

## RECENT ADVANCES IN KNOWLEDGE OF SOIL-TRANSMITTED HELMINTHS

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### ABSTRACT

New observations in recent years have accentuated differences between the two common hookworms, *Ancylostoma duodenale* and *Necator americanus*, with respect to modes of transmission and pathogenicity, and have established *Ancylostoma ceylanicum* as a species distinct from *A. braziliense*. Transmammary and paratenic transmission are now considered to be natural modes of infection in *Ancylostoma caninum* and possibly in other *Ancylostoma* species including *A. duodenale*, but not in *Necator*. The question of relative blood losses from laceration hemorrhage and blood-sucking in hookworm anemia is unresolved. The prevalence of Loeffler's syndrome in pulmonary ascariasis appears to be greatest in areas where transmission is sharply seasonal. Recent studies have failed to confirm reports of blood-sucking by *Trichuris*. Milk-borne transmission from mother to the newborn has been demonstrated for numerous species of *Strongyloides* not including *S. stercoralis*. Zoonotic soil-transmitted helminths of dogs and cats have become recognized as frequently causing visceral larva migrans and occasionally blindness in most parts of the world. Two major advances were made in diagnostic techniques — the Harada-Mori test-tube hookworm culture for species diagnosis and the Kato cellophane-covered thick fecal film for rapid and quantitative diagnosis of intestinal helminth infections.

### INTRODUCTION

The term "soil-transmitted helminths" came into common use in the early 1960's. At that time the World Health Organisation, Division of Communicable Diseases, under the leadership of Dr. N. Ansari was initiating plans for pilot projects for the control of ascariasis.

It was barely more than 10 years ago, in August of 1963, that the first

WHO Expert Committee on Soil-transmitted Helminths met, in Rio de Janeiro, just ahead of the 7th International Congresses on Tropical Medicine and Malaria. One year later, in September (21-26) 1964, the 1st International Congress of Parasitology was held, in Rome. Neither of these international congresses had a separate section for soil-transmitted helminths, but the three meetings collectively stand as an important milestone, as a very large number of review papers and original reports were contributed on different aspects of the biology, pathology, immunology, epidemiology, and control of the soil-transmitted helminths of man. For the WHO Expert Committee meeting alone there were 70 papers submitted as working documents. For the present meeting, I thought it would be of interest to review some of the newer observations on soil-transmitted helminths which have added significantly to the knowledge of 10 years ago. I am going to limit the review primarily to hookworms but will include some remarks about *Ascaris*, *Trichuris*, *Strongyloides*, and *Toxocara*. (There can be some doubt about including *Strongyloides stercoralis* in the soil-transmitted group. It might better be regarded as being transmitted through standing bodies of surface water, or through unfresh feces. Unlike those of hookworms, the larvae of *Strongyloides* species readily develop to infective stage larvae in the fecal mass and when placed in water both the free-living adults and larvae swim and thrive, whereas hookworm larvae in all stages of development fall to the bottom and drown, except at very shallow depths. As a matter of fact, the mode of transmission on which *Strongyloides* endemicity is most dependent remains to be identified for any local or general endemic area).

### THE HOOKWORMS

The most notable advances in the knowledge of hookworms have been made in the area of basic biology. At the International Congresses in Rio de Janeiro I recall that there was sharp disagreement on the question of modes of infection. Some could not accept that *Ancylostoma duodenale* larvae are infective by mouth. Further observations now leave no doubt that, whereas *Ancylostoma duodenale* larvae can infect either by mouth or percutaneously, *Necator* can infect by the percutaneous route only. It has been shown, moreover, that *Necator* larvae on reaching the lungs remain in the pulmonary tissues for several days where there is essential growth and development, whereas *Ancylostoma duodenale*, and all other species of *Ancylostoma* yet studied, pass through the lungs with little or no appreciable change and undergo corresponding developmental changes in the tissues of the small intestine. These facts have become established largely through observations on young dogs and human volunteers by Japanese workers (1, 2, 3).

As regards the species of *Ancylostoma*, many workers were reluctant to accept that for several decades they or others had done extensive research

on *Ancylostoma tubaeforme* of the cat believing that it was *Ancylostoma caninum*, and on *Ancylostoma ceylanicum* believing that it was *Ancylostoma braziliense*. It was Burrows who in 1962 recognized the distinct morphology of *A. tubaeforme* in the United States and removed it from synonymy with *A. caninum* (4). Similarly, Biocca in 1951 had redescribed *A. ceylanicum* and *A. braziliense* and given them distinct taxonomic states (5). Even after morphological differences were clearly and specifically pointed out by Biocca, some workers continued to publish reports on *A. ceylanicum* calling it *A. braziliense*. Recently, however, these workers have become convinced that the two are distinct species and that *A. ceylanicum* readily develops in man as well as in dogs and cats, whereas *A. braziliense* develops to the adult stage in the intestine of cats and dogs (6), while in man and small mammals it remains in the larval stage, and of all the known hookworm species it is the most prone to cause creeping eruption. Its behavior in this respect appears to be related to its adaption for transmission through paratenic hosts (2). Norris (7) found that a Florida strain of *A. braziliense* in mice tended to remain in hair follicles for long periods before moving on to the deeper tissues and he interpreted the long persistence in the issues of rodents (and man) as an adaptation for transmission by paratenesis.

The phenomenon of paratenesis is still not clearly understood, at least not as it applies to the hookworms. There appears to be a relationship between transmission from final host to final host through paratenic hosts, and transmission from the final host to the newborn offspring through the milk. Transmammary transmission of hookworm infection from mother to offspring was discovered by Olsen and Lyons in the early 1960's but was not fully described by them until 1965 (8). What they discovered was that in the Alaskan fur seal a hookworm, *Uncinaria lucasi* Stiles, 1901 occurs in the intestine of essentially all newborn pups, reaching maturity and producing eggs in 13 to 15 days, but in the adult seals only larvae are found, and that these are acquired percutaneously only and reside in the fat tissue and mammary glands until the young are born the following year. Larvae were demonstrated in the colostrum and milk. Following this demonstration, milk-borne infection has been reported for *Strongyloides ransomi* in the domestic pig (9); for *Ancylostoma caninum* in the dog (10); for *Toxocara canis* in the dog (11, 12); for *Strongyloides westeri* in the horse (13); for *Neoascaris vitulorum* in the cow (14); for *Strongyloides papillosus* in sheep and cattle (15); and for *Toxocara cati* in the domestic cat (16). In all of these examples except *Toxocara canis*, milk-borne infection may be the chief and possibly the only mode of infection, depending in the case of *T. cati* and of *A. caninum* on the circumstances which favor, or not, transfer through paratenic hosts.

In this connection, studies in progress in my own laboratory in collaboration with M.D. Little and K.T. Lee I believe will be of interest.

From the studies of Matsusaki (17) and Nichols (18) it was known that

the third-stage larvae of *Ancylostoma caninum* could persist in the tissues of rodents for more than a year. Several workers have also reported that, in rodents, after either cutaneous or oral infection *A. caninum* larvae migrate to and persist in the carcass. However, the exact location of the larvae and the type of tissue reaction induced by them were not studied.

About a year ago we investigated these two points (19). We found that in mice infected percutaneously with 500 to 1000 larvae each, larvae were present in muscles as early as 4 hours and persisted for at least 9 months. During the first few days they were found mostly near the site of penetration, but by 20 days they were nearly evenly distributed in muscles throughout the body. It was found too that the larvae were actually located within individual muscle fibers and that they caused essentially no tissue reaction. Following these findings we wanted to know whether *A. caninum* larvae would behave similarly in mammals other than rodents. A cat and a rhesus monkey were infected by the cutaneous route and at 16 and 17 days post-infection, respectively, larvae were likewise found within the muscle fibers. In a study just completed we found that this occurs also in the normal definitive host, the dog.

A phenomenon of great interest and possibly related to the persistence of larvae in the muscles is the high prevalence of very light human hookworm infections in certain areas where heavy infections are rarely seen. Surveys of populations in Pakistan and India have shown infection rates above 30% with few or none of the infections exceeding 2 eggs per milligram of feces (20). While investigating such a population in West Bengal, India, Schad and colleagues observed that egg-counts varied but little from season to season, being generally low with mean counts between 2 and 3 eggs per milligram (21). The interesting observation was that the lowest average level of infection occurred in February and March, 3 to 4 months after the end of the rainy season, which was more or less to be expected, but the surprising finding was that the egg-counts showed a sharp increase in April and May just before the season of transmission, at the onset of the rainy season. Schad interpreted this to indicate that the *Ancylostoma duodenale* larvae "acquired during the rainy season of one year remain dormant until just before the monsoon of the following year, when they resume development and mature."

Additional evidence of long-delayed development of *A. duodenale* was provided by an experimental infection in a human volunteer. About 230 larvae were placed on the skin on the 24th of June. At 22 weeks after exposure, stools were still negative and it was thought that the infection had failed. It was noted, however, that evidences of skin penetration were seen immediately after exposure and evidences of lung migration in the form of cough and pharyngitis were noted at 7 to 14 days. Eggs of *A. duodenale* may appear in the feces as early as 38 days after exposure. In this case, however, eggs were first found in the feces at 9 months, and during the next 3 months the counts increased to 5 per milligram. In a second volunteer the prepatent period also

was long — about 10 months (22). Parasitologists will be eager to have these observations confirmed and interpreted. A comparable rise in egg-output just prior to the season of transmission has been documented for certain trichostrongyles in sheep (the so-called “spring rise” in egg-counts) (23).

People who raise dogs are familiar with a disease of puppies referred to as “cotton mouth.” The term is derived from the appearance of the mucous membranes of the mouth and is an indication of profound anemia. The reason for bringing it into the discussion here, of course, is that the anemia of cotton mouth is caused by the dog hookworm, *A. caninum*. It is also caused by experimental infections of *A. braziliense* in young puppies, as described in several recent papers (24, 25, 26). Post-mortem examination of pups dying from cotton mouth disease will readily demonstrate that the blood losses are caused by hookworms. Close examination of the gut mucosa and of the worms themselves has led different observers to different and almost opposing interpretations of how the blood is lost (27). Impressed by the conspicuous presence of blood in the gut of some of the hookworms, and recalling Wells’ (28) dramatic demonstrations of blood flowing in measured amounts from the anus of hookworms (0.20 ml/day), and Roche’s even more dramatic illustrations of hookworms sucking blood, and expelling a great cloud of blood from the anus (29), some observers have readily concluded that the worms’ blood-sucking alone could account for the fatal blood losses. This interpretation has been challenged, however, and in one of my own studies the conclusion was reached that most of the blood seen in the lumen of the host’s gut came from bleeding mucosal lacerations, not from pumping of blood through the gut of the worm (30). The argument does not rest on the question of whether or not blood is passed through the hookworm’s gut. Though the amounts may be relatively trivial, some blood is taken from the mucosa of the host’s gut, passed through the gut of the worm, and expelled from the anus into the lumen. The central issue is whether observations made on the quantities of lost blood and the resulting anemia can be attributed to the worms’ blood sucking.

Direct examination of the opened intestine will confirm that the blood expelled in the feces of a heavily infected dog came from the small intestine. Always in such cases it will be evident that the mucosa is severely and extensively lacerated. The degree of laceration and the amount of bleeding from the mucosa will depend very largely on the age of the infection and the degree of crowding; the degree of crowding depends largely on the distribution as well as the numbers of worms in the intestine; and, the distribution of the worms in the first month or so of infection will depend on the mating activity of the worms.

In giving experimental infections to dogs there is a tendency to use relatively heavy inoculations. Rep (25), for example, in studies on blood loss and some other aspects of infection, gave pups weighing only 4 kilograms 10,000 infective larvae. Krupp (31) found clear evidence of a crowding effect

in heavy *A. caninum* infections, with some of the worms being displaced and forced into the colon when only 250 larvae were given by oral inoculation to 2- to 3-month old pups weighing 6 kg or less. It was shown in Krupp's experiments that, as would logically be expected, there is an optimum zone preferred by the worms, but there is also a space requirement ("lebensraum") which can only be satisfied by movement to suboptimal levels of the intestine. Shifting of the worms as they increase in size and reach successive stages of development, and expansion of the populated area as greater space is required by the maturing worms, was not documented in the study referred to (31), but observations on blood-loss as measured by isotope techniques do reflect this in two ways. First, blood-losses generally are more clearly attributable to worms when there is an appreciable degree of crowding. Second, when blood-losses are measured daily during the first 5 or 6 weeks of infection, there are distinct periods of 2 or 3 days during which blood-losses are markedly increased. In experiments by Miller (32) on *A. caninum*, for example, peak losses occurred at 13 to 15 days and again 10 days later. Roche and Layrisse (20) reported peaks at 12 days and 18 days. Rep (26) found that with *A. ceylanicum* in dogs, eggs first appeared in the feces as early as the 15th day and blood-losses were generally high for several days just before that time, and again later. In all such studies thus far reviewed, the peak blood-losses appear to correspond to the first two periods of mating. In some, there is an earlier period of loss which appears to correspond to a period of growth and maturation when the worms begin to require more space and respond to crowding by moving away from each other.

The first observations on mating in relation to blood loss were reported just 10 years ago (30). The studies were done on *A. caninum* in the dog. There is no reason to doubt that the findings apply to other species in other hosts, including *Necator* and *Ancylostoma* species in man. It was found that when sexes were balanced there was relatively little blood loss, except in the early period when the worms were crowded and mating was synchronous, i.e., when all worms reached maturity at about the same time and therefore all were moving about and mating in a disorderly and determined manner. Later, in balanced sexed infections, as the mating became less synchronous the peak periods of blood-loss gradually disappeared. Unisexual female infections caused greater blood loss than did all-male infections. Also, when the sexes were unbalanced, blood losses were relatively great, especially when males were in excess; ten or more males may be attracted to one ready-to-mate female.

In all of the above situations the blood flow from the tissues to the gut lumen was mainly through lacerations caused by the crowded and sexually aroused worms. In the discussion of these findings, a statement was made that was unacceptable to some of the readers then, and probably seems incredible to some even today. The statement was "... it is noteworthy that in most of the experimental infections a high proportion of the worms were unattached

to the mucosa, and even when attached relatively few of them had a visible amount of blood in the intestine. These conditions have been noticed also in natural infections (by Clark et al., 1961) (22). It may now be questioned whether hookworms actually suck blood to meet their physiological needs. The fact that the hookworm secretes an anticoagulant substance in the amphidial glands, as Thorson (1956) (34) has shown [also Eiff (35) and Spellman and Nossell (36)], may only indicate that this substance is used to prevent clotting of blood that is unavoidably swallowed and passed through the worm's intestine when it attaches itself at a newly lacerated point on the highly vascular intestinal mucosa." In citing or reviewing Wells' report (28), authors usually fail to mention that in 4 out of a series of 20 dogs he noted that "practically all the worms observed on each host were obviously much less active as regards blood sucking and blood ejection than the majority of worms in the other hosts of the series, and periods of complete inactivity were frequent and prolonged." He also reported that "worms will move about for hours without attaching themselves."

I have given the hookworms more time than can be given the other soil-transmitted helminths. Hookworms are, of course, important as a cause of disease in many parts of the world including Iran. They also as a group offer opportunities for interesting and useful research. Much of what is taken for granted about the hookworms has no firm scientific foundation and needs to be investigated. There is, for example, a general acceptance of the idea that a man and his parasites are engaged in a constant battle against each other. A healthy, well-nourished man can, in that view, cast off his parasites or at least reduce the worm population to a tolerable level. On the other hand, it is generally expected that a poorly nourished man, unable to cast off his parasites, can be easily overburdened with large numbers of worms that are able to overpower his defenses. When this concept was put to a test by correcting the malnourished state of 12 subjects with moderate to heavy hookworm infections (15 to 200 eggs per mg), the egg counts remained at the same level after repletion as before in all but one subject (37). In three whose blood losses were measured, the amounts after treatment were slightly less in one who harbored 475 worms, but sharply increased in the two others whose worm populations were 1217 and 2380, respectively. No worms were expelled in the feces during the period of repletion. These results were unexpected.

### *ASCARIS*

Among the recent reports on ascariasis, I would mention first a report that clarifies and confirms an observation made here in Iran during my first visit, in 1962. Biocca had just reported an extensive survey in Isfahan and had found *Ascaris* and *Trichostrongylus* infections extremely prevalent (38). In one section of the city, *Ascaris* was found in nearly 100% of all age groups. In

view of earlier findings by Vogel and Minning (39) demonstrating that as few as six larvae of *Ascaris lumbricoides* could cause Loeffler's syndrome in human volunteers, I was impressed with the apparent absence of Loeffler's syndrome in Isfahan. There was at that time also a recent report of hyper eosinophilia caused by a trichostrongyle infection (40). Eosinophilia was said to be uncommon in Isfahan and very high levels of eosinophilia were rarely seen.

Vogel and Mining's findings (39) were substantiated by a study by Gelpi and Mustafa (41) in which it was shown that in an area where transmission of ascariasis was limited to a brief annual rainy season of only 1 month or less numerous cases of severe pulmonary ascariasis were seen at that time. It appeared, therefore, that pulmonary ascariasis in the form of Loeffler's syndrome would be found only in areas where transmission was discontinuous and restricted to a relatively short period as it is in regions with a long winter or long dry season. A study by Spillmann (42), just completed in Colombia, has shown that in that region where ascariasis prevalence rates are high and transmission is more or less continuous throughout the year, as in Isfahan, Loeffler's syndrome is rare in both urban and rural communities. A screening program covering 12,000 clinic patients, 700 hospital patients, and 44 families with 328 members over a period of more than a year, detected only three cases of Loeffler's syndrome that possibly were caused by pulmonary ascariasis. Thus the conditions which favor tolerance of *Ascaris* larvae in the lungs, or produce a Loeffler's type of reaction, are beginning to be known and the knowledge will be useful in studies on pathogenesis and other aspects of the infection.

## TRICHURIS

There has been recent interest in the attachment and feeding habits of whipworms. The species of *Trichuris* found in the mouse, the dog, the pig, and man have all been described as inserting the thread-like anterior end of the body into the mucosal epithelium, only to the depth of the basement membrane of the epithelial cells. At the thicker levels of the esophageal region the worm induces the epithelial cells to form an expanded sleeve-like tunnel which holds the body firmly against the lamina propria. This relationship, along with the fact that the worm's esophagus is extremely narrow, makes blood-sucking and blood losses in significant amounts unlikely. Nevertheless, Burrows and Lillis (43) believed they saw blood in a whipworm, and a study was done by others to measure the amount of loss per worm (44). Two attempts to confirm the latter finding have failed (45, 46).

A most welcome recent development in regard to whipworms is the discovery of a drug, mebendazole, that is effective in removing them. Thus far it seems to be essentially non-toxic, differing in this respect from dithiazanine and others that were briefly popular (47).



## *STRONGYLOIDES*

It was mentioned already that milk-borne transmission has been described in several species of nematodes including *Strongyloides ransomi* found in pigs (9), *S. papillosus* of cattle and sheep (15), and *S. westeri* of horses (13). Other observations of interest are that the *Strongyloides* species found in African monkeys, *S. fuelleborni*, occurs commonly in humans in West, Central and East Africa, having been recorded in one report in 606 out of 4,577 people in 36 out of 45 communities surveyed. The prevalence rates range up to 30 percent where, in addition to transmission to man from monkeys and apes by fecal contamination of the environment, there apparently is true endemicity with man-to-man transmission (48). The prepatent period in an experimental infection in man was 28 days, which is longer than expected, and clinical signs were noted in the skin at the site of entry and in the lungs and intestine. Eosinophilia reached 48% at 7 weeks of infection (49). These observations and similar earlier reports point out the importance of accurate identification of *Strongyloides* species. From studies by Little (50,51), it is clear that this requires more knowledge and skill than can be expected of medical technologists. As in the case of *Trichuris*, there is now available a good safe anthelmintic, thiabendazole. This is of particular interest because the infection if untreated in patients on immunosuppressive drugs can be fatal (52).

## *TOXOCARA*

No new basic information has been published on *Toxocara* or visceral larva migrans (VLM) for several years. Case reports now emphasize the frequency of invasion of the eye and the presence of newly discovered infection in areas of enzooticity. Though many people are doubtful about the values of serological tests, and even more doubtful about skin tests for *Toxocara* infection, we can note with satisfaction that the epidemiological studies of Professor Woodruff (53) have had great value in calling attention to the need for community efforts to control soil contamination in public parks and play areas of towns and cities. In spite of numerous efforts to persuade parasitologists and others that the behavior of *Toxocara* larvae in humans is not that of an unnatural parasite in an abnormal host, the concept persists. The phenomenon of paratenesis seems to be gaining acceptance, but it is still somewhat unusual to see a report on VLM that does not in one way or other incorrectly stress the abnormal host-parasite relationship. From this I would further stress a point that I have been stressing for some years concerning host responses to parasites. The VLM studies led into the problem of diagnosing parasites in tissue sections, and this has been a major effort in parasitology laboratories for about 25 years. Early in this program we were repeatedly impressed by the striking fact that, although many of the host reactions can be recognized

as non-specific, especially the reaction to dead or drying helminths, every tissue-dwelling helminth, larva or adult, induces the host to react in a specific way, causing the host's cells and tissues to differentiate, as in embryological development, a structure that can be recognized as a specific characteristic of the parasite — and as clearly so as are the bursal rays or the cephalic papillae. This was a central theme of a recent review paper on "The nature of visceral larva migrans" (54). It has seemed to me that, like paratenesis, this admirable characteristic of well-adapted parasites is not enough appreciated and admired.

## DIAGNOSIS

The diagnosis of the three main soil-transmitted helminth infections—ascariasis, trichuriasis, and ancylostomiasis or necatoriasis — still rests as always on the detection and recognition of the characteristic eggs in the feces. For appraisal of clinical or public health significance of the infections estimates of worm burden are essential, and the only known practical way of making such estimates is by determining the egg-output in the feces. Inexperienced workers sometimes doubt the validity of the assumption that egg output can be interpreted in terms of worm burden, and there are a few clinical and public health workers who assert that any worms at all are bad and even one worm should in all circumstances be expelled, and any worm species causing even a few light infections in a community should be eradicated. Generally, however, it is accepted that egg-counts are meaningful to both clinical and public health workers.

The question to be debated always is how shall the egg-counts be made? By which technique must the eggs be counted? The choice itself, of course, is less important than is the skill and will of the technician doing the counts. At times, as during one session of the Expert Committee meeting in Rio de Janeiro, this may be overlooked and questions having no foundation are argued. Two questions which do have foundation are: first, are eggs randomly distributed in the feces? Second, if estimates of egg-output are reliable do they in fact indicate the number of worms in the intestine?

The first question was answered to my own satisfaction when I found that estimates based on 2-mg samples are as reliable as are those based on much larger samples (55,56). The question was answered more conclusively later by Martin, in a study designed specifically to examine the question of randomness (57). His work gave conclusive results on several points. First, small particles swallowed in food or liquids are randomly dispersed in the feces; second, ingested particles remain in the intestine on the average for 3 days; and third, the colon treats the three meals of a day as if all were taken at one time. A fourth interesting finding is that of all the particles entering the small intestine in one day, 15% to 25% will be passed in the stool of the

following day (in 24 hours), 40% to 60% the second day, and the remainder in the 3rd, 4th, and 5th days. However, up to 10% may be passed in the 5th day's stool and appreciable numbers may be evacuated as late as the 10th day. To be aware of the fact that the age of eggs of hookworms, *Ascaris* and *Trichuris* when seen in a fresh fecal sample vary as much as 10 days may assist someone in answering or in seeing an important question. The idea that eggs held in the colon by constipation may develop to a relatively more advanced stage can be discarded in light of this information.

A major advance in the technique of fecal examination for intestinal nematode parasites was made by Kato, who discovered that eggs could be easily found and diagnosed in a thick fecal film spread under a cellophane cover soaked in glycerine (58). In such a preparation the feces become clear, whereas the eggs do not and therefore are made conspicuous. The original Kato technique was adapted and modified slightly for a large scale survey in Japan (59), and Martin and Beaver (60) improved and standardized it for making egg counts in the quantitative diagnosis of *Schistosoma mansoni* as well as for the common intestinal nematodes. The Kato thick smear is now the technique of choice for the qualitative and quantitative diagnosis of most species of common intestinal helminths, and for some kinds of studies on *Schistosoma mansoni*.

One other advance in diagnosis should be mentioned. As the different species of hookworms cannot be reliably distinguished from one another on the basis of egg morphology whereas it is relatively easy to diagnose the 3rd-stage larvae of *Necator* and *Ancylostoma*, it has been extremely helpful to have a clean, simple, reliable method of culturing the larvae. The test-tube filter paper method developed by Harada and Mori in 1955 (61) was improved and redescribed by Hsieh in 1963 (62) and by Beaver and others in 1964 (63). Hsieh and others recently made extensive practical use of the Harada-Mori culture in determining the distribution of *Necator americanus* and *Ancylostoma duodenale* in Liberia (64).

As was stated already, a series of international meetings in the early 1960's marked the beginning of new interest in the soil-transmitted helminths. Some of the information on which the report of the WHO Expert Committee on Soil-transmitted Helminths was based came from surveys of intestinal helminths in Iran. The report stated that "...relatively high rates of hookworm infection are found in the Caspian region..., *Trichostrongylus* infection appears to be particularly common in parts of Iran, and ascariasis rates are high even in many of the more arid parts of the country" (62). In the 10-year interim since that report was published much has been done here to control the diseases caused by the soil-transmitted helminths. Hopefully, the discussions of these problems at the present seminar will again stimulate new interest and accelerate the progress of control programs currently underway here.

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