ANCIENT EGYPTIAN MODEL FOR THE BIOLOGICAL CONTROL OF SCHISTOSOMIASIS

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In 1971 I visited the Parasitology Laboratories of the U.S. Naval Medical Research Unit "NAMRU 3" in Cairo, where I was shown some interesting research being done on a local echinostome fluke. I was already aware of the studies of Dr. Lie Kian Joe in Malaysia on the antagonism within snail hosts between echinostome and schistosome larval forms. While in Cairo, I had opportunities to visit ancient tombs, as well as the wonderful Museum. I remember gazing at a wall painting at Saqqara which depicted offerings of food being borne by servants. The prevalence of fowl, especially ducks and geese, impressed me. Suddenly I realized that there might be a connection between these fowl of thousands of years ago and the apparent health and vigor of the Ancient Egyptians. The paper which follows is based on ideas from my stay in Cairo. The literature search was done at the University of Glasgow.

With the statement "as a cause of morbidity in these areas (tropical and subtropical regions) schistosomiasis is probably outranked only by tuberculosis and malaria", Jordan and Webbe (1) emphasize the seriousness of a disease which is increasing with the spread of irrigation, and against which only partially successful treatment and control are available. The contemporary situation is foreshadowed in a document of 4,000 years ago, the Ebers Papyrus, in which a remedy is given for "a man in whose belly there are (untranslated) worms; it is haematuria that produces them, and they are not killed by any remedy," (2). A recent, general discussion (3) describes no realistic solution to the complex problem. It is encouraging, however, that many experts are engaged in blood-fluke research, and that a variety of approaches are being explored.

Control of the snails which are intermediate hosts for schistosomes has been tried. Many different molluscicides have been formulated and tested, some quite successfully. But, the effectiveness of chemical control of snails depends on environmental factors which may be unique for each country or region. Rates of flow of water, amount and season of rainfall, and various behavioral and other biological details of the snails themselves may all be important to the success of molluscidal efforts. In Egypt, where over 16 million people have schistosomiasis, the use of molluscicides has proven both costly and relatively ineffective. In some parts of the world, biological control of snails has succeeded. Predation by natural enemies, competition with harmless species, etc., have been studied and, in some cases, applied. In Puerto Rico, for example, control of schistosome snails by introduced snails of other kinds has met with some success. In parts of the Republic of China, relatively unsophisticated methods are reportedly effective. Teams of workers "drain the ditches and dig in the snails", that is cover the snails with tamped earth. Stott (4), commenting on these activities, believes that the effectiveness of such methods derives from the workers' idealistic desire to serve their fellow man; he thinks such humanitarian approaches should be widely used. Certainly, control of snails should continue to be the subject of research and practical application.

Control of the transmission of schistosome eggs from man to snail-inhabiting water involves sewage regulation — very difficult in most developing countries — or treatment of infected populations. Effective therapy, until recently, required the use of compounds containing antimony or arsenic. These drugs, with a rather small margin between effectively therapeutic and toxic levels, are not readily accepted by patients because of unpleasant side-effects and the fact that they must be injected. Hycanthone (an aniline dye based compound) and related drugs are better than the antimony compounds, because they can be taken orally, and are effective in one or two doses.

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Evidence is accumulating, however, that hycanthone-like drugs cause chromosome breakage, an effect of which may be genetic damage. Thus, the search for a chemotherapy suitable for mass treatment continues. The hope of breaking the chain of infection at the human link has not yet been realized.

Immunological studies of schistosomiasis continue to be pursued. There is evidence of possibly protective host response. The immunological response is certainly useful in diagnosis. Attempts to stimulate the production of protective antibodies, however, are still in an experimental stage, with somewhat conflicting results from experiments with various laboratory animals and with different species or strains of schistosomes. The value of such results for planning some kind of immunity-testing in man seems not very clear. Practical "vaccination" against schistosomiasis is only a rather long range hope.

A promising and relatively new approach has been that of Lie and his associates (5-7). It was discovered that echinostomes compete with schistosomes in their larval (intramolluscan) stages. From the early 1960s evidence has grown that in areas where both schistosomes and echinostomes are present, the latter tend to flourish and the former nearly die out. This "natural experiment" in the biological control of schistosomiasis has been repeated in field trials by Lie and Ow-Yang (8), using echinostomes and a schistosome (*Trichobilharzia*, in ducks) with success. Intramolluscan competition has not yet been established as practical by field trials involving human infections. It may be well to examine its possibilities from a different aspect. Is there evidence of its worth outside the scientific literature? I believe there are facts about prehistoric and historic Egypt that provide such evidence.

Schistosomiasis existed in Ancient Egypt from very early times. While some have thought it originated there as a human infection, the accepted view today seems to be that the "Great Lakes of Central Africa" were the cradle of African schistosomiasis, and the Egyptian disease came from there with the movement of snails, people, and perhaps reservoir hosts northward along the Nile (9). Evidence for the presence of schistosomiasis in Egypt is clear. Ruffer's observation (10) of numerous terminal-spined eggs in the kidneys of two of six mummies (circa 1200 B.C.) proves that urinary schistosomiasis was present at an early time. The Ebers Papyrus and the Hearst Papyrus, both dating back to *ca* 1500 B.C., as well as the "Gynecological Papyrus of Kahun," about 1900 B.C., all earlier than Ruffer's mummies, contain prescriptions for the treatment of the disease called *"aaa"*, in hieratic script, which Egyptologists take to refer to urinary schistosomiasis (11). The papyri mentioned above are certainly copies, to a large extent, of much earlier medical writings, some perhaps going back to 3000 B.C.

Estimates of the prevalence or frequency of ancient schistosomal infections cannot be made directly. If prescriptions for treatment of all urinary disorders are compared in number with all other prescriptions in the Ebers Papyrus [which is probably the most complete of the medical writings coming from ancient Egypt according to Ebbell (2) and Leake (12)], the ratio is about 1:10. If one assumes that this ratio reflects the importance given urinary disease by physicians of those days, and if one further assumes that all urinary disease was of schistosomal origin, then perhaps it is reasonable to estimate that symptomatic schistosomiasis due to *S. haematobia* afflicted about 10% of the population. This figure may be too low, for then, as now, no doubt the majority of victims of schistosomiasis were poor farmers who daily came in contact with cercaria-infested waters, and acquired heavy infections, whereas the persons for whom the doctors prescribed, then as now, may have belonged to a class whose occupations prevented their acquiring symptomatic schistosomiasis. This occupational difference would be reflected in an underemphasis by physicians on a disease mainly prevalent among the poor. The figure may be too high, on the other hand, if a substantial percentage of urogenital disorders in ancient Egypt were not of schistosomal origin. There was probably confusion between venereal and parasitological symptoms. Jordan and Webbe (1), after discussing several references to urinary schistosomiasis in ancient Egypt, state "it is likely that the condition was widespread and probably a serious problem amongst the Ancient Egyptians." In comparison with the prevalence and seriousness of the disease among the modern Egyptians, however, who suffer a higher than 50% frequency of infection, the frequency and importance in ancient Egypt were relatively low.

A second estimate, based on historical impressions, supports the above conclusion. Egypt was one of the three great centers of civilization in antiquity, and retained its power for several millennia. Only twice was it conquered by invaders, once by Semites, who founded the Hyksos dynasty about 1800 B.C., and again by the Persians in 341 B.C., whose dominion ended shortly after when Ptolemy Lagos, Alexander's general, founded the Ptolemaic Dynasty lasting until Augustus' time. Successful defense of Egypt throughout most of its history certainly supports the view that Egyptians were not debilitated through disease. It may be argued, none-the-less, that the fellahin, upon whose labor the wealth of Egypt's rulers has always been based, may have suffered heavily from disease, in spite of the military vigor of the Egyptian state. The pharaohs hired mercenaries imported from other lands to fight for the empire. Thus the great wealth and military power of the country are not incompatible with the idea that schistosomiasis afflicted the laboring classes as much as it does today (13). On balance, however, I feel that today's level of disease was not present in what was for many centuries the strongest nation of its time. Hulse (11) supports this opinion by his interesting speculation that ancient Jericho fell to Joshua's army because its people were debilitated by disease. (He concluded that the disease was "urinary-genital schistosomiasis", and that the horrifying nature of the symptoms — impotence, reduced fertility, etc. — probably led to Joshua's exterminating the inhabitants and declaring the city "accursed.") If Hulse's speculation is correct, then Jericho's inhabitants had a level of disease — intensity of infection — that was remarkable in its time. Jordan and Webbe (1) state: "There is increasing evidence that the most important factor in the development of severe disease is a high intensity of infection." Taking this to be true, the presumed vigor of the ancient Egyptians is further evidence that the "intensity of infection" was not as high in Egypt then as it is today.

How can the difference between the old and new be explained? Among the factors thought to increase the intensity of infection in schistosomiasis are concentrations of population and increase in the numbers of the intermediate host. The population of Egypt has shown a remarkably rapid increase during the last century, but this growth has been largely accommodated by increasing urbanization. Crowding of the fellahin into villages was probably always a feature of the Nile valley, where the limited amount of agricultural land is a factor that determines the extent of space for housing. Thus, it is unlikely that significant change has occurred over even thousands of years in the concentration of people among the irrigated farm lands (14). No record has been kept of snail populations in Egypt; it is known only that *Biomphalaria* and *Bulinus* species were present in ancient times. Is there any evidence that snail populations have in fact increased? In other words, did some controlling factor existing in the past disappear or become reduced in recent times? Alternatively, did the transmission of schistosomes from man to snail, or from snail to man, change? I propose that two kinds of biological control, one, of the snail populations, the other, of the transmissions of the parasite, probably did exist, and have indeed been removed.

Snail populations in ancient Egypt were probably kept in check by predators as well as other natural causes. In prehistoric times the Nile flooded its valley unhindered, changing channels yearly, creating and obliterating swamps, ponds and lakes. In such a chaotic ecology, wild fowl, semi-aquatic rodents and insectivores, fish, even amphibians and reptiles, preyed on aquatic snails. The periodic drying of much of the flooded areas also tended to kill off susceptible snails. Permanent canals and drainage ditches, where snails could perennially multiply, were not a feature of that landscape. The natural control of snail populations, however, must have disappeared quite early. An essential feature of successful agriculture in the Nile valley was control of the flood waters, and this was accomplished before the reign of the semi-legendary King Scorpion prior to 3400 B.C. As soon as effective irrigation systems had been constructed, snail populations and their potential for transmitting schistosomiasis would have become stabilized at a high level. It is axiomatic that schistosomiasis spreads as man builds reservoirs (15).

Even after the physical environment became suitable, through irrigation, for large, sustained numbers of snails, predation may have kept snails in check for some centuries. The climate of early Egypt was such (16) that vast forests of reeds existed along the borders of the cultivated areas. Thus there was an available habitat, or refuge, for various kinds of predators, possibly in such numbers as to influence the populations of snails and the transmission of schistosomiasis. As the climate became drier, however, natural predation must have diminished, until, by the 25th century B.C., there may have been no natural check upon snail populations. Some predation by domestic fowl may have replaced natural predation, however. The goose was domesticated early; the Egyptians used it for food and consumed its eggs (17), and its fat was a favorite ingredient of the medicines of ancient Egypt (2). Domestic fowl, therefore, may have aided in the control of schistosome-bearing snails even after wild predators became unimportant.

Biological control of schistosomiasis is not synonymous with snail-control. Intra-molluscan competition between trematodes, which has interested parasitologists only recently, was described by Lie and others, who from the early 1960s have been studying the effects of echinostome flukes upon schistosomes in the snails which serve as intermediate hosts for both. Actual field trials (8, 18) have shown that high incidence of echinostomes can cause very low incidence of schistosomes in the snails of the test area. The rediae of echinostomes attack and destroy sporocysts of schistosomes (7, 19). A naturally occurring example of intra-molluscan competition may be present in Thailand. Bhaibulaya (20) reported that approximately 19% of the ducks reaching market in Bangkok were infected with echinostomes. This implies a liberal seeding of the environment with echinostome eggs, and, presumably, a high frequency of infected snails. Thailand is almost completely free of schistosomiasis (21); the presence of echinostomes in large numbers of ducks may help explain this fact. A similar condition, based on evidence of local snails being infected predominantly with echinostomes, was discovered by Chu *et al.* (22) in "a small focus of schistosomiasis in the Nile Delta". It appeared that natural biological control of schistosomiasis was being exercised by echinostome cercariae. (The latter encyst in snails, where they await being eaten by the final host. When they enter snails already infected with schistosome sporocysts, the latter die.) While more epidemiological work needs to be done, as Ferguson (23) suggested, still the principle can be considered well established that echinostomes may effectively control schistosomes where both are present.

Was schistosomiasis in ancient Egypt controlled by intramolluscan trematode antagonism? The answer depends on evidence for the presence of possible final hosts of echinostomes. Students of ancient cultures rely upon available pictorial information for data about the daily activities and environment of the people. Fortunately, Egypt is rich in sculpture and painting that describe, over a period of thousands of years, ancient life. Tombs were decorated with scenes of daily living and were filled with objects intended to prescribe and guarantee a good life for the dead in the land to which they were going. Characteristically, furniture, food, even slaves and concubines were supplied in picture or effigy. Prominent among the pictured goods were water fowl, the ordinary hosts of adult echinostomes. Hunting scenes in the Old Kingdom tombs at Saqqara show archers and net handlers taking wild fowl. Processions of gift-bearers include slaves holding ducks and other birds tied in bundles. Geese are prominent. The lid of a large wooden food box from a 19th century B.C. tomb, in the shape of a goose prepared for roasting, is exhibited in the Royal Museum in Edinburgh, along with a bowl of full-sized alabaster goose eggs and several small alabaster geese carved as having been plucked, stuffed and trussed for cooking. As mentioned before, wild fowl may have been plentiful in early times, as numerous hunting scenes in the tombs indicate. Therefore, if the sculptures and pictures fairly represent their subject, it may be assumed that these birds, including their echinostomes, were present.

Echinostomes in modern Egypt have only recently received attention. Jeyarasasingam *et al.* (24) described the life cycle of a new species, *Echinostoma liei*, showing that it is readily acquired by ducklings, *Rattus*

rattus, and *Crocidura olivieri* (an insectivore). Heyneman *et al.* (19) proved that the above trematode is capable of destroying schistosome larvae in mixed infections in snails. Chu *et al.* (22) studied seasonal fluctuation in cercariae coming from snails in a locality in the Nile Delta; they concluded that nature was "already exercising some biological control of *Schistosoma haematobium*, by means of echinostomes in one area in Egypt."

The purpose of this speculative essay is to urge a highly practical course — a new approach to controlling schistosomiasis in Egypt. Fluke control by flukes is a reality. It even may be working, effectively in Thailand, detectably in parts of the Nile Delta. The question of extending an intramolluscan control system to most of Egypt is answered in part by the arguments supporting the probability that such control did exist in ancient Egypt, where it depended on the prevalence of waterfowl. The following is an outline of how such control might be reinstituted.

First, a government sponsored program to encourage the rearing of ducks and geese should be started. Egypt depends on its farmers for economic prosperity. The development of a high-protein "cash crop", waterfowl, which could utilize some agricultural waste, and could be marketed easily in a protein-poor world, would benefit both the farmers' and the nation's economy. Even if the economic benefits were not great, such a program, if it brought the expected health benefits, would be less expensive than most imaginable public health efforts to control schistosomiasis. Ducks and geese, if they were allowed to feed on the vegetation and small invertebrates of the ditches and canals, would have a double effect on schistosomes. They would not only spread the competing echinostomes, but would also feed, as their ancient prototype in Egypt did, upon schistosome-bearing snails. Snail control would be an effective by-product of raising ducks and geese.

If the above results did not occur naturally from the planned increase in waterfowl with their echinostome parasites, the program could be augmented by deliberately seeding the waters with laboratory-produced echinostome eggs. This was done successfully by Lie and Ow-Yang (8) in Malaysia. The experiment showed that relatively light applications resulted in high infection rates for snails, with almost total elimination of the competing schistosome sporocysts. Lie (6) points out that heavy infections of echinostomes in snails are apt to cause considerable decreases in snail populations. This fact should be considered in any control program which aims at a steady balance among waterfowl, echinostomes, and snails.

Of course, echinostomes have a deleterious effect upon geese and ducks. Light infections such as usually occur are relatively harmless, however, and would probably produce no noticeable symptoms. The economic loss would not be great.

Maintenance of the control systems should become automatic. A natural balance among the hosts and parasites should persist, as I think it did in ancient Egypt. Human schistosomiasis would be reduced both in frequency and in intensity of infection. Public health agencies could steadily work through diagnosis and treatment of infected persons to lower the rate of contamination of the water with schistosome eggs. Eventually, with various drugs now known to be effective against schistosomiasis, the human disease might be eliminated.

There remains the problem of reservoir hosts. Ferguson (23) believes that there are few natural reservoirs of *S. haematobium* or *S. mansoni.* While troops of baboons which frequent lake shores have been found to be sometimes heavily infected with schistosomes, the possibility of human sources of these infections cannot be ruled out. Many kinds of rodents, including the common field rat of Egypt, *Arvicanthis niloticus*, can be infected in the laboratory, but naturally acquired schistosomes rarely occur in such animals. Since the proposed program area could not be quarantined against immigration or visitation from schistosome infested areas, human immigrants or visitors would fit the role of reservoir hosts by reintroducing the parasite into cleared areas. Thus public health maintenance of the program through diagnosis and treatment would have to deal with such human reservoirs. The search for animal reservoir hosts ought to be continued. But I think animal reservoirs would be irrelevant in a situation where the parasites themselves are under control. Human and animal hosts would be protected equally.

The proposed plan, of course, is necessarily imperfect. It cannot be considered an ideal solution to the problem of schistosomiasis, even in Egypt. Ideal solutions might be the following. First, a cheap, non-toxic, highly effective drug, usable for mass treatment, would be very desirable. Second, a specific, discriminating, cheap and easy-to-administer molluscicide might be considered an ideal. Third, immunological resistance through inoculation would be a desirable method of eradication or control. Yet none of these ideal remedies exists. Certainly the real possibility that one or more of these solutions will be found should not stand in the way of reasonable attempts at interim restraint of schistosomiasis. "The best (method) should not be the enemy of the good."

The pros and cons of the proposed program can be summarized as follows. In favor are the arguments that natural control of schistosomes by snail predation and intramolluscan competition exist today, as Lie and others have shown, and that they probably existed in Egypt during dynastic times. Favorable, too, is the economic soundness of stimulating the production of domestic ducks and geese along the canals and drainage ditches of the Nile Valley. Also, the proposal is ecologically sound, as it tends to restore faunistic balance to an agriculture that is rather specialized. Only three objections can be raised, in my opinion. One is that disease caused by echinostomes might become a medical threat to man. Another, through their effect on fowl, echinostomes could limit the economic productivity of the proposed program. A third objection is that the proposed method might not work. The first objection, based on human health considerations, I believe is trivial. Zoonotic disease acquirable only by eating raw snails can be easily prevented, or, if contracted, treated. Possible production loss from echinostomiasis in fowl is far outweighed by the health benefits from an even moderately successful program of schistosomiasis control. The third objection seems overly pessimistic. At a time like the present, when schistosomiasis is an increasing threat to human health nearly everywhere in the developing tropics, and when neither mass treatment nor snail-eradication appears feasible, with preventive inoculation a still more distant hope, any reasonable suggestion for other methods of alleviation or control ought to be considered.

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