

CONCLUSIONS

1. There exists a typical typhoid and paratyphoid blood-picture throughout the course of these diseases.

2. This blood-picture is characteristic of the obligate parasites of the typhoid-colon group and constitutes, probably, the counterpart to that usually found in colon bacillus infections.

3. The leukocyte reactions of typhoid and paratyphoid infections must be interpreted as group-phenomena.

4. In the pathogenesis of this typhoid-paratyphoid blood-picture, the germs and lymphatic tissues play a joint rôle, but the character of the intoxication determines the blood-picture.

5. The diagnostic value of the leukocyte-picture is particularly great during the first ten days, while its prognostic value is especially marked in the last ten or fifteen days of the disease.

6. Repeated, combined total and differential leukocyte-counts must be made throughout the course of typhoid or paratyphoid fevers. The cytology of these affections can be appreciated in no other way.

7. The immunity with leukopenia of the typhoid-paratyphoid group and the immunity with active leukopoiesis of the colon wing of this family are evidently the two extreme phases of one fundamental process.

8. Blood-charts and reasoning by analogy show that the conception of the typhoid blood-picture as a group phenomenon within the typhoid-colon family is correct.

9. Each member of the typhoid-colon bacillus group is able to produce either a toxic gastro-enteritis or a true typhoid affection.

10. The close or fundamental kinship between the numerous members of the typhoid-colon group of bacilli is proved, first, clinically by the time-honored name of typhoid fevers, second, pathologically by their common faculty of producing ulcers in the gastro-intestinal tract, third, cytologically by their blood-picture, fourth, serologically by the coagglutination of Pfäundler, fifth, epidemiologically by Hazen's theorem of the Mills-Reinke phenomenon of typhoid and general mortality.

11. The law of periodicity of inorganic chemical elements, enounced by D. I. Mendeleeff in 1869, is in my opinion applicable to the distinct group-arrangement of organic, living microorganisms.

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REMEDIES FOR ANIMAL PARASITES

A STUDY OF THE RELATIVE EFFICIENCY AND DANGER OF
THYMOL AS COMPARED WITH CERTAIN OTHER
REMEDIES PROPOSED FOR HOOKWORM
DISEASE *

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Thus far I have experimented with about twenty different remedies for ankylostoma aside from the action of various chemicals on the eggs and larvae. It is desired to consider more in detail four of these remedies which at present seem to me to be of particular interest in treating hookworm disease, to call attention to some of the dangers accompanying the use of each and to suggest what laboratory experiment and clinical experience have shown to be the best method of expelling hookworm by these particular remedies. What I shall have to say,

then, is of the nature of an experimental criticism interpreted in the light of many experiments on dogs, especially, infected and studied under conditions that admitted of proper control.¹

THYMOL

One of the first substances to be used with any degree of success is thymol, which is one of the higher phenols known as isopropylmetakresol. It is difficultly soluble in water, 1 gm. in 1,100 c.c., but is very easily dissolved in alcohol, and less so in castor oil, olive oil and fats, than in alcohol. When the dry powder is taken after a twelve-hour fast, with the alimentary tract cleaned out by a saline or calomel purge, but little thymol is absorbed, most of it leaving the intestine by way of the feces. After 3 gm. doses daily for a long period of time, Blum was able to recover from human urine sufficient thymol compounds to analyze. These appear in the urine as thymolsulphuric acid, thymolglycuronic acid, thymolhydrochinonsulphuric acid, and a thymol chromogen. During twenty-four hours after taking 3 gm. of thymol one man eliminated thymolglycuronic acid equivalent to 0.2025 gm. dichlorthymolglycuronic acid.

When absorbed in sufficient quantities it causes marked depression, nausea, vomiting, severe headache, roaring in the ears, weak heart-beat, resulting in a thready pulse, muscle weakness, lowering of the body temperature, dizziness, and general collapse. In my experiments on dogs, the myocardiograms show the heart muscle largely responsible for most of the graver symptoms, its contractions grow more and more weak, resulting in a gradually lowered blood-pressure, until finally, if the amount of thymol in the blood is sufficient, the animal dies from low blood-pressure, due to diminished ventricular output. Thymol also acts on the mucous membrane, stimulating secretion of mucus and causing burning sensations and sometimes vomiting, in which case the patient may suffer intensely from its irritant action on the membranes of the mouth, nose, and throat. Should the drug be accidentally drawn into the lungs it may cause grave complications, even consolidation of that part of the lung tissue with which it comes in contact. In general, then, it may be said that thymol resembles phenol (carbolic acid) in action, but is less easily absorbed and is about one-fourth as toxic.

Bozzolo, in 1881, had occasion to treat ankylostomiasis, and discovered that thymol was efficient in expelling the parasite. At first he gave 2 to 10 gm. of the powder a day, followed by a weak alcoholic beverage, so as to have a weak solution of the drug in the alimentary tract. Later he gave 2 gm. every two hours until 12 gm. were given. In the hands of later workers this treatment proved effective, but too drastic, and after a number of mishaps smaller doses were recommended, the use of all thymol solvents forbidden, and more emphasis placed on vigorous purgatives to expel the parasites and diminish the possibility of further absorption of the drug after its function as a vermifuge had been fulfilled.

With thymol treatment, as with most treatments for intestinal parasites, too much emphasis cannot be placed on the proper preparation of the alimentary tract and the parasite before administering the antihelminthic. Since thymol combines with proteins and other substances taken as food, and by dilution alone is kept away from the parasites, the alimentary tract should be as empty as possible. To this end only sufficient food is

* Read in the Section on Pharmacology and Therapeutics of the American Medical Association, at the Sixty-Second Annual Session, held at Los Angeles, June, 1911.

* From the Hygienic Laboratory of the U. S. Public Health and Marine-Hospital Service.

1. The details of the experiments, along with a discussion of the other remedies studied, will appear in a bulletin from the Hygienic Laboratory in the near future.

eaten at noon on the day before taking thymol to insure against faintness. The evening meal ought to consist of beef broth, or some form of gruel. At about 8 or 9 p. m. a compound cathartic pill is taken. The following day the treatment proper begins, the best of which seems to be that so clearly outlined by Stiles,² in substance being that recommended by the Porto Rican Commission which has reported thousands of successful treatments. It is as follows:

At 6 o'clock in the morning, one-half of the dose of thymol is taken in flat, 5-grain capsules, the finely powdered thymol being thoroughly mixed with one-half to one-third its bulk of milk-sugar to insure rapid disintegration of the mass in the stomach and intestine. The patient should lie down until some time after the drug has passed into the intestine; at 7:30 or 8 a. m. the second half of the calculated dose is taken and at 10 a. m. a vigorous purge, either of magnesium sulphate or of compound cathartic pill, is taken. The feces from now until the day following ought to be collected, washed and examined for parasites, and a week later a fresh sample examined for eggs to make sure of the efficiency of the method.

The dose of thymol should depend on the age and condition of the patient. Since absorption is much more rapid in young animals than in adults, and their protoplasm reacts more vigorously, the dose must be reduced. The body cells of badly infected individuals are also less able to withstand the toxic action of the drug, the numerous wounds in the intestinal mucosa favoring increased absorption of thymol, just as in the case of abraded surfaces in contact with phenol. Experiments on animals and clinical experience teach that the dose of thymol for both young animals and those weakened by disease must be only one-tenth to one-fifth that of a vigorous adult. The following doses represent the maximum amount of thymol recommended by the Porto Rican Commission and by Stiles to be given during one day for the age groups, respectively, to be given in two doses and modified, not to the age, but to the apparent maturity and vigor of the patient:

Age, Years.	Grains.	Grams.
Under 5.	7½	0.5
From 5 to 9.	15	1.0
From 10 to 14.	30	2.0
From 15 to 19.	45	3.0
From 20 to 50.	60	4.0
Above 60.	30-45	2.0 to 3.0

Treatment with submaximal doses of thymol expels only a fraction of the parasites and renders the residue in some way less susceptible to subsequent doses. Though only a part of the parasites are expelled, the patient at once reacts to the improved conditions of nutrition, the hemoglobin content is increased, the heart strengthened, and in general the bodily health is improved. For this reason instead of following within a few days the first treatment with a second, it seems best to wait and take advantage of the host's increased resistance to the drug because of the increased bodily vigor. Then if tolerance is developed by the parasite, use may be made of one of the other vermifuges discussed later.

Although thymol is generally conceded to be one of the most active hookworm expellants, it has certain drawbacks, chief of which are its irritant action, its toxicity when absorbed, and its tendency to cause tolerance in the parasite in excess of that which it develops for the host. These objections have encouraged the trial of other phenol compounds, but with little success, since those that are less soluble are likewise less active vermicides. Beta-naphthol, however, has been tried and with considerable success.

BETA-NAPHTHOL

Beta-naphthol is a naphthalin derivative, soluble at 25° C. in 950 parts of water and 0.61 parts of alcohol, is quite soluble in olive oil, castor oil, fats, and difficultly soluble in the saliva and in the acid gastric juice. Part of the beta-naphthol is absorbed in the intestine; just how much seems never to have been determined, but that which is absorbed is, according to Edlefsen, excreted by the kidneys as beta-naphthol gluconic acid, beta-naphthoquinon, and possibly in other slightly modified forms. One of its chief dangers is that the kidney cells are apt to be affected, resulting in nephritis and subsequent albuminuria. The mucous membranes are affected by it, but there is not that intense burning of the mouth, throat, and stomach, following contact with the dry powder, which is experienced with thymol; on the contrary there is more of a numbing sensation of the tongue. Thus far I have found in the literature no cases of severe poisoning from its internal administration. Most of the cases of poisoning recorded are of patients treated for skin disease, this drug being, like phenol, readily absorbed by the skin when applied in ointments.

Colbert, after trying thymol in a few hundred cases of ankylostomiasis with a number of unpleasant results, employed beta-naphthol. Out of 5,000 patients, 4,056 were cured. A large number, however, had to be treated four or five times before the feces no longer contained eggs. Beta-naphthol is a weaker vermicide than thymol, consequently slower to effect a cure. In spite of this, Colbert recommends it above thymol because of the absence of the more objectionable properties of the latter. Fort, of Georgia, reports 374 successful treatments and recommends it highly.

The experiments in this laboratory confirm the reports of clinicians. Dogs stand beta-naphthol much better than they do thymol. It does not cause vomiting except with large doses and in prolonged treatment. It does, however, frequently produce considerable irritation of the genitalia after urinating, but thus far none of the animals developed either immediate or remote symptoms of a grave character. Since the parasites likewise react less vigorously toward this drug, and in equal doses beta-naphthol seems to be less active than thymol, probably the difference in activity is in proportion to their relative toxicity for the host. If further experiments prove this to be true there is no advantage in substituting beta-naphthol for thymol; less thymol should be used at a time and the number of treatments increased. But should the ratio of relative efficiency and that of the relative toxicity of these two compounds be in favor of beta-naphthol, then it is the more desirable and safer remedy in cases of children, anemic, and aged patients. This point I hope to prove in the near future.

In general the procedure of treatment and the precautions to be taken are the same as those described for thymol. For a vigorous adult the procedure is as follows:

The patient is placed on a liquid diet; at 3 p. m. a mild cathartic of calomel or salts is given. On the second day at 7 a. m. 1 to 2 gm. of beta-naphthol, mixed with about one-third its weight of milk-sugar, is given in a gelatin capsule; at 8 a. m. 1 to 2 gm. more are given; at 11 a. m. a vigorous cathartic of salts or compound cathartic pill; at 12 a glass of milk and bread may be eaten, and after that the regular diet (Clayton, Fort).

MALE FERN

In Europe there is perhaps no vermicide so widely used as the ether extract of male fern. In the more northern portions of Europe it seems relatively easy to

2. Stiles, C. W.: Bull. U. S. P. II and M.-II. S., 1910, No. 30.

obtain very active samples of the rhizome, but in this country a high quality of it is difficult to purchase on the open market. To insure an active extract the best quality of rhizome, showing the characteristic green fracture, is necessary.

Its active principles readily deteriorate with age, not only when isolated as such, but also as the crude extract and even as the dried rhizome itself. The extract is a mixture of substances, amongst which the most important are filicic acid (Lach), aspidin, albuspidin (Boehm), aspidinol (Boehm), flavaspidinic acid (Boehm), aspidinin (Boehm). Poulsson, Boehm, and Straub think that aspidin, albuspidin, and aspidinin are powerful smooth-muscle poisons, and Straub has later shown that male fern is primarily a plasma poison, attacking both smooth and striated muscle without destroying nervous conduction. These properties make it, theoretically, a powerful and effective poison for ankylostoma, and if the amount absorbed by the host can be controlled it has most of the essentials of a good vermifuge.

With due precautions against solvents and against too long contact with the mucosa of the alimentary tract, the factor of absorption can in part be controlled, but even then there is usually enough of the drug absorbed to enable one to detect it in the tissues of various organs, and filicic acid along with some of its split products appears in the urine. With moderate doses mild poisoning is very common, and large doses are attended with considerable danger. When poisoning occurs the patient experiences severe abdominal cramps, catarrhal and diarrheal conditions of the intestine, headache, dizziness, shortness of breath, yellow vision, and sometimes amblyopia and even temporary blindness. In the severest cases the person becomes delirious, is attacked with severe muscle-cramps which may develop into tonic spasms, and even death may ensue. In the severe cases in which recovery takes place, permanent unilateral or bilateral blindness results. Sidler-Huguenin, 1898, compiled seventy-eight cases of poisoning and twelve deaths; Nieden compiled forty-seven cases of injury to sight from male fern; nineteen cases showed double-sided, and fifteen one-sided amblyopia. According to Kalayama and Okamoto, in 32.5 per cent. of the cases of male fern poisoning there were varying degrees of visual derangement. Like thymol, then, this remedy is not absolutely safe, for only 5 gm. has caused severe poisoning in man. Various attempts have been made to eliminate the poison that is injurious to the host, retaining the substance that has a selective action for the parasite, but thus far these so-called active principles have been found unreliable.

Male fern extract had long been known as a teniacide, but Perona and Perroncito about 1881 brought it into prominence as a substance highly toxic for ankylostoma. Since then its efficiency as a vermicide has been amply demonstrated.

Fickerman treated 534 patients, the first dose curing 83.9 per cent. Laplanche found that the first dose cured 75.9 per cent. of 1,648 patients. Nagel compiled the results of about 4,000 cases, his observations extending over several years of time; mild poisoning was common. Tenholt treated about 10,202 worm patients, 74 per cent. requiring but one dose. Birgmann treated 22,000 patients with ankylostomiasis and observed only four cases of permanent blindness.

In treating hookworm disease by male fern it is not only essential to have a fresh ether extract, but it is necessary to prepare the alimentary tract for its recep-

tion. The mucosa should be free from mucin and from fatty foods. All solvents of male fern such as alcohol, fats, and oils, must be avoided, just as with thymol. Then in order to avoid unnecessary absorption after the drug has fulfilled its function of poisoning the parasite, it should be expelled as quickly as possible. Compound cathartic pills or magnesium sulphate seem to be the best cathartics. Since ether extract of male fern has a very disagreeable taste, it ought to be put up in capsules. Glutinous capsules have been recommended, but when taken in these, larger doses seem to be necessary. The following procedure used in part by Goldman seems to be a good one:

For a vigorous adult 8 to 16 gm. of ether extract of male fern is put up in 1 gm. gelatin capsules. First day: Evening meal of meat broth or light soup; compound cathartic pill later, say about 8 p. m. Second day: 7 a. m. 1 gm. male fern every ten minutes until 4 to 8 gm. have been taken. One-half hour is then allowed to elapse and if no undesirable symptoms develop the remaining 4 to 8 gm. are taken, 1 gm. every five minutes. One to two hours later a vigorous purge is taken (calomel or salts). The feces should be washed and the worms counted; three to ten days later the feces are again examined for eggs, and if necessary the treatment repeated.

EUCALYPTUS AND CHLOROFORM

Another mixture known as "Hermann's Mixture" is of considerable interest. It is composed of 3 gm. of chloroform, 2 gm. of oil of eucalyptus, and 40 gm. of castor oil. This is divided into two doses and given at hour intervals.

Thus far I have been unable to find any cases of acute poisoning from pure oil of eucalyptus mixed with castor oil. It is known to have a local action on the skin, but otherwise little is known of its pharmacologic action. Two and one-half c.c. of oil of eucalyptus globulus in 10 c.c. of castor oil, given in a gelatin capsule to a 5 or 6 kilo. dog, causes vomiting. Judging from the contents of the vomit, the mixture caused an abundant flow of mucin, slightly tinged with blood. The same animal can take, apparently with little inconvenience, the same amount of eucalyptus oil if given at hourly intervals in doses of 1 c.c. mixed with 5 c.c. of castor oil.

It cannot, however, be said of chloroform that it is a harmless drug when taken in doses as usually recommended for expelling intestinal worms. As is well known, chloroform alone is a powerful irritant to all parts of the alimentary tract. It acts locally on the mucosa, causing lesions therein, and stimulates both the stomach and the intestine to very active movements. Being absorbed from all parts of the alimentary canal, especially the upper portion, it reaches the liver by a rather direct route and may result in acute poisoning. A 10 kilo. dog may show no outward signs of intoxication after ingesting 3 c.c. of chloroform thoroughly mixed with 10 c.c. of castor oil. Hookworms may be expelled within two and a half hours after giving the mixture. If, however, a second dose be taken three to four hours afterward, a dog, before lively and playful, soon ceases to be so, food is refused, vomiting may set in, and some hours later the animal is seized with acute mania-like symptoms and eventually dies. The post-mortem findings of such animals reveal profuse lesions in the liver, the lobules, and in many places groups of them, being distinctly outlined by their yellow color, the pericardium shows a peculiar mottled appearance, and there is hemorrhage in the lungs, diaphragm, stomach and intestines.

There can be no doubt about the chloroform being responsible for these pathologic conditions, and such

results place one on his guard in using chloroform internally. Its invidious action on the internal organs may not result in symptoms gross enough to be observed until considerable time has elapsed, thus tempting one to administer a second dose, the summated action of which may bring things to a crisis at once. Acute mania is reported in the case of a boy after taking for hookworms the prescribed dose of "Hermann's Mixture." The dose was probably that supposed to be taken by an adult, and should have been modified according to the age and condition of the patient, a matter to be considered at all times. Even then patients seem to rebel against a second treatment, and Colbert, Key, and Law each speak of it as dangerous and less efficient than beta-naphthol. Thus far I have found the remedy more efficient for dogs than beta-naphthol, and an excellent substitute for thymol in very refractory cases.

It is not quite clear just what part oil of eucalyptus plays in expelling ankylostoma, but until further data are at hand I am inclined to think it is simply an irritant to the parasites, causing in them rapid vermiform movements, and making them loosen their hold and change their position, in which case a vigorous purge may sweep them alive out of the intestine. The chloroform not only does this, but also anesthetizes them sufficiently to render them incapable of again taking hold of the mucosa while being expelled by the purgative action of the ricinolic acid. When quickly expelled in this way the worms are not at first very active, but placed in saline solution they soon become very active and may live twenty-four hours.

That chloroform is the most important constituent of this formula can easily be demonstrated by taking two infected dogs A and B. A is treated with 15 c.c. of castor oil plus 3 c.c. of eucalyptus globulus, in 3 doses an hour apart. After a second treatment only thirteen live worms were obtained. B is treated with 15 c.c. of castor oil and 3 c.c. of chloroform in doses one hour apart. Inside of $3\frac{1}{2}$ hours after the last dose, feces were obtained containing 133 hookworms, and a few hours later 150 more were expelled, all of which were very active after being in water ten minutes. A second treatment some days later secured twenty-five hookworms; subsequent examination of the feces showed it free from eggs, and later after using the animal for a blood-pressure experiment, careful examination of the stomach and intestines showed the animal to be free from hookworm. Dog A was then treated with 15 c.c. of castor oil and 3 c.c. of chloroform, in three doses an hour apart; hookworms were obtained, and after the second treatment the feces showed no hookworm eggs.

These experiments seem to represent in general the relative action of eucalyptus and of chloroform. With some dogs a larger number of worms may be obtained after eucalyptus, but in such cases there is considerable blood in the feces, whereas chloroform is quite uniform in its action and always expels the worms more efficiently. So that one is justified in concluding that the oil of eucalyptus globulus is probably superfluous and at best simply an aid to the chloroform during the stage of irritation in causing the worms to loosen their hold on the mucosa.

CONCLUSIONS

1. Any practical vermifuge to be effective in expelling uncinaria or ankylostoma must be an irritant of sufficient intensity to cause the parasite to loosen its hold.
2. It should paralyze the neuromuscular apparatus to hinder the parasite from making fresh attachment.

3. Its relative toxicity for the parasite must be either much greater than that for the host or be much more readily absorbed by the former than by the latter.

As has already been pointed out, each of the above remedies is absorbed more or less from the alimentary tract, and Tenholt has even gone so far as to assume that only such drugs as are absorbed can be active in expelling ankylostoma. Since their method of taking food is by way of the mouth they must of necessity be poisoned by ingesting the tissues of the host already impregnated with the toxic substance, and if the host does not absorb sufficient thymol, beta-naphthol, male fern, etc., they remain fixed to the intestinal mucosa and are not expelled by the purgative.

My present experimental data suggest that this is at best only a part of the truth. It happens that drugs like thymol when combined with iodine or the benzole radicle are much less active vermicides than thymol itself. It is also true that thymol iodid, being much less soluble than thymol, is absorbed to a less extent by the intestinal mucosa. *A priori* this would seem to support the idea of Tenholt that thymol iodid has no action on hookworms because none of the drug is absorbed by the host. But if the worms themselves be studied in contact with solutions each of thymol and thymol iodid it is possible to explain the reaction of the worms towards the two drugs on the basis of amount of drug in actual contact with the parasite and the effect of introducing the iodine atom into the molecule, and thus lowering its toxicity. While, therefore, the drug absorbed by the host and ingested by the parasite as a part of the cell and plasma may have a toxic action on the worms, it seems that such drugs as thymol, male fern, chloroform, and beta-naphthol, act by direct contact with the worms, causing rapid vermiform movements, and if the irritation is sufficiently great the worms finally attempt to escape. From now on until paralysis sets in not a little of the surrounding media is ingested, since the mouth parts of the parasite are kept in constant action. At this stage the intestinal contents of the host ought to be expelled so as to get rid of the surplus drug and the poisoned or anesthetized worms. Judging from the action on the worms *in vitro*, two to three hours seem to be about the time when the cathartic should begin its work: Although in the case of chloroform and eucalyptus the cathartic in the form of castor oil works hand in hand with the chloroform.

In conclusion it may be said that at present thymol is one of the most toxic vermicides for ankylostoma thus far proposed. It is easy to obtain, keeps well, is cheap, and is easily administered; it kills the parasites instead of merely paralyzing them. When taken under the care of a physician who is careful to gauge the dose in accordance with the physical condition of the host, it seems to be the best all-around remedy thus far studied. While dangerous in large doses, it differs from beta-naphthol, male fern, and chloroform, in that the danger is at once apparent and can be controlled by heart stimulants and by methods that help maintain a good blood-pressure until the drug has killed the parasite and the cathartic has removed the excess of thymol. Whereas, with the other remedies just mentioned the danger signals are less obvious and usually it is only after irreparable damage is done that one is aware that his patient is in danger of any after-effects.

Beta-naphthol is probably the next pure chemical substance that ought to be tried more extensively on human hookworm subjects. Persons affected with kidney lesions ought not to take it, and when used the urine

should be examined to determine whether it causes albuminuria. If the maximum dosage of 2 to 4 gm., divided in two parts and given an hour apart, does not cause renal disturbances in adults, beta-naphthol has much to recommend it as a hookworm remedy.

Male fern at present has not much promise in this country because of the lack of care in collecting the rhizome and in preparing an active ethereal extract. This, however, is a condition which doubtless would soon be remedied if once considerable demand existed for an active extract.

At present there is but little reliable data on how efficient "Hermann's Mixture" is for expelling human hookworms, or what percentage of cases might show after-effects. It seems unnecessary to add such an irritating oil as eucalyptus globulus, and if chloroform is used it ought to be given with plenty of oil. It is best to divide the maximum 3 c.c. dose, for a vigorous adult, into 3 parts, 1 c.c. of chloroform to 10 c.c. of castor oil, given at hour intervals. Should vomiting occur before the chloroform is taken, stop the treatment, and if necessary change to thymol or beta-naphthol. By thus regulating the dose of chloroform, I have had excellent results with dogs, it has proven rapid in its action and thus far not followed by any evil after-effects. Should the chloroform-castor oil mixture act as favorably in human beings as it has for me in dogs, it will prove a universal worm remedy of great importance.

Finally it may be said that the best of remedies are but weak instruments of defense in stamping out this degrading disease. The weapon of offense must after all be proper disposal of fecal matter so that infection is rendered impossible. And what can be more effective in accomplishing this than the cultivation of a healthy public sentiment which will insist on its communal rights in this matter, protect the innocent, and by proper police regulation quickly punish the offender? To this end it would seem that the most effective line of attack is that led by Stiles and others who are endeavoring to educate the masses as to the importance of proper sanitation.

MY EXPERIENCE WITH HOOKWORM INFECTION IN THE DEEP GOLD MINES

OF CALIFORNIA *

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The physician practicing medicine in the interior of the North American continent may have meager opportunity for the application of tropical medicine or meet few diseases foreign to the locality, but as new diseases, new industries, and a changing population take effect, then he may anticipate new enemies on which to test his skill.

I offer this paper without any anticipation of presenting anything new, but with the hope that my experience with uncinariasis, or hookworm infection, together with the few suggestions that I can make, in relation to its cure and particularly its prevention, may prove of value to the fraternity. I think that I can positively state, without fear of contradiction, that many individuals have gone down to an untimely end from hookworm infection, and we have helped to bury our mistakes by

signing a death certificate for "miners' consumption" or some other disease, diagnosed symptomatically; while in many other cases, hookworm has been a contributing cause of death and has gone unrecognized, unheralded and unappreciated.

I may be radical when I say that I doubt if there are any deep mines in the United States, which have been in continual operation for a number of years, and which employ foreign laborers—miners who have worked in the mines of Cornwall, Austria, Italy or South Africa; and perhaps many other places before coming to this country—that are not more or less infected. In the mines along what is called the "mother lode," the deep gold-mining district of California, laborers of this class are employed.

These foreigners, without exception, come to the Pacific Coast from eastern ports, mostly from New York. They frequently stop *en route* at eastern mines, in Pennsylvania, Michigan and other places, and there is no reason to believe that they do not infect these mines.

These miners become infected by working from childhood in infected mines in the old country, and all are carriers, in the same sense as the typhoid carriers that we occasionally see. It is not only my opinion, but also that of Dr. Gunn, of San Francisco, whom I consider an authority on hookworm, that most mines in operation for a considerable length of time, employing this class of labor, where the conditions are favorable to their development, are infected with hookworm.

It might be well to quote at this time from Frohlich, Raillet, Stiles and others, that there are two distinct species of hookworm, the European and American, but I wish to say that if the European are not American, they should be, for they have been in this country long enough to be naturalized. These authorities state that the effects of the two species are not distinguishable and the treatment is the same.

Hookworm infection, if suspected, is not difficult to diagnose, but by the neophyte it may be overlooked. One may stand on the streets of any mining town along the "mother lode," when the miners come from and go to work, and with little chance of mistake point out the men infected with hookworm. Their skin has an appearance as peculiar to their trouble and as characteristic as is the cachexia of cancer.

When a patient complains of symptoms referable to gastro-enteritis, appendicitis, functional heart trouble, etc., the stools should be examined for the ova of hookworm. After an ordinary laxative the worms themselves are not found in the stool, only the eggs. Having once seen the ova, which are clearly pictured by recent books on the subject, there is little chance for mistake. Many cases of apparent heart trouble, gastro-enteritis, appendicitis, anemia, malaria, etc., yield like magic to hookworm treatment. I recall one case in which a miner, supposed to be dying of "miners' consumption," who was too weak to cross the street, was found to be infected with hookworm and responded nicely to the treatment; he is now back at work in the mine, doing hard manual labor, and is well and hearty.

It is not necessary to give a laxative to secure a sample of the stool. The patient can pick up a small amount of an ordinary stool on a toothpick and place it in a clean vial. A thin film of this spread on a slide, and examined under a $\frac{1}{8}$ inch objective, without cover glass, will disclose the ova if they are present.

Eosinophilia is diagnostic evidence of hookworm infection; however, we must keep in mind the fact that eosin-

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