

carefully observed, as any marked alteration either in the direction of slowing or quickening is an indication for ceasing administration for a time. With overdosage the pulse rate is increased and the respiration rate slowed, and therefore a watch should be kept on any disturbance of the ratio between the two. Usually there is at first some slowing of the pulse rate, probably from the previous excitement and subsequent quietude. When once the pulse rate has settled down, however, it should not alter greatly.

Unfortunately patients are very variable in their response to hyoscine; most of them conform to the type described—sleepy or drowsy between pains but roused by them. Some, however, may remain awake and yet be found afterwards to have complete amnesia, and others may become restless and troublesome. There is always considerable mental confusion, but unless it is associated with excitement and difficulty in controlling the patient, it is not an indication for interfering with the injections. Some degree of restlessness is usual in the early stage, before the complete effect of the drugs is obtained, but in occasional instances it may become very troublesome. It is an indication of overdosage with hyoscine, and may require further administration to be discontinued. A watch must be kept on the bladder, and if the patient is unable to empty it voluntarily the catheter must be passed. Thirst is always well marked and leads to frequent drinks being given. Food, usually liquid, must be given in all lengthy cases.

It will be clear from this general account of its administration that the amnesic narcosis calls for the continuous observation of the patient by a skilled nurse and constant attention by the practitioner in charge. The patient may appear quiet and yet wake up suddenly and, in her mental confusion, get up and wander about and do strange things—for example, hide herself or try to escape. No bowls of poisonous lotion should be left within easy reach, for thirst may drive her to sample the first fluid that comes to hand. Also, to get good results calls for experience in the method.

There are sundry modifications that make its partial use easier to those with little experience of it. Its effects are most valuable in the first stage of labour. In the second stage when the stronger expulsive pains and the distension of the outlet are likely to rouse the patient, resulting in her reconstructing the whole labour and making the induction a failure, it is often easier to fall back on a light general anaesthesia, especially once the outlet begins to gape and birth is imminent. If that is done, it may not be "twilight sleep," but amnesia is secured. Also, if the injections have been discontinued or the patient is out of control, chloroform anaesthesia may be induced—just sufficient to allow of a full examination being made—and if the os is not fully dilated or the head not deep in the pelvic cavity, another injection of morphine—a small dose, say 1/8 grain—may be given which will take effect before the general anaesthesia is recovered from.

The great objection to the routine adoption of this form of narcosis in labour is, to my mind, its undoubted effect in lessening the expulsive contractions of the uterus and voluntary bearing-down efforts, and thereby increasing the number of low forceps operations. The effect on the child—which appears to be almost entirely due to morphine—is of minor moment, as, though born apnoeic and disinclined to breathe, if left alone respiration will be established in a short time. The injection of pituitrin 1/2 c.cm. (that is, up to 5 units) will reduce the number of forceps deliveries, but leave them still above the average, as we found when the method was tried out in a series of cases not specially selected as suitable. The effects on the third stage are not noticeable. Hence my view is that both a careful selection of cases should be made and strict adherence to Gauss's method left to those with long experience of it.

Selection of Cases.

It is valuable for all patients in whom a long and tedious labour may be anticipated, particularly cases of slight disproportion between the head and pelvis, when a long time for moulding is essential. Many of these cases would be of the kind designated as "trial" labours, and

in them it is undoubtedly of great service in lessening fatigue; as soon as the head is well down further administration of hyoscine may be stopped and, if the patient delivers herself, a little chloroform given during the birth of the head. If delivery by forceps is required, anaesthesia is necessary. It is also useful in cardiac cases that have been under ante-natal treatment for decompensation, by lessening fatigue and strain during labour.

Apart from cases in which there is a cause or clear reason for avoiding fatigue, this method is adopted occasionally for cases in which the temperament or excitable state of the patient, especially if associated with a slow and erratic onset of labour, suggests it. It is often asked for by women who have either had a trying experience in a previous labour or have a great dread of what is before them and are without confidence in their unaided powers of going through it. It is always advisable in a medical school to select cases of this type now and then for instructional purposes, so as to keep nurses and students acquainted with the method.

SUMMARY.

Fatigue is of the mind as well as of the body, and is hastened and aggravated by continued pain without relief, by fear, and by loss of self-control, and is a potent factor in the production of inertia and other disorders of uterine function.

With experience on the part of doctors and nurses, success in obtaining amnesia will be attained in nearly three-quarters of the cases, and some relief in the remainder. A great saving of nervous strain is undoubtedly effected by this form of narcosis, but if carried through to the end it has the fatal objection of increasing intervention in labour. For that reason, save in a few special cases, such as I have indicated, I prefer to use morphine, with or without a sleeping draught, or the single initial injection of morphine and hyoscine as and when it seems to be required.

It will be clear that much patient study and observation is required before a solution is reached of the problem of how the relief of the pains of labour and the avoidance of fatigue and nervous strain can be secured without interfering with normal function. Much more must be done in exploring the causes of failure to complete a natural function among physically well-formed women, and so long as the artificial substitute of the forceps is acquiesced in, so long will obstetric practice fail to become saturated with the principles of preventive medicine.

EPIDEMIOLOGICAL OBSERVATIONS ON HOOKWORM INFECTION.

DISCUSSION OF THE QUESTION OF IMMUNITY AND SPECIFIC
REACTIONS OF THE HOST IN HELMINTHIC INFECTION.*

BY

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At the invitation of the Government of the Argentine, two years ago, I had, together with Dr. Roberto Dios and Juan Zuccarini, the opportunity of studying the hookworm question in the northern departments of the province of Corrientes, immediately adjacent to Paraguay. The Argentine is in general practically free from endemic hookworm infection, although the frontiers between it and Paraguay are heavily infested with the worms, especially *Necator americanus*. According to Soper (1925) *Necator* seems to have been introduced from the north by African negroes; Paraguay was infested with the same parasite apparently only fifty to sixty years ago by Brazilian negro soldiers. *Ancylostoma duodenale* has apparently a much longer history in South and Central America, and either was brought over by the Spaniards or, as suggested by Soper (1927), is indigenous to the Indian race. In Paraguay and North Corrientes, however, only 5 to 6 per cent. of the expelled human hookworms belong to this species.

* Being a lecture delivered, under the auspices of the University of London, at the London School of Hygiene and Tropical Medicine on March 12th, 1929.

In the north of Corrientes we found not only that practically 100 per cent. of the rural population was infested with hookworms, but that egg count (by Stoll's method) revealed an unusually high degree of egg output, corresponding to an average of approximately 430 hookworms per person—so far as such estimates can be exact.

I cannot discuss here the details of our results. The most striking fact was that, in contrast to nearly all the other hookworm-infested countries, we found everywhere in North Corrientes an average egg production about two or three times as high in children and young adolescents of both sexes as in persons over the age of 20 (see Table I).

TABLE I.—Average Output of Hookworm Eggs per gram of Mushy Stool per Person from 396 Inhabitants of North Corrientes.

| Age (Years). | Males. | | Females. | | Total. | |
|-------------------|--------|-----------------|----------|-----------------|--------|----------------------------|
| | No. | Hookworm Eggs. | No. | Hookworm Eggs. | No. | Hookworm Eggs (Hookworms). |
| 3 to 10 ... | 56 | 4,356 | 47 | 5,757 | 143 | 4,816 (ca. 330) |
| 11 to 20 ... | 127 | 5,949 | 48 | 9,350 | 175 | 6,885 (ca. 550) |
| 21 to over 50 ... | 47 | 1,565 | 31 | 2,437 | 78 | 2,152 (ca. 170) |
| 3 to over 50 ... | 270 | 4,697 (ca. 380) | 126 | 6,313 (ca. 510) | 393 | 5,205 (ca. 430) |

The figures in brackets are rough estimates of the number of hookworms present.

Among the latter group we found no cases with more than approximately 800 hookworms, although they may occur occasionally (see Fig. 1). But, even if we omit the

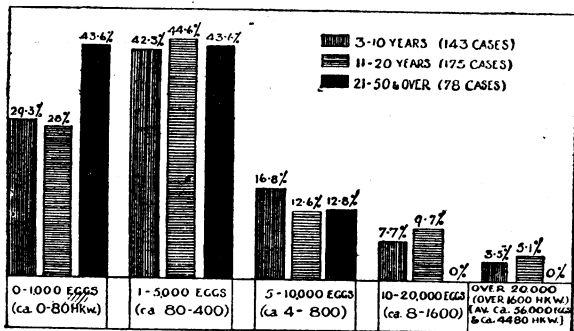


FIG. 1.—The same material as in Table I, arranged according to the output of hookworm eggs in relation to age groups.

unusually high infections with over 1,600 hookworms occurring in some of the young people, the degree of infection drops very decidedly after the twentieth year (see Fig. 2).

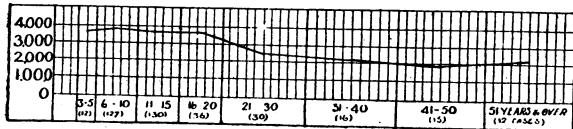


FIG. 2.—The same material, less 13 cases each with an output of more than 20,000 hookworm eggs per gram of faeces (equivalent to over 1,600 worms).

It may seem strange that, in contrast to our findings in Corrientes, the degree of infection among adults examined by Soper in Paraguay was three or four times as high as among children. The latter, however, were living under the hygienic conditions of a splendid orphan asylum, which precluded new infections, and we can corroborate the statements of Mhaskar and of Chandler that, under such conditions, the number of hookworms diminishes rapidly even in a few months. Indeed, when Soper was making his excellent and very careful examinations, he could not have known of Chandler's observations on this rapid "hookworm loss": observations which are absolutely in contrast to the previous statements of Smillie. If Chandler's observations are confirmed, many of the previous statistics will be practically useless in so far as they are based on the

examination, not of the general population, but of prisoners, orphans, and so on.

While North Corrientes, like Paraguay, may be one of the most heavily hookworm-infested countries of the world, the clinical damage among the population is apparently much less in evidence than that reported from other Necator countries (such as Brazil) having a much lighter infection. This is probably because of the better standard of life, especially the better nutrition, of the Corrientes people (they consume a great deal of meat), which makes them more tolerant to their parasites than is the case with the Brazilian peasants, who, according to Smillie, are badly nourished and much overworked. That malaria, so frequent in many hookworm-infested countries, seems to be practically absent among the population of North Corrientes is doubtless another important factor in their favour, and perhaps the admixture of much Indian blood also increases their tolerance.

At any rate, the people of Corrientes in general give one the impression of being healthy, intelligent, and lively. In spite of their intense hookworm infection, their average haemoglobin rate, measured with the same individual instrument, was almost the same as among the healthy members of our institute at Hamburg, being 81.7 for the males and 74.6 for the females on the old scale of Sahli. Among the children and young adolescents of North Corrientes it is true there occur very heavy and even deadly cases of hookworm anaemia. On the other hand, only about 10 to 15 per cent. of the young people showed a loss of 10 units or more of the Sahli scale, the tolerance of the older ones being so remarkably high that the boys—but not the girls—between the ages of 10 and 20 could, without any average loss of haemoglobin, stand an infection with approximately 160 to 240 hookworms, although 100 Necator or less is considered in other countries as the limit. Moreover, the body size and weight of the school children corresponded closely to those of hookworm-free districts, such as Buenos Aires and Paris.

Surely, one can feel weak and miserable enough even without anaemia or any other objective symptoms of illness—a fact apparently also true of many hookworm cases. Nevertheless, one becomes more and more convinced, I think, that in the past the damage caused by a slight hookworm infection in native populations has often been overestimated, at least as far as Necator is concerned; *Ancylostoma duodenale* is doubtless by far the more dangerous parasite.

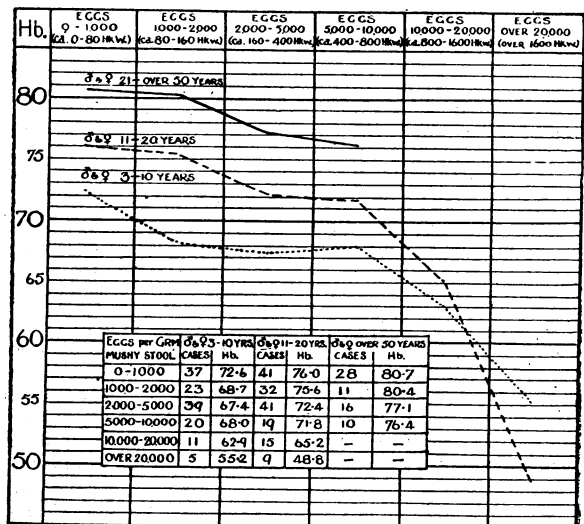


FIG. 3.—The average haemoglobin index (old Sahli scale) in 357 persons in North Corrientes, arranged according to the output of hookworm eggs.

Figure 3 shows in the vertical columns the haemoglobin value, according to the old Sahli scale (with about 80 for the normal blood of an adult); the horizontal divisions correspond to the "egg output," and therefore approximately to the number of hookworms present.

In contrast to the less tolerant children (up to 10 years), the adolescents from 11 to 20, as well as the adults, tolerate about 80 to 160 hookworms without an appreciable loss of haemoglobin. An egg production corresponding approximately to 160 to 400 hookworms is associated in all the age groups with an average haemoglobin loss of about 4 to 5 points; but it is remarkable that it is not higher in an infection with about 400 to 800 worms, the curve falling decidedly only above this limit.

The fact that the figures of Smillie from Brazil and of Carr from Mexico show the same tendency as found in Corrientes seems to justify the hypothesis, indicated by Smillie, that the host infected with a certain number of hookworms insufficient to overwhelm its resistance acquires the faculty of compensating in some way for the blood damage. Some of our preliminary experiments seemed to point to the formation of antibodies against haemolytic substances produced by the parasite.

As is well known, a haemolytic substance has been extracted from *Ancylostoma* by various workers; and my collaborator Dr. Kikuth found it several times in quite high concentration in the Ringer solution in which living *Ancylostoma caninum* had been kept at body temperature for some days, although for some unknown reason the haemolysin was not always present. The substance, not being destroyed by boiling, is apparently not of an albuminous nature; this fact, however (as will be discussed later), would not exclude our haemolysin from still acting as a "true antigen" producing antihaemolysin. But this possibility is apparently not realized; since the serum of our *Ancylostoma* dogs did not fix the haemolytic principle more than does normal blood serum. Moreover, the erythrocytes of the infected animals were destroyed by the haemolysin to the same degree as those of normal ones. Whether the haemolytic substance is active only *in vitro* remains to be investigated. However, according to de Langen and Djamil there is no evidence of chronic haemolysis in hookworm disease; apart from the intestinal bleedings there is apparently only toxic damage to the haemopoietic organs. If this view is correct, our haemoglobin curves from Corrientes, etc., would indicate only that the bone marrow can adapt itself, to a certain extent, to this chronic intoxication.

The literature concerning other specific helminthic products has increased so greatly that I can point out only some of the more important facts.

The precipitin reaction, and especially the complement-fixation test, are of some practical value for the diagnosis of *Echinococcus* and *Bilharzia* infections. Often the complement-fixation reaction is present also in patients harbouring *Ascaris lumbricoides*, and we found it positive in experimental animals repeatedly injected with Ringer's solution containing the products discharged *in vitro* by this parasite. The fact that after the removal of the *Echinococcus* cyst the complement-fixation test soon becomes negative, while, on the other hand, the "Casoni reaction" of the skin remains positive for a very long time (possibly for ever), seems to indicate that the two reactions are of a different nature, although they may be produced by the same worm products.

The active principle of the fluid from *Echinococcus* cysts causing the "Casoni reaction," like the antigen of other cutaneous reactions, is not of an albuminous or lipid nature, because, as shown in 1926 by Lemaire and Thiodet, it passes through a dialysing membrane. According to the recent excellent paper of W. Jadassohn and our own experiments, this holds good also for the *Ascaris* substance, which provokes an itching urticaria-like swelling with an erythematous areola when put in superficial scarifications of a reacting skin. This substance, present not only in the body of *Ascaris*, but also in its secretions discharged *in vitro*, is absolutely stable against boiling. On the other hand, the volatile substances of *Ascaris* are unable to provoke such a skin reaction. As shown by Coventry and Taliaferro, and confirmed among others by W. Jadassohn and my collaborator Dr. Kikuth, the "Prausnitz-Kuestner reaction" is positive—that is to say, the sensitiveness is transferred with an intradermal injection of the serum

from a reacting person to the injected area of the skin of a normal individual. Moreover, our experiments confirm Jadassohn's statements that the sensitizing property of this serum can be destroyed by adding a certain quantity of our thermostable *Ascaris* substance and that the latter becomes ineffective with the serum of a reacting person. In other words, the "antigen" and the "antibody" fix each other, and therefore, according to von Pirquet and others, the reaction is of the "allergic" type.

From the clinical point of view it will be advisable to suspect an *Ascaris* infection in cases of urticaria, and perhaps also in cases of asthma or other "anaphylactic symptoms," as will be discussed later. Furthermore, a *Strongyloides* infection is often associated with a peculiar type of urticarial eruption. In chronic infections with the parasite the skin can become so highly hypersensitive that even the extremely small quantity of "antigen" secreted by a single filariform larva can provoke an intense reaction; because, if a larva is wandering in the subcutaneous tissue of such a person, its way is marked by a quickly progressing urticarial streak. Spontaneous urticarial eruptions occur occasionally in nearly all my European cases chronically infected with *Strongyloides*; and these eruptions, being confined only to the buttocks and their vicinity, are of considerable diagnostic value. I think they are caused by filariform *Strongyloides* larvae developing in faecal particles, which even with apparent cleanliness can still adhere to the anus; it is clear that such larvae will enter the skin of these parts, which, in consequence of the repeated invasions, must become more and more "locally sensitized," as did the skin of my own forearm after many laboratory infections of my hand. The daily morning bath not being a sufficient prophylactic, washing must be repeated at least every evening; "Heliobrom-Teichgräber" mitigates the violent nocturnal itching. The constant reinfection with these larvae may contribute also to the remarkable persistency of a *Strongyloides* infection, lasting in one of my patients for twenty-six years; he has the honour, I think, of holding the "world record."

Although antigens provoking a more or less specific skin reaction may be present in every helminthic parasite the practical value of the method must not be overestimated. For example, we do not know how far a positive reaction to *Ascaris* antigen is specific in its nature; even if it were so, it would perhaps take some time for the skin of the host to become sensitized; on the other hand, the skin may stay sensitized long after the expulsion of the parasite, as shown by the Casoni reaction. Furthermore, one has to consider individual factors, and the skin of different races may not react in the same manner to helminthic antigens. It is important also in our test to take into account "group reactions." For example, the *Strongyloides* antigen is a very reliable diagnostic aid in chronic *Strongyloides* cases, and did not give a positive reaction if the person was infected only by *Ascaris*. On the other hand, the skin of *Strongyloides* carriers has reacted in my experiments not only to the *Strongyloides* antigen, but also to the antigen of *Ascaris*, and even to that of *Trichinella*, and of *Echinococcus*, although a former infection with the two latter parasites was very improbable.

At any rate, I think that at present the skin reaction has a practical value in helminthic diagnosis only for infections not easily detected in any other way. For the diagnosis of *Echinococcus* it is apparently superior to the complement-fixation test, and according to a recent publication of Fairley (1927) is very promising for the detection of *Bilharzia*; how the fallacy of the cutaneous method can be avoided in clinical use is also discussed in his valuable paper.

Instead of injecting worm extracts into the skin I prefer to introduce into a superficial scarification a trace of a powder prepared from the dried body of the parasite. This "Full-Antigen," as I call it in contrast to extracts, is very effective, can be kept for a long time, and is handy for clinical use. It may be advisable to heat the antigen powder to 100° C. to evaporate its volatile components, which are possibly associated with the "anaphylactic symptoms" that have in a few cases followed the skin reaction with *Ascaris* antigen.

As already discussed, the volatile substances of the *Ascaris* body, chemically determined so carefully by Flury, cannot provoke the skin reaction. Yet it is very difficult to understand how substances other than volatile can be involved in the frequent cases in which merely entering a laboratory where horse *Ascaris* has been dissected is sufficient to cause urticaria, erythema, asthma, and other anaphylactic symptoms. The same holds good, perhaps, for those cases in which the mere presence of a horse provokes

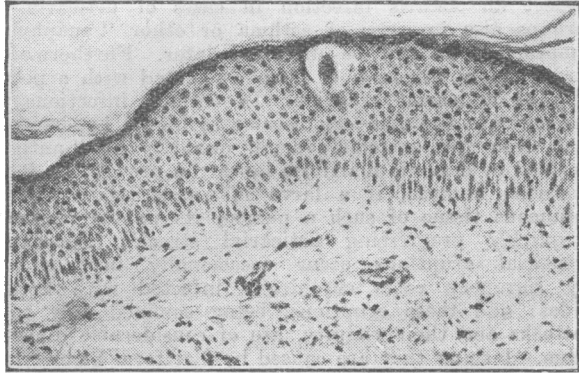


FIG. 4.—Section of skin with a larva of *Uncinaria stenocephala* under the stratum corneum. (Photograph $\times 150$.)

such attacks. At any rate, our own experiments are not in favour of the assumption that in these cases the air may contain sprayed droplets of *Ascaris* fluid.

As found recently by Dr. Borchardt of our institute, some volatile aldehydes of the fatty acids (prepared in our laboratories by Dr. Oesterlin), which according to Flury are contained also in the body of *Ascaris*, produce in the cat a marked eosinophilia; on the other hand, the *Ascaris* tissue loses this faculty after boiling. We do not know if these volatile substances can provoke anaphylactic symptoms in experimental animals, but, at all events, eosinophilia is very closely associated with anaphylaxis. The erythema, urticaria, asthma, and other general symptoms, so often accompanying the perforation of the skin by the Guinea worm, and attributable, according to Fairley's classical investigations, to secretions discharged by the parasite, clinically resemble an anaphylactic shock. They, like other "allergic stages," are cut short promptly by adrenaline, as shown by Fairley. It would be interesting to try adrenaline in the Calabar swellings of *Filaria loa* infection, in which the very high eosinophilia is, I think, suggestive of an "allergic" nature. It is remarkable that the symptoms of anaphylactic shock occur not only after the rupture of an *Echinococcus* cyst, but, according to W. Jadassohn, even after merely touching the scratched skin with body fluid of the horse *Ascaris*. Further, according to Kellaway, a general narcosis not only prevents the anaphylactic shock in *Echinococcus* patients, but often inhibits also the development of the Casoni reaction—an observation suggesting that the skin reaction may be controlled by the nervous system. (The same seemed to be the case in our experiments in which the cutaneous reaction was negative in an area of skin previously injected with adrenaline; but the exudation involved in blister formation after a burn with hot water equally failed on such a treated area.)

The eosinophilia, so characteristic of helminthic infections, may be connected with the defence of the host against the toxic worm products, but, according to Sandground, hardly with immunity against the parasite itself. Indeed, our knowledge about such an immunity in helminthic diseases is very scanty. The fact that when many

parasites of the same species are present the individual worms do not attain their usual size—as in the liver infected by many *Clonorchis sinensis*—suggests that the metabolic products of a parasite can prevent the normal development of its companions. This may be one of the reasons why in some helminthic infections hyperparasitism

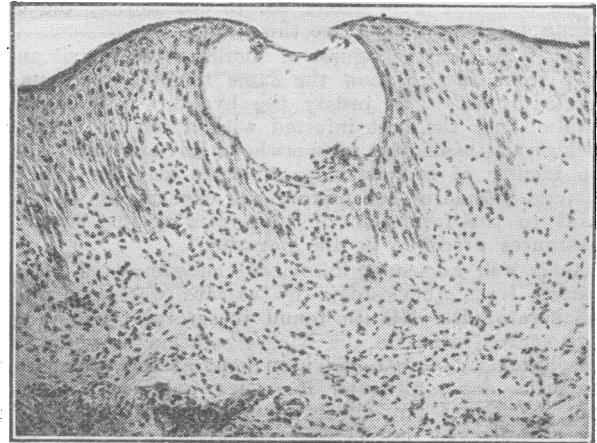


FIG. 5.—Section of the larval tract further backwards than Fig. 4 (Photograph $\times 150$.) The pressure of the accumulating fluid has progressively enlarged the tract with flattening of the lining epithelial cells.

is possible only to a limited extent, as pointed out for *Filaria bancrofti* by Sir Patrick Manson, and found true also for *Taenia solium*, *Schistosomum*, and other parasites.

The immunity against hyperparasitism is comparable to a certain degree with the "immunitas non sterilisans" of Ehrlich, as seen in lues and other microparasitic infections; but the experiments of Gordon and Blacklock with the fly larva, *Cordylobia anthropophaga*, prove that in metazoan parasites also we have to consider an immunity persisting after the parasite's removal. The recent experiments of Sandground with *Strongyloides stercoralis* in the dog suggest that such a type of immunity can occur also in nematode infections, and I agree with Yokogawa that the very low susceptibility to *Toxocara canis* of dogs more than a year old is also a consequence of the prenatal infection of practically all our puppies, and not merely an "age resistance," as Martin has suggested in the case of swine *Ascaris*. But it is very difficult to exclude an "age resistance" in such cases, as is lately apparent from Herrick's experiments with hookworm larvae fed to dogs of different ages, although some of his experiments seem to indicate the presence of an "acquired immunity" in hookworm-infected dogs.

According to Ohno, by feeding with the parasite, immunity against *Toxocara canis* can be obtained in the dog. However, our similar experiments with *Ascaris lumbricoides* and rabbits were not conclusive, and Martin reports that his experiments with *Ascaris* extracts injected into pigs were negative.

The experiments of Hiraishi, who succeeded in infecting his pigs with human *Ascaris* only when their food did not contain vitamin A, suggests that deficient nutrition may diminish the host's natural resistance against the parasites. These findings are in accordance with recent experiments by Sollazzo in Claus Schilling's laboratory, which indicate that the natural resistance of pigeons against *Trypanosoma brucei* can be broken down by deficiency of vitamin B or by starvation. Moreover, one of my dogs, apparently immune to hookworms after repeated infections, became susceptible again when deprived of vitamin A; but, of course, such a single experiment cannot be considered conclusive.

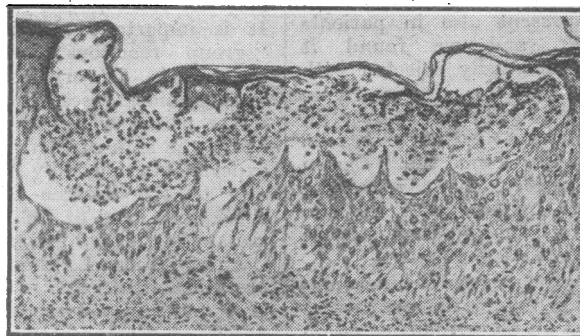


FIG. 6.—Section of another portion of the infected skin. (Photograph $\times 150$.) Leucocytes progressing under the corneal layer: the continuity of the epithelial cells has been rent asunder by the tension of accumulating fluid.

The suggestion that the blood serum may be involved in the protection of the host against the parasite could be demonstrated neither in the case of *Cordylobia* immunity nor, according to Sandground, in the acquired immunity of the dog against *Strongyloides*; while in my own experiments the filariform *Strongyloides* larvae were agglomerated by normal as well as by specific serum. A "local tissue immunity" in Besredka's sense is apparently present in the skin previously infested by *Cordylobia*; possibly it is also found in the tissue of the intestine protecting it against parasites entering the mucosa (as *Strongyloides* does), and according to Holplli also feeding on its tissue (as hookworms do, or *Ascaris* and related forms). But the experiments of Herrick and Allen Scott, showing that a certain percentage of hookworm larvae in dogs do not even begin to feed on the tissue, but remain undeveloped for a long time in the intestine, are not in favour of this assumption. In addition, the bile secretion may have a "specific" influence, and some observations suggest that parasites can react to volatile substances. These are so highly characteristic for every species that the dog, for example, can distinguish by means of them not only the species, but actually the individual.

On the other hand, the experiments of Steiner and others with plant nematodes, and the behaviour of the various *Strongyloides* strains, tend to show that a parasite can adapt itself to the biochemical conditions of a new host; that such an adaptation precedes morphological changes is evident, the *Ascaris* of the man and the morphologically identical form in the pig being a suggestive example. But in spite of the fact that the biochemical processes of host and parasite seem to influence each other in many ways, there is so far no evidence of the production by the parasite of "antiferments" against the peptic ferments of the host. In any case, the *Ascaris* experiments of Weinland do not constitute such evidence, since, according to F. Einstein, *Ascaris* is protected against digestion by the impermeability of its cuticle.

Finally, some further remarks on hookworm epidemiology. As the "age resistance" to hookworm infection is so pronounced in dogs, one might expect the human child to be more liable than the adult. In nearly all the hookworm countries, however, the percentage of infected children is much lower than that of the adults. But the defecation habits of primitively living people have such a decisive influence in hookworm epidemiology that the relatively low infection of the children may be merely a consequence of the use of defecation places less contaminated with excrement (and therefore with infected larvae) than are the places frequented by the adults. As it is practically impossible to decide to what extent such habits may influence the hookworm statistics in different countries, we must be very careful in drawing general conclusions from any given material. Therefore the following deductions may, perhaps, not be conclusive.

So far as I know, apart from North Corrientes, an infection of young people higher than that of adults has been reported only from Mexico, by Carr, and from the rural population of Alabama, by Smillie and Augustine. In Alabama, however, the hookworm diminution after the fourteenth year of life is explained by the fact that shoes are used only after this age; in North Corrientes and Mexico, however, such differences between the habits of younger people and adults were not noted.

It is quite remarkable that just in North Corrientes and Mexico (where, in contrast to the other hookworm countries, the infection spontaneously decreases in the adults) the infection of the younger individuals reaches so high a degree as reported from nowhere else, a fact which suggests that the reduction of infection in the adults may be caused by an "acquired immunity" in consequence of the high and continuous infection during earlier life. Herrick points out that the epidemiological observations of Sawyer, Hill, and Dochter are also in favour of the assumption that, under the influence of a continuous hookworm infection, a certain degree of immunity against further infections is developed, especially when the former infection has been a high one. That the same seems to hold good for the hookworm-infected dog has already been noted.

The question of the varying susceptibility to hookworm infection in different races is of great economic importance. According to a very important paper by Smillie and Augustine, the negro children in Alabama are much less infected with *Necator* than are the children of the white farmers, and this in spite of the fact that they live practically under the same conditions. The authors suggest that since the epidermis of the negro children is thicker than that of the whites it is not so easily perforated by the hookworm larvae. The same, I think, may hold good perhaps for the skin of other coloured races. That the skin structure can influence the degree of hookworm infection is proved by the experiments of Looss and myself, which show that the tender skin of young individuals is more easily infected than is that of older persons.

Another clinical observation suggests a higher mechanical resistance of the negro epidermis against hookworm larvae than obtains in Europeans. Kirby-Smith, Dove, and White have described from Florida and its vicinity a type of "creeping eruption" clinically resembling the skin affection caused by the migration of a *Gastrophilus* larva. In the Florida cases, instead of a fly larva, the larva of *Ancylostoma brasiliense* of the dog was found in the epidermis. However, this species of hookworm larva may also find difficulties in boring into the negro skin, because the affection, although very common in the skin of whites, is practically absent in negroes.

About two and a half years ago the same affection developed on the forearm of an assistant and myself after some skin-penetration experiments with the larvae of the dog hookworm *Uncinaria stenocephala*. As this species is found also in European dogs, one has to consider the possibility of such skin infection in Europe. On the other hand, according to White and Dove, in contrast to *Ancylostoma brasiliense*, the larva of *Ancylostoma caninum*, so common in most countries, is not involved in "creeping eruptions." This evidently is true also of the larvae of the human species. I have studied the normal course of the affection in my own skin, and although bacterial activity cannot be excluded, of course, I think that the essential cause of the peculiar pathological changes is a toxic secretion of the larva, small as this may be.

TUBERCULOSIS IN CHILDHOOD.*

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THE high incidence of tuberculosis in childhood, its characteristic forms which differentiate it so markedly from the consumption of adults, the inevitable fatal prognosis of some types and, with correct treatment, the favourable outlook of others, make the subject of considerable interest and of the utmost importance. Reference to the Registrar-General's annual report for 1926 gives ample evidence of the frequency of tuberculosis in children. In that year tuberculosis was responsible for 8.3 per cent. of the total deaths in England and Wales, whilst 14.5 per cent. of all the deaths from tuberculosis occurred in children under the age of 15.

The susceptibility to the tubercle bacillus is not spread evenly over all the years of childhood. The disease is uncommon during the first eight months of life; but thereafter the liability to infection rapidly increases, reaching its height at the age of 2 years. From then onwards the body gradually acquires a certain degree of immunity. The lack of resistance to tubercle at an early age accounts for the marked difference of the life-history of the disease in children and in adults; in the young child it rapidly assumes a generalized and fatal form, whereas phthisis, the more characteristic adult type, is rarely seen in childhood. As the child grows older the lymphatic system comes to play a more important part. The lymphatic glands act as a powerful second line of

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