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Suggestions and observations on the treatment of trichinosis and its experimental premises

Adolpho Lutz
Introduction

Although the discovery of the etiology of an unexplained disease is justly hailed as a great triumph, there is no denying that on such occasions the question of treatment is often left aside. Fortunately, the latter follows its own path and often takes the right route by empirical means, even though some questions may still remain about the origin of the disease. Thus, rheumatic polyarthritis, syphilis, and other diseases have been successfully treated, although their etiology is either unknown or incompletely known, whereas with other diseases, such as cholera, tuberculosis, and other bacterial invasions, we are as powerless as before, despite discoveries of recent years.

In the empirical realm, one single felicitous coincidence may prove decisive; as time goes by, this is what has happened now and again, in the midst of many failures. Directed research, on the other hand, works with much more restricted factors, in terms of quality, quantity, time, and place. Under these circumstances, so as not to lose this imbalanced battle, it is absolutely necessary that from time to time the researcher examine the true nature of the problem undertaken, and that from among his store of treatment resources, he choose only those agents that promise some success. This process is of course empirical as well, but it follows certain lines prescribed by theory; thus, it shortens the way, as we see best in the example of surgical sepsis, which in a very short period gained much better results by using different methods and different routes than the results that had been obtained in centuries of unplanned empiricism.

It is from this point of view that I would like to make some observations and suggestions in regard to a disease in which results obtained so far have been limited to a prophylaxis that has been efficacious but not wholly sufficient in itself – I refer to trichiniasis. I am quite aware of the fact that in so doing, I may be undertaking a difficult and possibly thankless task, and also that a positive result, even if ever so small, would be of more use than the best-founded proposals. For this reason, I have intended for several years to test my views on experimental animals and, if possible, at the bedside. However, nearly insurmountable difficulties currently prevent me from undertaking this very exacting work, which requires a great deal

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of time and is largely dependent on external circumstances, so I feel it is almost a
duty to call the attention of others, better positioned than I am for investigating this
object.\(^1\)

The tasks met with in the treatment of trichiniasis are of several kinds.

The first is, of course, prophylaxis; we intend to achieve this chiefly through
inspection of meat for Trichinae and by teaching the public about the danger incurred
from eating pork that has been insufficiently cooked or smoked. Much has already
been accomplished in regard to both these particulars, and the public in general
understands this rule of hygiene better than any other. Nevertheless, these measures
are not quite enough; such examinations of meat may prompt a not wholly justified
lack of concern; this is why new cases of trichinosis are reported every year. Although
I lack data on these numbers, I cannot deem them insignificant, judging from
newspaper articles. Besides, milder, isolated cases probably remain undiagnosed.
Although mortality seems low in most instances, damage to health is usually quite
substantial, even when the outcome is favorable.

One is consequently justified in expecting medical science to seek new
medicines, so that, at least in the case of early diagnosis, a fatal outcome may be
safely prevented. After all, the etiology and cause of the disease are as plain as
day, and our task is not hopeless, at least when undertaken at the beginning of the
disease.

A priori this seems to be relatively easy; even when a large number of
experiments appear to prove the contrary,\(^2\) we have several paths left to examine
before calling their results into question. I need only remind the reader of
ancylostomiasis, the treatment of which appeared hopeless for so long, but has
now become simple and safe.

In the discussion that follows, general knowledge of the history of the
development of trichina and of the manifestations of trichiniasis are presupposed.
The latter, in a broad sense, falls naturally into the following stages.

The Different Stages of Trichiniasis and their Treatment

1 – From the introduction of the encapsulated Trichinae to their liberation in
the host's intestinal tract.

2 – From the beginning of development of the intestinal Trichinae to the
birth of the embryos.

3 – From the beginning of the emigration of the young brood to the
disappearance of the symptoms.

It need hardly be pointed out that these stages are not clearly separated
chronologically, but overlap in part; however, this does not impair the usefulness of
subdivision into stages.

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\(^1\) In my present field of work, Brazil, Trichinae are unknown in man and animals. My endeavors to
obtain living muscle-Trichinae from Europe have met with no success. In the cited observations
undertaken in Europe, I used the flesh of an infected rabbit, which I owed to the kindness of Professor
Leuckart; having died by accident, the animal was used for some feeding experiments. [A.N] [E.N.: to
infect other animals]

\(^2\) See especially Fiedler: "Zur Therapie der Trichinenkrankeit," Deutsches Archiv für klinische Medizin,
v. XXXVII. [A.N.] [E.N.: In English, “On treating trichinosis,” German archive for clinical medicine]
Except in the case of a direct experiment, the first stage is seldom observed, because of its short duration and its lack of symptoms; it can only be deduced by finding muscle-Trichinae in samples of meat of the same origin as that eaten. Through direct experiments, Leuckart was able to show that free Trichinae can be found in the stomach already after three to four hours, but release may take much longer if they are enclosed in tough pieces of meat. Consequently, energetic treatment meant to eliminate the parasites is in order during the next hours or even during the following days. It is self-evident that the fastest-acting purgatives must be employed; the same applies to emetics and even to the use of stomach pumps, when there is still hope for results.

In the second period, our task is still relatively simple, since we need only endeavor to kill the parasites in the intestine. It is doubtful whether they can be driven out alive; nor is it necessary to take steps to expel dead parasites, unless they are wanted for examination.

In the third stage, treatment becomes much more difficult, and complete cure by getting rid of the whole brood of immigrated Trichinae is not a serious alternative. Even destroying them is for the present a rather hopeless prospect. Any substance able to kill the worms inside the tissues would have to be introduced more or less directly into the circulation, and it probably would not be easy to find a substance that could be admixed to the blood in sufficiently high concentration to destroy the tough little parasites without also harming the host. Methods of a more physical nature are not promising either.

If, however, we give up attempts to destroy the young during migration, there remains the task of abating this process as much as possible, by getting rid of the intestinal parasites so as to put a stop to further multiplication. It is known that migration does not occur in one levy but in successive ones, and for this reason, the stage of the illness during which characteristic symptoms of trichiniasis are manifest may last fairly long. The fact that diagnosis is mostly made only after migration has begun does not mean that the time for combating the disease is over; in short, therapeutic indications will probably coincide with the second period, especially when the suspect food was eaten not once but several times during several days. Before going into the treatment of the second stage, I want, however, to make a few remarks on diagnosis, because it is only through the most accurate diagnosis that we can hope to obtain worthwhile results.

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3 According to Leuckart, one occasionally finds live encapsulated Trichinae living in the intestine of the experimental animals even on the third day. [A.N.]

4 After more than 20 hours, Merkel succeeded in obtaining feces containing various Trichinae that had left the capsules, by administering 300 grs. infusion of Sennae composita (see Fiedler j.c. and also Deutsches Archiv für klinisches Medizin, vol. 36, p. 357. [A.N.]

5 Also in the case of parasites that live outside the intestines, some success has been obtained by using antihelminthics, e.g., against distomes of the gall-ducts in man, by Chabert (using Oleum chabeti) and, unless I am mistaken, once in Italy as well (using Extr. filicis). According to Grassi, Calandruccio, and Perroncito, it is also possible to drive out liver flukes in sheep using Extr. Filicis, with ethereal tincture or turpentine oil (see Cbl. f. Bakteriologie etc., 1887, v. 1, p. 725). Benzine seems to have the same effect and perhaps Asa foetida as well. The latter even seems to drive Strongylus microirus from the bronchia of horses (see Davaine, Traité des Entozoaires, Paris, 1877). However, the Strongyli do not seem to be killed; success with trematodes hardly justifies the hope of similar results in muscle-Trichinas.
Diagnosis

The presence of Trichinae in the human organism can be ascertained by several methods, which cannot, however, be used in every case, nor at all times.

The first – i.e., demonstrating that living muscle-Trichinae have been swallowed – was mentioned above. In our studies, it has proven valuable above all in experimental work, because an almost precise estimate of the number of specimens taken into the organism allows us to judge the extent of the infection in animals that are still living. In careful treatment experiments, a preliminary examination must therefore be made; even so, a source of error may arise from the unequal distribution of the Trichinae in the muscular system; moreover, in some cases, only a relatively small portion of the parasites ever develop.

The second method entails demonstration of Trichinae at any stage of development, or of characteristic fragments of them in the stool; this will be discussed below.

A third way is to look for Trichinae in fragments of muscles, obtained by excision or with a hook, or to find them in the blood or in the fluids of serous cavities. This method only offers prospects of success when migration (and the consequent reaction of the organism) has already begun and when infection is intense. The result obtained is always relatively late, if not altogether too late, and when the symptoms are pronounced, it becomes rather superfluous. Moreover, this examination is very unpleasant for the patient and in human beings can only be used in a rather restricted way. On the other hand, it can be employed extensively in helminthological experiments, and is highly useful in these cases.

In the fourth place remains the possibility of diagnosing the disease from the symptoms. This will become all the easier, the more frequent the cases are, since one clear-cut case is enough so that even less characteristic cases can be recognized.

Diagnostic Evaluation of Symptoms

The symptoms may develop as early as the 2nd or 3rd day (Leuckart), that is, at a time when there cannot be any real migration as yet. According to Kuechenmeister and Zuern (Die Parasiten etc., 2nd ed.) it can even start within a few hours. Symptoms are mainly limited to the intestinal tract (nausea, vomiting, diarrhea, and sensations of discomfort); the more general symptoms are those also observed in other diseases of the digestive system (general malaise, headache, thirst, fever). In extremely rare cases, the symptoms may have such a violent, cholera-like character, from the start, that death may supervene before the more general symptoms occur; it is stated that during the epidemic of Hadersleben three victims died on the 6th day after infection, i.e., during a stage when, according to the current hypothesis, it is highly unlikely that the birth of the new generation had begun. In experiments on animals, death may occur as early as the 4th day (Leuckart).

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6 The birth of young Trichinae begins on the 6th day (Leuckart) and, more rarely, on the 5th (Vogel and Pagenstecher). [A.N.]
It seems to me as yet unclear how the severe symptoms and death occurred in these cases. The supposition that the number of intestinal Trichinae must have been much greater than in cases where the same stage involved latent, less pronounced symptoms seems a valid and fair supposition, but in my opinion it does not provide an explanation. The mere presence of microscopic or macroscopic roundworms, albeit numerous and mobile, does not necessarily bring such symptoms about, as long as the histological elements of the intestine remain intact; moreover, intestinal Trichinae are far too small to produce mechanical irritation of the kind produced by *Ascaris* and *Taenia*. It is not unlikely that some vital action of the Trichinae, perhaps even an irritating secretion, may play a role. In any case, the human intestine is able – without any reaction – to harbor myriad so-called *Anguillula stercoralis* (larvae of *Rhabdonema strongyloides* Leuckart), similar in size and number to the intestinal *Trichinae* and far more mobile than they; similarly, there may be a very great number of *Oxyuris vermicularis* in the cecum without provoking local symptoms, and the larvae of *Filaria bancrofti*, i.e., *Filaria sanguinis hominis*, do not produce any general symptoms, though they may circulate in endless numbers in the blood or be found in ascites chylosus.

During the first week after infection, there is nothing at all pathognomic about symptoms and so even when several cases occur together, only rarely are they accurately interpreted. They become more characteristic from the second week on. In simpler cases, they may occur only then or even later. A very striking symptom is the swelling of the eyelid, which, according to Kuechenmeister, almost always occurs about the seventh day, disappearing after some days to reappear later. Despite its early appearance, this should be considered a sign of the invasion of the muscles of the eyes by some forerunners (as Leuckart has suggested), since functional disturbances of the eye muscles are also observed around the same time.

Oedemata in other parts of the body come later. The muscles swell, becoming hard and stiff; as a result, they are generally held in the most relaxed position while movements are drastically reduced. Further consequences of the infection of the muscles are hoarseness, problems swallowing, and labored breathing. Of the other symptoms, only profuse sweating, and, to a certain degree, insomnia, are characteristic. Observed in the most severe cases, the other symptoms – fever, rapid pulse, thirst, sparse and concentrated urine, delirium, decubitus ulcers, heavy diarrhea (not constant), bronchitis, and pneumonia are not peculiar to trichiniasis, but reminiscent of typhus illnesses and may lead to confusion.

Hydropsis, at the end of the disease, must be regarded as the consequence of generalized illness, especially the effects on circulation, whereas oedemata observed at the beginning should be considered as side-effects or induced by the plugging of the lymphatic vessels.

The later course of the disease and the various degrees of severity will not be discussed here; they are dealt with at length in books on medicine and parasitology. Here we are concerned only with the symptoms that make diagnosis possible and point to the seat of the trouble.

7 Friedel was the first to voice this supposition. [A.N.]
All that has been said of intestinal Trichinae applies in even a higher measure to migrating larvae; in other words, the parasites are not simple foreign bodies acting mechanically and producing symptoms because of their great numbers – rather, active pyrogenic substances are at work; these are a result either of the parasites’ vital processes, of material alterations to the tissues of the host caused by the parasites, or of the millions of foci of infection, since the worms in the intestinal tract either pave the way for pathological agents or spread them directly. Therefore, one cannot regard the entire process as one derived from multiple microscopic lesions, but should take into account that they are instrumental in producing infection. This is corroborated by the symptoms of peritoneal irritation (redness or cloudiness), as found at the end of the second week in Leuckart’s experiments. In man, the inflammatory nature of the process can be recognized from fever, swollen glands of the mesenterium, and the parenchymatous degeneration seen in postmortems. It is generally recognized that pulmonary affections are only an indirect consequence of invasion by Trichinae and not caused by specimens who have lost their way.

**Final Part**

Treatment. Preparation of the intestine.

Let us now move on to treatment itself, in which, as already indicated, special attention must be given to preparation of the intestine. Since we presume that the Trichinae are lodged in the mucus of the intestinal wall, we must do our best to choose laxatives that will dislodge them. Based on a rather long series of experiments that I conducted on cases of ancylostomiasis, I decided that alkalis [Alkalien] and salicylates [Salina] are unsuitable for this purpose. Of the many substances tried in experiments, calomel and podophyllin produced the best results. The former is also very well suited for animal experiments (e.g., rabbits); its use in human cases is somewhat restricted because of the danger of stomatitis. Consequently, a supplement that reinforces its action is advisable. To this end, *Extractum thei* and *pulvis folium Sennae* extract have proven suitable. These can also be used for several days, thereby prolonging their effects. Unfortunately, when administered in large doses, podophyllin easily produces cramps and vomiting; in smaller doses, it can be used continuously as a laxative for some time. The use of calomel is only appropriate in the case of patients whose digestive organs are not highly sensitive.

Further experimentation is highly desirable, and I would like to recommend the continuous use of larger doses of sulfur in these cases.

Experiments should also be conducted using keratin-coated pills in conjunction with the abundant administration of hydrochloric acid; these experiments may, for example, test salicylic acid as a descaling agent.

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8 Part published in *Deutsche Medizinal-Zeitung*, no. 15, 20 Feb. 1888. [E.N.]

9 Of course they would be more likely to prove efficacious if introduced directly into the intestine. [A.N.]
This treatment may be enough to expel a number of intestinal Trichinae, especially with the help of calomel (which also has some anthelminthic properties); this result would in itself justify the experiment. For this purpose, stools would have to be sampled immediately, in the manner mentioned above. Even if the result of the treatment were negative, the way would have been prepared for a subsequent anthelminthic.

This brings up the question as to which anthelminthic offers the greatest prospects of success, a point that can be approached in several ways. One of them, which has been tried several times, consists of studying the effects of each drug directly on living Trichinae. For this purpose only intestinal Trichinae should be used, both free ones and those enveloped in mucus. The results obtained will be no more than reference points and not applicable results. The conditions inside the intestine are often quite different from those outside and the use of certain substances will in the first case be precluded – at least in the doses and concentrations needed. On the other hand, it is possible that some drug which did not seem very promising in experiments outside the intestine may prove effective. My efforts to avoid the influence of gastric juice and excessive dilution by employing keratin-coated capsules, as Fiedler suggests, have so far been in vain, because of the technical imperfections of the capsules.

The drugs whose effects on intestinal parasites are in part known and in part probable may be divided into several groups, albeit not always sharply delimited ones. Of these, I recognize the following:

1 – Dehydrating substances that attack the worm’s integument directly. One substance in this group was tried on isolated Trichinae and then on patients, i.e., glycerin. The first to use it, Fiedler did not obtain satisfactory results, as he states quite openly in his recommendations, even in experiments on animals (which permit less careful use). Merkel, however, believes that the satisfactory outcome of one case must in part be ascribed to this substance. I believe (as does Fiedler) that this assertion does not have a sufficiently sound basis.

It would be easy to obtain a definitive answer to this point if, in experiments upon animals, the glycerin were directly injected into the affected part of the intestine. Should this, or another drug, yield reliable results without any substantial side-effects, it might then be tried out in appropriate human cases (continuous application may be possible through a stercoral fistula). Carried out by practiced hands, today such a procedure should hardly be more dangerous or less justified than liver surgery to treat echinococcus. However, until experiments with animals provide a good foundation for this treatment, it would seem more advisable to test more promising drugs, since glycerin has not yet proved to be a good anthelminthic. The same applies to alcohol, which is also recommended by Fiedler.

2 – In the second group we may place numbing and narcotizing drugs, some of which, such as chloroform and ether, have found favor in the treatment of Taenia. I believe carbon sulfate to be especially effective, but of course it could only be

10 See Fiedler, cit. (second note). [A.N.]
used in very reduced doses. Alcohol may also be placed in this group, so long as its action is not through dehydration. This drug does hold some possibilities – especially if directly introduced into the intestine – but local effects are by no means irrelevant, and the danger of general symptoms likewise limits the dosage used, even if those needed should be smaller than expected a priori.

3 – The third group is composed of parasiticides themselves.

Among the large group of aromatic substances (i.e., ethereal oils, metals and their salts, and so on), there are many bodies that are decidedly toxic for lower organisms. It must, however, not be overlooked that different zoological and botanical groups react in quite diverse ways to such substances and that conclusions drawn from one group may not be applied to another. Even though some insecticides and fungicides might be well worth testing, they should be relegated to a second plane (in part, they are very poisonous, and in part, perhaps without cogent motives, they have only been tested in minimal doses). We shall first concentrate our attention on the drugs tested specifically as vermifuges.

Here again, we must distinguish several groups, which are by no means equally promising, namely those that are toxic to all intestinal worms, or at least to species belonging to different orders, and those that have only proved toxic for a certain species. Of the latter, we are especially interested in the ones that are effective against round worms, especially species that are difficult to expel, whereas drugs against Taenia in the narrower sense are not very promising. I often do not have enough observation material to define more precise divisions, which would probably require a series of new experiments, but I will nevertheless attempt to make a quite provisory grouping.

Among widely tested drugs, I would include firstly thymol, as it has never failed entirely against any kind of intestinal parasite. In the case of Taenia and Bothrioccephalus, segments are most certainly expelled following the single administration of 4 to 6 grams (divided into 2 or 3 doses); the head is often missing but relapses did not always occur (though I did observe these in the case of Botriocephalus). The segment is sometimes torn and the individual proglottides highly contracted. Repeated use would probably bring sure success.

With Ancylostoma, thymol has also proven very effective as long as the appropriate preparation measures are taken (see Volkmann’s Sammlung klin. Vortäge no. 365). I have also seen equally firm results with Rhabdonema, though one cannot be fully certain, most likely due to the habitat conditions mentioned. Ascaris are wholly expelled, if necessary through repetition of the dose. In the case of Trichocephalus, the eggs completely disappeared from stools during various trials, thus proving that thymol is effective even in the cecum. In other cases, the treatment was not successful; the treatment was of course only continued when other intestinal parasites were present. Thymol treatment often leads to elimination of Oxyuris as well, and it seems to be the most effective among oral medicines. If used in combination with purgatives, it should lead to a total cure, which is hard to say about other medicines.

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11 Collection of clinical conferences by Volkmann [T.N.].
It can thus be seen that thymol is categorically efficacious; any failures are probably due to insufficient contact with the parasites. If simple contact can be assured, there does not seem to be any reason why intestinal trichinae should be the only parasites able to resist its effects. It is not at all likely that they are especially resistant. Moreover, treatment may be repeated or continued, which of course increases the prospects of success. I have not seen adverse effects, even when using it for a number of days. I would, however, recommend that the patient’s urine be tested for albumen daily.

Thymol is quite like Extractum filicis alber in terms of its efficacy; good preparations of the latter seem superior to it from a number of angles (Taenia). In many places, however, such preparations are hard to obtain, a fact which, taken in conjunction with insufficient preparation of the intestine, may explain the failures observed so far. An inherent immunity of intestinal Trichinae also seems unlikely in this case. Extractum filicis may also be treated during several days; compliance with the same recommendations applicable to ancylostomiasis are decisive. I will refer to my detailed description in the references above.

These two drugs exhaust our list of universally effective anthelmintics. At most, the obsolete Oleum chaberti and kamala12 might be mentioned, which are said to affect A. caris, in addition to their effect on Cestodea. In kamala the effects also seem highly dependent on the quality of the product; perhaps it is for this reason that we as yet have no definitive guarantee in treating Ancylostoma and Trichinae.13 Of the rest of the drugs that have proven efficacious against tapeworms, we may place some hope in benzene14 and turpentine oil.15 However, neither have presented guaranteed results to date, and it would appear that they will only be effective if used in a modified way.

Among medicine that is efficacious against tapeworm, santonin, in combination with calomel, has produced only a few positive results in cases of ancylostomiasis, but as a rule has proven wholly ineffective. The possibility of achieving better results by using keratin-coated pills or by directly introducing it into the intestine cannot be entirely excluded. On the other hand, the other medicines used against Acsaris show no particular promise; in part, it is hard to obtain them in such conditions that they will be effective.

We can make no recommendations about the other substances which, not being considered vermifuges, are noxious to lower organisms. If directly introduced into the intestine, some of them might prove effective, but precisely because of their toxicity, they may only be administered in restricted doses. Picric acid and its derivatives (first recommended by Friedreich) are no longer considered efficacious. Antipyrine and acetanilide may be useful for symptomatic treatment of trichinosis.

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12 The glands and hairs of the capsules of Mallotus philippinensis, an East Indian shrub. It is purgative, and is used mainly against Taenia and lumbrici. [E.N.]
13 Camala and calomel are also recommended by Davaine, cit. [A.N.]
14 Tested by Mosler and other authors. [A.N.]
15 This is supposed to be effective against Ascarides and, in veterinary medicine, against several roundworms (see Davaine cit.). [A.N.]
Of all these substances, I would only recommend the first two for experiments on patients, even without preliminary experimentation on animals, and I believe that cautious use would be quite justified. Should they, contrary to my expectations, turn out to be completely ineffective, I believe this negative result would not be an entirely useless step forward in research of Trichinae.

This ends my observations, based on a painstaking examination of the extensive literature. My goal has merely been to lay before practitioners the current state of questions, as I see them. Specialists will have no trouble separating new ideas from common scientific knowledge. Any inadequacies in my presentation will perhaps be excused, for the humane reasons that led me to publish these views. Should my suggestions be considered worthy of experimentation under circumstances more favorable for this purpose (even though running the risk of disappointment), I would feel fully compensated for my frustration in not being able to put this project personally to the test of experiment.