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EXPERIENCE FROM ROCKEFELLER FOUNDATION STUDIES ON THE CONTROL OF HOOKWORM

K.S. Warren
The Rockefeller Foundation
New York, USA

The first great attempt at control of a major helminth infection globally was initiated by the Rockefeller Foundation at the time of its birth in 1913. The Rockefeller Sanitary Commission, which had been working on the control of hookworm in the southern United States, was merged with the Foundation and christened the International Health Board. The leader of this organization, Wickliffe Rose, immediately conceived of the idea of extending the work of eradicating hookworm infection. As stated by Fosdick in his History of the Rockefeller Foundation, "In the years that followed, Rose's daring enterprise was extended to 52 countries, "six continents and to twenty-nine islands of the seas" (Fosdick, 1985). As the work of the International Health Board developed around the world, it became customary in heavily infected tropical countries to dispense with individual examinations, and the people were treated en masse without preliminary diagnosis. The plan was first tried out in Japan and elsewhere in the Dutch East Indies, and was later put to extensive use in India and Siam. The primary reason for the adoption of this practice was the growing belief that in hookworm control the essential thing was not so much to aim at the absolute cure of every infected person in the community as it was quickly to remove the largest possible number of worms from the largest possible number of people, and thus to lower the severity of infection. But even this theory yielded to later ideas as new evidence was obtained. Fosdick, a lawyer, then observed,

> In the earlier days, Rose and his associates spoke of the eradication of hookworm; the original Rockefeller Sanitary Commission used that word in its title. It is a goal that has never been reached. Social patterns and habits cannot be changed overnight, and discouraging reinfestation can occur where adequate sanitary arrangements are not maintained. Moreover, as the years went by, it began to be clear that there was a distinction between hookworm disease and a comparatively harmless hookworm infection. Laboratory investigation proved that people with a limited number of hookworms are not necessarily ill.

To understand this crucial statement it is necessary to be familiar with the life cycle of the human hookworms, *Ancylostoma duodenale* and *Necator americanus*. Larvae hatch from eggs in faeces deposited onto soil. After two moults, the larvae are infective for humans and are able to penetrate the skin within five to ten minutes. The larvae are then conducted by the circulatory system to the lungs, make their way through the alveolar walls to the bronchi and trachea and are carried with the swallowed secretions to their final habitat in the small intestine. Two further moults occur in the intestine before the parasites reach maturity and start egg production (four to six weeks after skin penetration).

The adult worms measure 5 to 13 mm in length and are found largely in the jejunum, where they attach to the mucosa by toothlike structures. Blood and mucosal substances are ingested, and much of this material is excreted. The average blood loss and egg output in A. duodenale infection (0.15 ml of blood per worm per day; 25,000 eggs per worm per day) are several times greater than in N. americanus infections (0.03 ml of blood per worm per day; 7000 eggs per worm per day). Hookworms do not multiply within the human host, and the average lifespan of N. americanus is reportedly two to six years; that of A. duodenale is supposedly shorter (Lozoff et al., 1978).

Although hookworm infection exists with the establishment of a single worm in the body, hookworm disease occurs only when infection is heavy enough to result in clinical manifestations. The majority of people with hookworm have light infections without disease. For instance, in Venezuela 726 of 796 individuals (91%) with N. americanus infections had low egg counts and no anaemia. Only egg counts of greater that 2,000 x gm of faeces in women and children or greater than 5,000 x gm of faeces in men were associated with anemia. The only clinically significant consequences of chronic heavy hookworm infection are iron deficiency anaemia and occasionally hypoalbuminaemia (Lozoff et al., 1978).

Most of these facts were known early in the Rockefeller Foundation hookworm campaign and were used to develop an optimal, cost-effective means of control. This was clearly described by Wilson G Smillie in 1924. In a paper in the Southern Medical Journal he noted that, in approaching the control of hookworm disease in south Alabama, he was influenced in part by observations that had previously been made in Brazil. These included (Smillie, 1924):

> A distinction must be made between hookworm infection and hookworm disease. Light hookworm infection may be and commonly is acquired casually by all classes of people in a zone infected with hookworms. Actual hookworm disease, that is, an infection which is severe enough to be of real harm to the individual, occurs only in that group of individuals in the infected area whose bare skin has long and continuous contact with infected soil.
>
> Massive infection from a single or occasional exposure to hookworm infected soil is rare.
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> Hookworm infection is slowly acquired and slowly lost. Thus a severe degree of infection is rare in a child under five years of age, and even in a heavily infected zone. The number of hookworms harboured by a child does not increase and decrease with each season, but increases gradually in number year by year. As a rule, therefore, the older the child, the heavier the infection.

Smillie then noted that only a small proportion of town dwellers are infected with hookworm and the average number of worms harboured is small. In rural areas adults, who usually wear shoes, rarely show hookworm disease (Smillie, 1924).

> Hookworm disease, that is, an infection which is severe enough and widespread enough to be an important economic factor in the lives of the people, should be found almost exclusively in the rural children of school age (6-16 years) because their bare feet are almost continually exposed to hookworm infected soil throughout the warm season of the year.

This was shown by large numbers of egg and worm counts. Thus, the disease may be controlled by devoting our attention to this age and class group (Smillie, 1924).

> It is true that sanitation alone will control hookworm disease. But this method is extremely slow. To be effective, at least 80% of the rural homes and all the rural schools must have sanitary toilets, and these must be used. This necessitates a changing of habits and customs of a lifetime and can scarcely be accomplished in a decade.

Hookworm disease can best be controlled by mass treatment of the heavily infected group of individuals. One single treatment of the rural school children will reduce the actual number of worms harboured by more than 90 per cent. New infection is slowly acquired. The children are relieved immediately of the great burden they have been carrying and sanitary measures can be undertaken to prevent reinfection.

Finally, Smillie noted, "We may establish the axiom that hookworm treatment should be used to control hookworm disease; the infection rate is controlled by sanitation." (Smillie, 1924).

This targeting of treatment and use of single doses to reduce drastically the intensity of infection rather than multiple doses to achieve a cure is particularly poignant in that the treatment of choice for hookworm in 1925 was carbon tetrachloride. Smillie observed that it is not only unnecessary but fruitless to attempt to treat all cases to a cure. One treatment will remove most of the worms, and "it will be necessary to re-treat children of school age every two or three years until sanitation is well-established. As sanitary toilets are installed in the rural district, the hookworm infection rate will gradually decrease. When the infection rate of the rural school children reaches 25%, there will be no hookworm disease in the community and hookworm treatment may be entirely stopped" (Smillie, 1924).

It seems that this rational approach described in 1924 and based on knowledge of the biology and epidemiology of the parasite was not universally understood or adopted. There was great disagreement with Smillie's approach even at the time. When similar strategies were developed for schistosomiasis almost 50 years later, the concept was essentially rediscovered and underwent the same criticisms. Now the World Health Organization has specifically adopted a strategy of disease control for schistosomiasis targeted at high risk/high intensity of infection groups (WHO, 1985). It is somewhat ironic too realize that the switch from blanket mass immunization to surveillance and containment has led to the eradication of smallpox.

This brings us to a new association of the Rockefeller Foundation with hookworm in its present Great Neglected Diseases of Mankind programme devoted to bringing state-of-the-art modern science to the study of the major diseases of the developing world. At Rockefeller University, Mr Peter Hotez, a graduate student in Dr Anthony Cerami's laboratories, has isolated an anti-coagulant from hookworms, purified and characterized it chemically, done preliminary testing by injecting it into dogs to determine whether it induces protective immunity against canine hookworm, cloned the gene for it in bacterial vectors in Dr Nina Agabian's laboratories and sequenced it (Hotez et al., 1985). Further studies are being performed to see if the large quantities of antigen now available will function as a vaccine for hookworm. Then, its back to biology and epidemiology to determine optimal use of such a putative vaccine or others that may be produced in the great age of biotechnology, if only scientists will consider hookworm, still an infection of 800 million people, to be worthy of their interest.

REFERENCES

Fosdick, R.B. (1985) The Story of the Rockefeller Foundation. Harper, New York

Hotez, P.J., Letrang, N., McKerrow, J.H., & Cerami, A. (1985) Isolation and characterization of a proteolytic enzyme from the adult hookworm Ancylostoma caninum. Journal of Biological Chemistry, 260: 7343-7348

Lozoff, B., Warren, K.S., Mahmoud, A.A.F. (1978) Hookworm. In: Geographic Medicine for the Practitioner, Warren, K.S. & Mahmoud, A.A.F. (eds). University/Chicago Press, pp 102-105

Smillie, W.G. (1924) Control of hookworm disease in South Alabama, Southern Medical Journal, 17: 494-499

World Health Organization (1985) The Control of Schistosomiasis. Report of a WHO Expert Committee. Technical Report Series, 728, Geneva