of Parasitology (1914)	0.8
Journal of Tropical Medicine and Hygiene (1898)	0.5
Lancet (1823)	12.3
Medecine et Maladies Infectieuses (1971)	0.3
Molecular and Biochemical Parasitology (1980)	2.5
Parasite Immunology (1979)	1.9
Parasitology (1908)	1.7
Parazitologiya (1966)	0.1
Proceedings of the Helminthological Society of Washington (1934)	0.2
Reviews of Infectious Diseases (1979)	2.3
Systematic Parasitology (1979)	0.4
Transactions of the Royal Society of Tropical Medicine and Hygiene (1907)	1.2
Tropenmedizin und Parasitologie (1949)	1.2
Tropical and Geographical Medicine (1948)	0.3
Zentralblatt fur Mikrobiologie (1887)	1.2

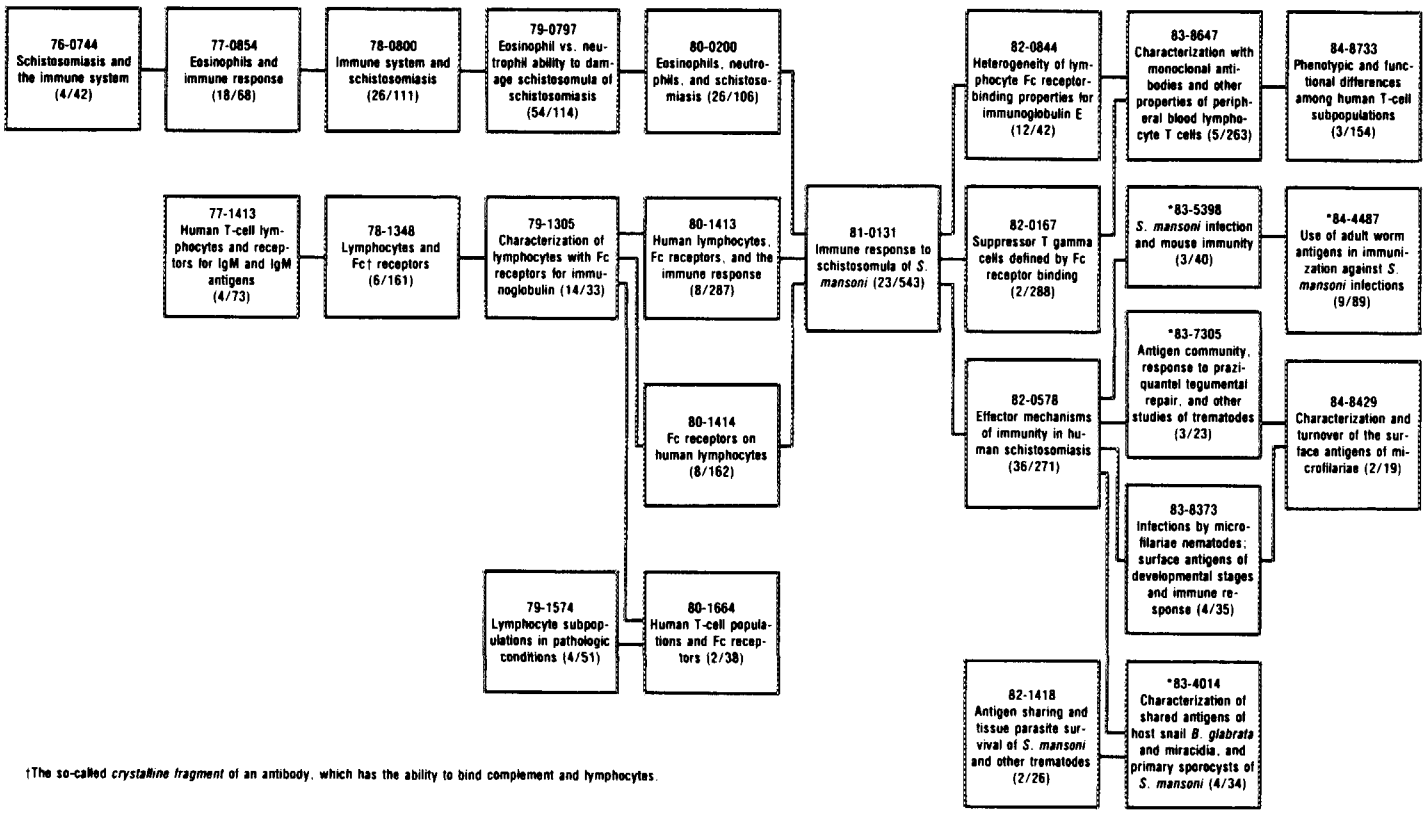
Table 3: *SCI*® research fronts on schistosomiasis. A = number. The first two numbers indicate the year of the research front. B = name. C = number of core papers. D = number of citing papers for the year indicated.

A	B	C	D
83-0192	Cell-mediated and antibody induction in schistosomiasis; antigens of eggs and the detection via ELISA	7	88
83-0738	Analyses of praziquantel as a treatment for cysticercosis, schistosomiasis, and toxocariasis	31	116
83-0900	IgE and other circulating immune complexes in schistosomiasis	2	23
83-1830	Histochemical effects of cholinergic, anticholinergic, and other neuropharmacologic drugs in schistosomes	2	9
83-2726	Homeostatic and renal disorders in cirrhosis, schistosomiasis, and hepatic portal hypertension; hepatorenal syndrome	2	23
83-3592	Observations on cattle schistosomiasis in the Sudan	5	30
83-3897	Studies on the activation of eosinophils, basophils, and other aspects of the immune response; role in immunological resistance to *Schistosoma mansoni* and infection by other parasites	2	34
83-4014	Characterization of shared antigens of host snail *Biomphalaria glabrata* and miracidia, and primary sporocysts of *Schistosoma mansoni*	4	34
83-4704	Changes in hepatic protein synthesis after *Schistosoma mansoni* infection in mice	2	12
83-5398	*Schistosoma mansoni* infection and mouse immunity; immune induction with irradiated parasites and complement dependent killing	3	40
83-7305	Antigen community, response to praziquantel tegumental repair, and other studies of trematodes, including *Schistosoma mansoni* worms	3	23
84-2173	Surface antigens, intestinal migration patterns, and other aspects of larval *Toxocara canis* infection	8	32
84-2855	Comparative treatment of schistosomiasis infections with praziquantel, oltipraz, and other anthelmintic drugs	19	94
84-3204	Use of praziquantel in treatment of cerebral cysticercosis, schistosomiasis, and other infections	6	41
84-4487	Use of cercariae, schistosomula, and other adult worm antigens in immunization against *Schistosoma mansoni* infections	9	89
84-8985	Clinical characteristics and treatment of schistosomiasis and other parasite infections	2	9

preliminary journal list. We examined core and citing papers from the current schistosomiasis research fronts, and the journals that appeared most frequently were added to the preliminary list. In addition, the 1984 *Science Citation Index*® (*SCI*®) journal guide was examined for relevant journals, which were also added to the list. Warren reviewed the list and made additional suggestions. By this time, many journal titles were recurring and a fairly long "core" list was established that required careful editing. Preference was given to journals covered by ISI. The final list provides as wide a geographic spectrum as possible and an inclusive representation of all facets of schistosomiasis research.

Warren is not only a dedicated schistosomiasis researcher, but he has also taken a special interest in information methodologies and medical communication. For example, he edited *Coping with the Biomedical Literature*,[31] to which 12 authors, myself included, have contributed chapters.[32] He has also compiled a computerized schistosomiasis bibliography containing a keyword title index. The original two-volume set in this series, coedited with Vaun A. Newill, currently associate director, Medical and Environmental Health Department, Exxon Corporation, New York, covers the literature published between 1852 and 1962.[33] Published in 1967, it contains about 10,300 references relating to both human and animal schistosomes and their snail vectors. A second two-volume set in this series, edited by Warren and Donald B. Hoffman, Jr., Edna McConnell Clark Foundation, New York, was published in 1976 and covers the literature between 1963 and 1974.[34] These volumes also include abstracts of the 3,558 cross-referenced articles cited. In 1978 Hoffman and Warren

Figure 1: Historiograph of schistosomiasis research. The number of core/citing papers is given in parentheses after the research-front title. An asterisk next to the research-front number indicates that it appears in Table 3.



†The so-called *crystalline fragment* of an antibody, which has the ability to bind complement and lymphocytes.

published two companion volumes that update the literature to 1975 and provide an overview of the diverse areas of schistosomiasis research by condensing journal articles.[35]

Warren also published a selected schistosomiasis bibliography in 1973 containing abstracts of the most significant schistosomiasis literature from 1852 to 1972.[36] A panel of 47 experts selected only about 4 percent, or 400, of the 10,300 papers reviewed. The literature is organized by subject matter, and reading a single chapter reveals the evolution of that subfield of schistosomiasis research.

Research Fronts

Table 3 shows the 1983 and 1984 *SCI* research fronts on schistosomiasis. Certain core papers identified for 1983 continued as such in 1984. These are then linked to form cluster strings called historiographs, as shown in Figure 1. Each box includes the research-front name, the number of core articles, and the number of citing papers. The fronts that are included are determined by the continuity of the core literature from year to year.

Four of the eight core papers from "Analyses of praziquantel as a treatment for cysticercosis, schistosomiasis, and toxocariasis" (#83-0738) continued into 1984 to help identify "Surface antigens, intestinal migration patterns, and other aspects of larval *Toxocara canis* infection" (#84-2173). In addition, the 1984 research front "Comparative treatment of schistosomiasis infections with praziquantel, oltipraz, and other anthelmintic drugs" (#84-2855) contains four core papers from #83-0738, two from #83-3592, and one from #83-4704.

Figure 2: The C2-level map of research front #84-0894, "Anthelmintic drugs in the treatment of schistosomiasis and other parasite infections." Number of core/citing documents is given in parentheses. The size of the box around the number indicates the relative size of the citing literature. Asterisks in front of the titles indicate that the research fronts appear in Table 3.

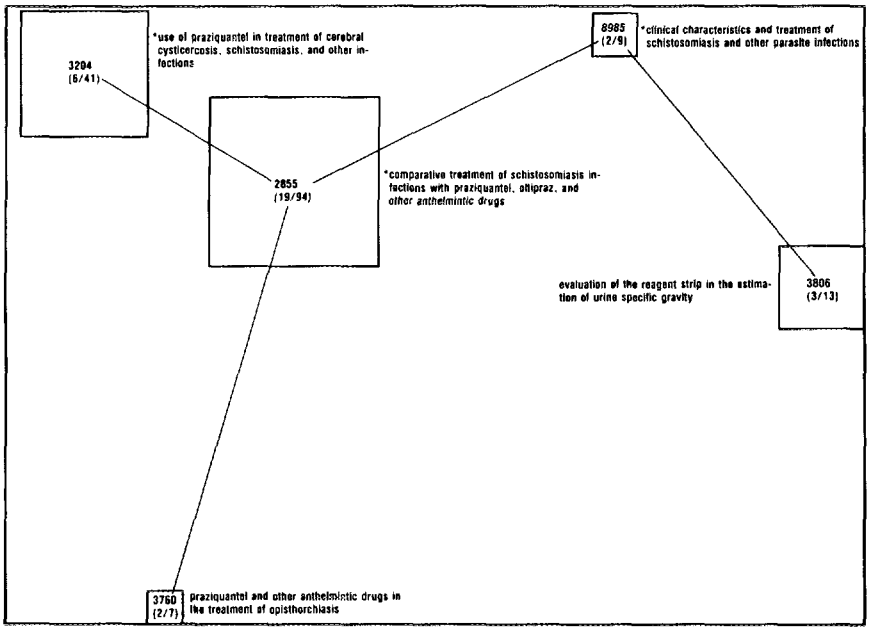
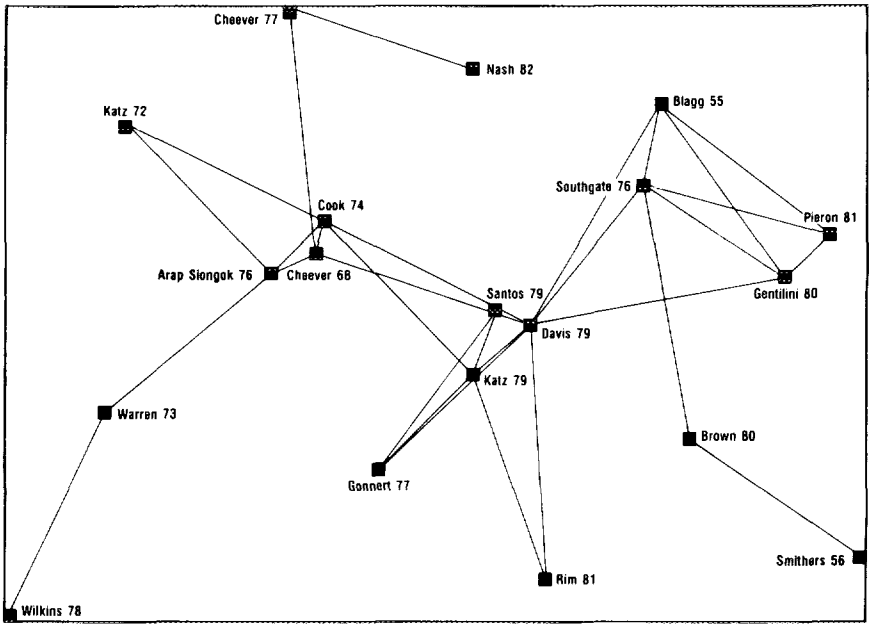


Figure 3: Multidimensional scaling map showing links between core papers of research front #84-2855, "Comparative treatment of schistosomiasis infections with praziquantel, oltipraz, and other anthelmintic drugs." Full bibliographic data are given in the key.



Key

Arap Siongok T K, Mahmoud A A F, Ouma J H, Warren K S, Muller A S, Handa A K & Houser H B. Morbidity in schistosomiasis mansoni in relation to intensity of infection: study of a community in Machakos, Kenya. *Amer. J. Trop. Med. Hyg.* 25:273-84, 1976.

Blagg W, Schloegel E L, Mansour N S & Khalaf G I. A new concentration technic for the demonstration of protozoa and helminth eggs in feces. *Amer. J. Trop. Med. Hyg.* 4:23-40, 1955.

Brown D S. *Freshwater snails of Africa and their medical importance.* London: Taylor & Francis, 1980. 487 p.

Cheever A W. A quantitative post-mortem study of schistosomiasis mansoni in man. *Amer. J. Trop. Med. Hyg.* 17:38-60, 1968.

Cheever A W, Kamel I A, Elwi A M, Mosimann J E & Danner R. *Schistosoma mansoni* and *S. haematobium* infections in Egypt. II. Quantitative parasitological findings at necropsy. *Amer. J. Trop. Med. Hyg.* 26:702-16, 1977.

Cook J A, Baker S T, Warren K S & Jordan P. A controlled study of morbidity of schistosomiasis mansoni in St. Lucian children, based on quantitative egg excretion. *Amer. J. Trop. Med. Hyg.* 23:625-33, 1974.

Davis A, Biles J E & Ulrich A-M. Initial experiences with praziquantel in the treatment of human infections due to *Schistosoma haematobium*. *Bull. WHO* 57:773-9, 1979.

Gentilini M, Duflo B, Richard-Lenoble D, Brucker G, Danis M, Niel G & Meunier Y. Assessment of 35972 RP (oltipraz) a new antischistosomal drug against *Schistosoma haematobium*, *Schistosoma mansoni*, and *Schistosoma intercalatum*. *Acta Trop.* 37:271-4, 1980.

Gonnert R & Andrews P. Praziquantel, a new broad-spectrum antischistosomal agent. *Z. Parasitenk.—Parasitol. Res.* 52:129-50, 1977.

Katz N, Chaves A & Pellegrino J. A simple device for quantitative stool thick-smear technique in schistosomiasis mansoni. *Rev. Inst. Med. Trop. Sao Paulo* 14:397-400, 1972.

Katz N, Rocha R S & Chaves A. Preliminary trials with praziquantel in human infections due to *Schistosoma mansoni*. *Bull. WHO* 57:781-5, 1979.

Nash T E, Cheever A W, Ottesen E A & Cook J A. Schistosome infections in humans: perspectives and recent findings. *Ann. Intern. Med.* 97:740-54, 1982.

Pieron R, Lesobre B, Mafart Y, Meyniel D, Lancastre F, Renard A, Simon J, Gregoire J & Basset P. L'oltipraz en traitement d'un jour dans la bilharziose a *Schistosoma haematobium* (donees pharmacocinetiques, effets therapeutiques) [Oltipraz in one-day treatment of *Schistosoma haematobium* bilharziasis (pharmacokinetic data, therapeutic effects)]. *Rev. Med. Intern.* 2:231-7, 1981.

Rim H-J, Lyu K-S, Lee J-S & Joo K-H. Clinical evaluation of the therapeutic efficacy of praziquantel (Embay 8440) against *Clonorchis sinensis* infection in man. *Ann. Trop. Med. Parasitol.* 75:27-33, 1981.
Santos A T, Blas B L, Nosenas J S, Portillo G P, Ortega O M, Hayashi M & Boehme K. Preliminary clinical trials with praziquantel in *Schistosoma japonicum* infections in the Philippines. *Bull. WHO* 57:793-9, 1979.
Smithers S R. On the ecology of schistosome vectors in the Gambia, with evidence of their role in transmission. *Trans. Roy. Soc. Trop. Med. Hyg.* 50:354-5, 1956.
Southgate V R, van Wijk H B & Wright C A. Schistosomiasis at Loum, Cameroun: *Schistosoma haematobium*, *S. intercalatum* and their natural hybrid. *Z. Parasitenk.—Parasitol. Res.* 49:145-59, 1976.
Warren K S. Regulation of the prevalence and intensity of schistosomiasis in man: immunology or ecology? *J. Infec. Dis.* 127:595-609, 1973.
Wilkins H A. Variation and stability in *Schistosoma haematobium* egg counts. *Trans. Roy. Soc. Trop. Med. Hyg.* 72:397-404, 1978.

Figure 2 is a multidimensional scaling map for the C2 research front "Anthelmintic drugs in the treatment of schistosomiasis and other parasite infections" (#84-0894). The map shows the relationship between five 1984 C1 fronts, including three directly related to schistosomiasis. The amount of literature on each topic varies considerably. This is shown graphically by varying the size of the boxes for the research-front nodes.

Front #84-2855, found in Figure 2, is also the C1 research front mapped in Figure 3. The front has 94 citing and 19 core papers, including Warren's 1973 paper "Regulation of the prevalence and intensity of schistosomiasis in man: immunology or ecology?"[37] Only 9 citing papers on "Clinical characteristics and treatment of schistosomiasis and other parasite infections" (#84-8985) were found in *SCI*-indexed journals in 1984, and 15 in 1985. The two core papers for this front describe various treatments used for schistosome-infected patients, including a paper describing the quick Kato smear test described earlier.[3]

Conclusion

Despite improved treatment and control measures, the number of people with schistosomiasis may be growing. This increase is due in part to population growth in endemic areas and widespread water confinement due to dam construction. The effectiveness of controlling this disease will depend on the knowledge of local conditions as well as an accurate understanding of today's transmission dynamics.

* * * * *

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4. **Deelder A M & Kornelis D.** Immunodiagnosis of recently acquired *Schistosoma mansoni* infection. A comparison of various immunological techniques. *Trop. Geogr. Med.* 33:36-41, 1981.
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