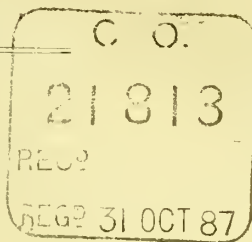


99a
LVII.—1886.

CEYLON. C. O. D.
c



REPORT

ON

ANÆMIA, OR BERI-BERI, OF CEYLON.

BY W. R. KYNSEY,

*Fellow, King and Queen's College of Physicians; Principal Civil Medical Officer and Inspector-General
of Hospitals, Ceylon.*

Ordered by His Excellency the Governor to be Printed.



Colombo:

GEORGE J. A. SKEEN, GOVERNMENT PRINTER, CEYLON.

1887.

CONTENTS.

	PAGE
REPORT	1
APPENDIX.—Translations from the German by J. D. Macdonald, M.D., of—	
(1) Dr. A. Lutz's Treatise on <i>Anchylostoma Duodenale</i> and <i>Anchylostomiasis</i> ...	7
(2) Dr. Schulthess' Contributions on the <i>Anchylostoma Duodenale</i> ...	46
(2) Dr. Erni's Report on the <i>Trichocephalus Dispar</i> and <i>Beri-Beri</i> in Sumatra ...	53

NOTE.

AFTER this report was in print the *Lancet* of July 23 reached me. Drs. Slater and Oliver, of Newcastle-upon-Tyne, describe in it an outbreak of beri-beri on a Chinese transport which visited that port. The symptoms detailed, with the sudden deaths from syncope, or embolism, agree in every particular with the Ceylon disease; and I feel sure if the *anchylostoma duodenale* were sought for they would be found in large numbers. There is also in the same *Lancet* the first of a series of papers on Kakké, or Japanese beri-beri, in which it is apparently shown that a deficiency of nitrogen with an excess of carbon caused the disease; and that an increase in the former element with a diminution in the relative proportion of carbon was followed by a decrease in the number of cases and deaths; that, in fact, beri-beri was a dietetic disease. The same conditions as regards the actual and relative quantity of nitrogen and carbon exist in the food of all the rural population of Ceylon; but beri-beri is never produced unless the *anchylostoma duodenale* are present in the intestinal canal. I have no doubt good food may prevent the development of the serious symptoms of beri-beri, and an increase of the nitrogenous elements will retard them, even when the parasites are present, unless they are in large numbers.

In a very able and suggestive inaugural address by Dr. Walter Dickson, R.N., before the Epidemiological Society of London, beri-beri in its paralytic and dropsical forms is discussed, and the statement is made that its first appearance in the Antilles, Guiana, and Brazil was almost simultaneous with the introduction of cooly labourers from Asia. The foot-note on page 3 of this report refers to the introduction of the disease into Mauritius by the same means, and the worst cases that I have seen in Ceylon were among Tamil immigrants employed on coffee estates. It is highly probable that the cold climate of the estates, and the great range of temperature, from the intense heat of the day to the bitter cold of the night, aid in the development of the dropsical symptoms. The curious and rare cases given in Dr. Dickson's address, which were due to contagion, can be explained by the parasitic nature of the disease.

The importance of the beri-beri question to other countries, as well as to Ceylon, may be judged from the statement in the *Kölnische Zeitung*, as quoted by Professor Maclean, that in the four years from 1879 to 1883, 17,722 soldiers of the Dutch army in the East were under treatment for beri-beri, and the annual loss from deaths and invaliding amounted to 1,100, and more than half the force was unfit for active service from the sequelæ of the disease.

W. R. K.

ERRATA ET ADDENDA.

Page 1, para. 2, line 2, *for* "treaties" *read* "treatises."

Page 2, para. 9, line 12, *for* "kake" *read* "kak-ke."

Page 2, para. 11 (2), line 4, *for* "jegunum" *read* "jejunum."

Page 3, *add* to foot-note || "Cf. article by Sir Joseph Fayrer on Acute Œdema: Beri-Beri. *Medical Times and Gazette*, June 12, 1880, page 631.

Page 4, para. 19, line 23, *after* "development" *insert* "into larvæ."

Page 5, para. 26, line 11, *for* "dyspnoa" *read* "dyspnœa"; line 14, *for* "conjunctiva" *read* "conjunctivæ."

Page 6, para. 29, last line, *for* "figs. D and E" and "figs. M and N" *read* "figs. *d* and *e*" and "figs. *m* and *n*."

Page 6, para. 31, line 4, *for* "jegunum" *read* "jejunum."

Page 7, para. 39, line 2, *for* "nervous" *read* "motor paralytic."

Page 7, para. 42, line 2, *for* "22" *read* "23."

ANÆMIA, OR BERI-BERI, OF CEYLON.

THE object of this report is to point out the existence in Ceylon of the condition known formerly as Beri-Beri, and now usually described as Anæmia, with its ætiology and treatment, and the prophylactic measures which are necessary to prevent its occurrence or spread.

2. The term beri-beri is frequently met with in old returns of disease, and it is described in many treatises on medicine as "the endemic disease of Ceylon"; but in recent years it has ceased to be used, and if most of the members of the profession practising in the Island were questioned on the subject they would probably answer they had never seen a case: still, there is no more fatal disease in the Colony than the form of anæmia, under which name beri-beri is now usually described.

3. The cause of the discontinuance of the term is, that several separate and distinct diseases were included under it. No one reading the old descriptions of the affection can doubt this; but, owing to more accurate knowledge of disease, and more careful diagnosis, cases formerly described as beri-beri are now separated into the different forms of dropsy, paralysis, rheumatism, anæmia, &c. And this also accounts for the difficulty in reconciling the great variety of symptoms recorded by different observers.*

4. It will, I have no doubt, be found on investigation that the "endemic cachexia" of all countries can be resolved into a number of different diseases or conditions. This was the case with the parangi of Ceylon, which included syphilitic and skin diseases, as well as framboesia, or yaws, which is the disease which should alone be included if the term is to be continued in use at all. Many of the so-called sequelæ characterised by ulcerations on various parts of the body, followed by peculiar cicatrices and deformities, have probably little connection with the original yaws, beyond their occurrence in persons who once had that disease; but are caused by lupus or tubercular disease of the skin and mucous membranes in the ill-fed people of the interior, who, for the greater part of their lives, live on innutritious food and drink bad water. With the improvement in both, under the wise policy of the Ceylon Government, in extending irrigation works throughout the provinces where it was most prevalent, the disease is rapidly disappearing. It is of course possible, and even probable, that the original attack of parangi, or yaws, may leave behind it some injury to the skin, which predisposes to lupoid ulceration.

5. After separating the different well-known forms of dropsy, paralysis, rheumatism, and other diseases included under beri-beri, there are left those conditions known as anæmia, the ætiology of which has given origin to a literature of its own; but as to its pathology little advance was made until quite recently.

6. The term beri-beri† is not found in any Sinhalese medical work, nor is it found as the name of a disease in Sanscrit, Páli, or any of the prakrit languages of India, so far as I have been able to ascertain. The Sinhalese word "beri" (බරි) is derived from the Sanscrit "bhara" (भार), meaning a load or weight; the adjective බරි means heavy or weighty. The reduplication would be very heavy, or extremely heavy. "Bé" (බේ), or "beriya" (බේරිය), or "behé" (බේහේ) are different forms of the same word, and mean that a thing or work is heavy or difficult, or cannot be done. It is used in the sense of being unable to do a thing from weakness. According to Marshall, natives in his time, when confined to bed used the following expression in a tone of great agony: "*Mata bé,*" or "*Mata beri*" (I am unable). To render the word more intensive, it is sometimes repeated as *bé bé, beri beri*.‡ The Portuguese used *Non pode* in the same sense, or *Non merito pode*. The term as the name of a disease in Ceylon first occurs in Rebeiro's history,§ and it was subsequently used by Dr. Christie for the disease, the leading symptoms of which were anæmia, numbness and feebleness of the limbs, disinclination to move followed by œdema and general anasarca.

7. The term beri-beri of the Malayan Archipelago means "sheep," from the persons affected walking like sheep. This disease was first described by Bontius, a Dutch physician of Batavia, thus:—"Affectus quidam ad modum molestus hic homines infestat qui ab incolis beri-beri, (quod ovem sonat) vocatur. Credo quia quos malum istud invasit nictando genibus ac elevando crura tanquam oves ingrediuntur. Estque species paralyseos seu potius tremoris: nam motum sensumque manuum ac pedum immo vero aliquando totius corporis depravat ac tremere facit.....Quamvis autem hoc malum plerumque per gradus ac pedetentim homines invadat, tamen aliquando valde subitum est.....Porro signa hujus mali aspectu obvia sunt. Adest enim spontanea universi corporis lassitudo; motus ac sensus præcipue manuum ac pedem depravatur, ac hebescit: ac in iis sentitur plerumque titillatio talis quædam, qualis in Patria frigida ac hyemali tempestate manuum ac pedem digitos corripit, nisi, quod hic

* Professor Aitken, in his well-known work on medicine, remarks:—"The name beri-beri was given by the Malabar physicians, and has been handed down to us by writers on Indian diseases as a name for almost every fatal disease of debility, paralysis of various kinds, reflex paraplegia, dropsy, anasarca, cachexia, scurvy, and anæmic rheumatism, with various diseases of the heart and pericardium, which have all at some time been included under the common name of beri-beri."

† The information relative to the term beri-beri was kindly obtained for me by Dr. S. Fernando, my Office Assistant, from two learned Sinhalese gentlemen, Baṭuvantudāve Pandit and Mudaliyār Bartholomew Gunasékara Pandit.

‡ "Medical Topography of Ceylon" (p. 208), by Henry Marshall, Surgeon to the Forces. London, 1821.

§ "History of Ceylon," by Captain John Ribeiro. Translated by the late G. Lee, Postmaster-General of Ceylon.

tantus dolari non adsit. Tum etiam vox aliquando ita impeditur, ut aeger vix articulate loqui possit: quod mihi ipsi accidit, dum hoc morbo laboranti vocis sonus per integrum mensem tam exilis esset ut me vel proxime assidentes vix intellerent."*

8. It will be seen that the Ceylon disease and that described by Bontius are different, the leading symptoms of the latter being paralysis or tremor: in the beri-beri of Ceylon there is no true paralysis nor tremor that I have seen. There are numbness and feebleness of the limbs, and a disinclination to move,—a paresis, or "slackening of strength,"—but no more: the patient seems to be constantly saying, "Let me alone, and I shall be satisfied." And I have no doubt he thinks so. The term beri-beri of Bontius is of Malay origin, and the paralytic symptoms described by him and by Marshall† attacked the Malay soldiers. It is therefore very probable that these men in Ceylon used the word beri-beri as they did in their own country, and it became confused with the beri of the Singhalese expression of weakness. Herklots, who wrote on the disease in India, derived the term from the Hindustani word "bharbari," meaning "œdematous swelling."

9. On reading descriptions of beri in other countries (the Straits, Japan, Brazil) after the time of Bontius, and comparing them with the Ceylon and Indian disease, the only essential difference is the prominence given to the paralytic symptoms. In the beri-beri of Ceylon, as I have previously stated above, while there is paresis and difficulty of locomotion from weakness and the œdematous condition of the feet and legs, there is no true paralysis. This shall be alluded to again.

Dr. Aitkens gives a classification of Dr. Paterson, of Bahia (Brazil), where the disease is prevalent, in which three forms are given:—

- (1) Where dropsy is the prominent symptom.
- (2) Where paralysis is the leading feature.
- (3) The mixed form, where dropsy and paralysis are equally prominent.

In Japan, where the disease is known as "kake," a distinction is drawn between the "dry," or paralytic, and the dropsical, or "wet." The latter is essentially the same as the Ceylon disease, and we now know its cause; but affections in this country where true paralytic symptoms are present, can be resolved into well-known forms of cerebral, spinal, or peripheral paralyses, and I cannot help expressing the belief that the same will be found to be the case in other countries, after careful investigation.

10. The winds known in Ceylon as the "long-shore" and "land wind," which are very dry and disagreeable, and probably at certain times charged with malaria, give rise to rheumatic attacks with partial and temporary loss of power. This was alluded to by Dr. Lind, as quoted by Marshall in his account of the diseases incidental to strangers in different parts of the world. He says:—"Barbiers (evidently beri-beri) is a species of palsy, a disease most frequent in India. It distresses chiefly the lower class of Europeans who, when intoxicated with liquor, frequently sleep in the open air exposed to the land winds. Its attack is generally sudden, and entirely deprives the limbs of their motion: sometimes all the extremities of the body are affected; sometimes only part of them."

Dr. Macdonald informs me that when he was Port Surgeon of Colombo, sailors frequently complained of similar attacks after sleeping in the open air on deck; and I was also informed that in our prisons, before the introduction of cots, when the prisoners slept on the cold ground, such attacks were not infrequent.

11. There are at least two principal forms of anæmia included under descriptions of the beri-beri of Ceylon:—

(1) That form which is the result of malarial poisoning. There is in such cases a distinct history of attacks of malarial fever, or of residence in a malarial district where such attacks are common in persons using improper or innutritious food. The symptoms are extreme debility, impoverishment of the blood, invariably accompanied by enlargement of the spleen, often followed by dropsy, and rarely by paralysis, which apparently depends on functional disturbance of the spinal cord, is rapidly developed, is intermittent, and quickly disappears by removal from the malarial district and by the administration of anti-malarial remedies.

(2) That form with which this paper is mainly concerned, and which depends on the presence in the intestinal canal of parasites, mainly of the *anchylostoma duodenale* and possibly of the *trichocephalus dispar*, both nematoid worms, the former occupying the duodenum and upper part of the jejunum, the latter the colon and cæcum, both being conveyed into the system by impure drinking-water. The form of anæmia is an oligo-cythæmia, or an oligochromocythæmia, the result of loss of blood.

* Jacobi Bontii in "Indiis Archiatri de Medicina Indorum," edito ultima. Parisiis, MDCXLV. (Cap. I.—De paralyseos quadam specie quam Indigenae Beri-Berii vocant.)

The following will express what Bontius meant:—Men here are affected with a certain painful disease, called by the natives beri-beri (a word that means sheep). I fancy it is so named from the fact that those it affects walk like sheep, staggering on their knees and raising their thighs. This is a sort of palsy, or rather tremor, for it impairs the moving and feeling powers, not only in the hands and feet, but even sometimes in the whole body, and it occasions trembling.....The invasion of this malady is in most cases gradual: yet sometimes its attack is sudden.....Now, the symptoms of this malady are easily observable. First, a sudden sense of weariness comes over the whole body: the power of motion in the hands and feet is impaired, and the sense of feeling blunted, and a tickling sensation is experienced, not unlike to, but less sharp than, the pain felt in our cold climate during winter time in the fingers of both hands and feet; and lastly, the speaking organs become so impeded, that the patient can hardly articulate. This happened to myself when suffering with this disease: my voice was so feeble that it could hardly be heard by persons sitting near by.

† *Op. cit.*, page 161, chap. iii. (Of a particular kind of Palsy.)

12. It was long suspected that beri-beri was due to a parasite. Sir Joseph Fayrer* suggests that a similar hæmatozoon to the nematoid embryo found in the blood of persons suffering from chyluria might be the cause of beri-beri. Dr. H. Erni, in his contributions to the beri-beri question,† reports the results of post-mortem examinations made on the bodies of persons who died of beri-beri in Sumatra. The anchylostoma duodenale was found in the upper part of the alimentary canal, and the trichocephalus dispar in the cæcum and colon: he regards them as "genuine parasites living at the expense of the blood of their host," and causing extensive lesions in the intestinal canal. He remarks:—"In more than fifty post-mortem examinations of beri-beri I have never missed these intestinal lesions, whilst they do not occur in patients dead of other diseases. The parasites are indeed to be met with also in such, but without any lesion of the intestine. This makes me assert that beri-beri is helminthiasis, the cause of which is the destructive process in the intestinal canal caused by these parasites. Reflex symptoms arise from the lesions, whilst through the loss of blood and impaired digestion anæmia occurs. This chronic anæmia has, in its turn, a deleterious effect upon the different organs, and degeneration of the heart with atony, and dilatation of the blood vessels, particularly of the aorta, result. Finally dropsy supervenes, œdema of the ankles, feet, legs, and face, &c., as well as hydropericardium, less seldom ascites; and death results from œdema of the lungs and paralysis of the heart. Should the patient survive the dropsical stage, general symptoms of atrophy, the atrophic stage, set in."

13. The influence of various intestinal parasites in the production of anæmia has recently claimed much attention; and I believe it will be found a more successful field of investigation in this condition than the search after bacteria. Herr Runeberg ("Berliner," Klin, Wochenschrift, October 4, 1886) brought forward cases before the meeting of German scientists in support of the view, that the presence in the intestine of the bothriocephalus latus was a cause of pernicious anæmia, and was cured by the exhibition of anthelmintics. Hirsch ("Geographical and Historical Pathology") gives a quotation, that children sent home from Ceylon often have bothriocephali. This parasite is, I believe, unknown in the Colony, which is remarkable, as a large proportion of the population live on fish.

14. The trichocephalus dispar, known as the "whip-worm," is found principally in the cæcum, often in large numbers. Davaine calculated that one-half the Parisians were infested by it;‡ but Cobbold remarks, that "clinically its importance by no means corresponds with its prevalence." Mr. Gibson§ gives a case of paralysis, with loss of speech, from the intestinal irritation of the trichocephalus dispar, in a female child aged six. After treatment she passed several chamber-vesselsful of trichocephali, with a gradual disappearance of the paralysis. This parasite is common in the bodies examined in Ceylon, and I am inclined to believe its influence in the production of disease has been on the whole under-estimated.

15. There can be no doubt about the deadly effects of the anchylostoma duodenale on the system, when present in large numbers. The disease known as "Egyptian chlorosis" and the anæmia of the workmen employed in the construction of the St. Gotthardt tunnel, and in mines, are caused by the presence of this parasite; and, in my opinion, anchylostomiasis and the beri-beri of Ceylon are absolutely identical: are, in fact, one and the same disease.||

16. It is very probable that the benefit derived from the use of the preparations alluded to by Professors Aitken and Maclean, under the names of "Oleum Nigrum" and "Treak Farrook" (and of purgatives), in the treatment of beri-beri, is due to their anthelmintic properties, both containing turpentine or some similar drug.

17. Anchylostomiasis is the only disease in Ceylon which meets the descriptions of beri-beri. The definitions and description of beri-beri given by Sir Joseph Fayrer in Quain's Dictionary, by Professor Aitken in his "Practice of Medicine," and in the classical lectures of Professor Maclean, stand for anchylostomiasis, the word paresis, feebleness or weakness, being substituted for paralysis; and as regards the symptoms, the elaborate treatise of Lutz, translated by Dr. Macdonald (annexed to this report), should leave no doubt in the minds of the most sceptical.

18. Both are most prevalent in the tropics, but may and do develop beyond these regions: both prevail most extensively in seasons characterised by a high degree of atmospheric moisture and temperature: both are most prevalent on the sea-coast and along the banks of great rivers, dampness, wetness, or swampiness being the characteristics of the soil; but there is no connection with malaria. The areas or centres where both prevail are often narrowly circumscribed, while adjoining districts with the same climatic influences escape: both attack bodies of men collected together under bad hygienic conditions, and those of strong physique are equally liable to be attacked with the weak, but those living on innutritious food, or food not corresponding to the metabolism and blood-making, or to the needs of the body, such as rice and dried fish,¶ suffer the most severely: both are due to the use of bad drinking-water, and both recover if the anæmia has not advanced too far, on leaving the focus of the disease and changing the mode of living, particularly by the use of nutritious blood-forming food: both attack at all ages, but adults and males are more frequently affected than females or very young children; but the latter frequently suffer when crowded in schools or reformatories with bad sanitary arrangements. In

* Beri-beri in Quain's "Dictionary of Medicine," page 104.

† "Berliner Wochenschrift," No. 37, of September 13, 1886. Translated in Appendix.

‡ Quain's "Dictionary of Medicine": article on Trichocephalus, by Dr. Cobbold, page 1659.

§ *Lancet*, vol. ii. for 1862, page 139.

|| The outbreak of "acute anæmic dropsy" in Mauritius, reported upon by Dr. Davidson in the *Edinburgh Medical Journal* for August, 1881; and the outbreak of the "New disease" in Calcutta, recorded by Dr. Macleod in the *Indian Medical Gazette*, were no doubt anchylostomiasis, or the dropsical form of beri-beri, or the beri-beri of Ceylon.

¶ Hirsch's "Handbook of Geographical and Historical Pathology," vol. ii. New Sydenham Society edition.

both, predisposition increases with the length of time spent at the focus of the disease, and a residence of some months is necessary before the disease is developed; and as regards race, the natives suffer more than Europeans, but the latter living under the same conditions as the natives suffer equally. In both, the *anchylostoma duodenale* is found: in mild cases in small numbers, in severe cases in large numbers; and in old atrophic cases there is evidence they were present, although none are found on post-mortem examination: neither are communicable from person to person. In both, anthelmintic remedies give relief or cure, and in both sudden death, so prominently alluded to in old descriptions of beri-beri, and by Professor Maclean, is appallingly frequent.

19. The comparatively more frequent occurrence of beri-beri among men as compared with women and children, is because adult males come more in contact with the sources of infection by working away from home on brickfields, mines, roads, and paddy or rice fields, where they drink impure water. Women and children, if equally exposed, would contract the disease. If the men of a family are alone infected, it points to the source of infection being outside the dwelling; if all the members of a family suffer, the source of infection is close by. The difference in the effects of the parasites on women and children depends on the number present in the intestines, the amount of work, and the nature of the food. Race offers no immunity: Europeans suffer equally with natives,—this was so in the army in Ceylon in the old pre-sanitary period. The occurrence of the disease on board ship is due to the fact that the men come on board with the parasites, or contract these on board from impure drinking-water. In the first case, the disease used to break out when the men began to feel the effects of deficient or bad rations. The women and children suffered less, or not at all, because they had fewer or no parasites. The difference in the effects of the parasites in the tropics and in Europe is one of degree, and depends on their number and the nature of the food. The rapid recovery in recent cases on leaving the focus of the disease is due to removal from the sources of infection combined very frequently with better living. The embryos of the *anchylostoma* develop more rapidly in rainy weather, when the temperature is between 25° and 30° C., and the atmosphere moist: a lower temperature delays or stops the development altogether. They develop well in moist earth: consequently, in seasons and places where these conditions exist, persons are most frequently attacked; a cold dry season often brings an outbreak to an end. The disease is frequent along the banks of rivers, particularly those liable to overflow their banks, as the ova are carried away from their source and deposited in shallow places, where they undergo development and gain entrance into the human system in the water used for drinking.

20. In this report it is only necessary to give a brief description of the parasite and the disease produced by it, and a summary of Lutz's observations: for fuller details I must refer to his admirable and exhaustive treatise, which leaves nothing to be desired.

The *Anchylostoma duodenale*, or *Anchylostomum duodenale*, or *Sclerostoma duodenale*, or *Dochmius duodenalis*—Lutz adopting the first form—was discovered in Milan by Dubini, in 1838. It belongs to the genus *Dochmius*, order Nematodes, family Strongylidæ, and, along with the order Acanthocephala, forms the class Nematelminthes. The disease produced by its presence is called anchylostomiasis, or anchylostomoses.

21. It is scarcely possible to mistake the *anchylostoma* for any other human parasite. "The form of the body is fairly compact, cylindrical; the length exceeds the breadth twenty times; whitish ash-coloured, reddish, or black. The head is plainly seen bent towards the dorsal side. The posterior extremity is not bent—is pointed in the female and broad in the male; length varies from 6 to 15 mm. The smallest female observed was 7 mm. in length, the largest among several hundred 15 mm." Leuckart found the length of the female 10 to 12 mm., rarely 18 mm.; the greatest thickness 1 mm. He found the male 6 to 8 mm. in length, rarely 10 mm. They are found in the upper part of the small intestines in the duodenum, and particularly in the upper part of the jejunum, where they avoid, according to Bilharz, the direct effect of the bile.

22. By suction the blood is taken into the intestines, and, according to Grassi, it is probable it is again evacuated, more or less unchanged, when a new supply is taken in. "The worm apparently lives on the blood plasma without interference with the blood corpuscles, so that an absorption, not a digestive process, occurs. It becomes as it were an addition to the vascular system of its host, whose blood circulates in it." Lutz makes the following calculation of the loss of blood from the suction of these parasites:—"Supposing even the daily requirements of each only amounted on an average to one drop, which probably is too small an average, the daily loss caused by five hundred worms would amount to 20 grammes (5 drachms), which, considering the rich supply of nourishment this blood contains, is sufficient in time to cause a pronounced form of anæmia. Five hundred *anchylostoma*, the intestines of which are empty, weigh 2 grammes, and double this probably when full of blood. Now, supposing this blood is renewed every two hours,—a supposition which has nothing impossible about it,—the loss is seen to be considerable." "The parasite bites its way into the mucous membrane, pierces the submucous cellular tissue, and subsists on the blood. After its removal there remains an ecchymosis, the size of a lentil, the centre of which presents a white spot of the size of a pin's head with a fine hole; out of these wounds blood oozes into the intestinal cavity." (Wagner.)

23. The larvæ of the *anchylostoma* are found wherever there are accumulations of fæces, on moist, uneven ground containing water, in localities occupied by men and animals where there are no latrines, or badly constructed ones. Such conditions exist in the villages of Ceylon, and on many of the coffee estates, and in such, a number of the inhabitants are found to suffer from anchylostomiasis. The number of larvæ is found to be enormous, and, according to Lutz, may be counted by millions. The larvæ find entrance into the body in the drinking-water, or from the soil itself, or from soiled vessels or clothing. Labourers who take their meals on the spot, and carry their food to their mouths with soiled fingers; children, after crawling on the dirty ground on their hands carry them to their mouths and become infected.

24. A few anchylostoma present in the intestines may give rise to slight or no symptoms at all, and even many may not be felt for a time if the food is good and varied; but should the infected person become weakened by illness, such as an attack of ague, or exposed to bad food, as often occurred in old days on board ship, severe and even dangerous symptoms may rapidly develop: the number of parasites present may vary from a single worm to upwards of three thousand. It has been established by Lutz that the presence of five hundred produces severe disturbance even in the strongest adult, and if the individual be unfavourably placed as to diet and bad hygienic surroundings, a much smaller number will do the same. He adds: "The idea that the worms are not the cause but the consequence of the disease seems, after all our pathological experiences, rather an unintelligible anachronism. To retain such an idea, knowing what we do of its mode of development, its mode of infection, and its mode of living, would be something strange." The variety and severity of the symptoms in anchylostomiasis depend mainly on the number of parasites present. Sometimes severe symptoms are coincident with the presence of a few parasites. Lutz states that when this is the case we have to do with old cases in which the anchylostoma had either been expelled or disappeared in the course of time. In children a few parasites often give rise to severe symptoms.

25. The symptoms of anchylostomiasis may be divided into three stages:—(1) the dyspeptic; (2) the anæmic; (3) the dropsical.

26. The patient very often looks robust, with a fair development or even an increase of subcutaneous fat,—so much so, that on superficial inspection there are no signs of illness. He will probably state he always enjoyed good health, and never had malarial fever, but that for some time past his strength has been gradually failing, and that the least effort fatigues him; he feels weary and sleepy, and is unable to work. His appetite has not diminished, and may even be increased, and is frequently perverted by a desire for unripe fruit or vegetables or uncooked food. Among children, geophagy is common, and even among adults it is not unknown. He complains of disturbance of digestion with pains increased on pressure in the right and left hypochondria, and at the ensiform cartilage, meteoric distension of the abdomen, flatulency, nausea, vomiting, and the bowels are either obstinately constipated or there is constipation alternating with diarrhœa. In the anæmic stage there is cardiac pain with palpitation and dyspnoea on exertion. Lutz attributes the cardiac pain to exhaustion of the heart, and classifies it with the pain felt after violent walking, riding, or rowing. The face has usually a yellowish tint; the eyes are bright, and the conjunctiva pale and bloodless to a remarkable degree, well seen on everting the lower lids. There is well-marked pallor of the mucous membrane of the mouth and tongue, which strikingly contrasts with the apparently good condition of the patient. If the disease is not recognised and treated, œdema of the face and extremities sets in, occasionally attended with a certain amount of fever. He now complains of giddiness and dimness of vision, with a tendency to syncope on sitting up, headache, tinnitus aurium, muscular pains, and inability to move, or even partial loss of power over the limbs with numbness. This weakness no doubt results from the diminished supply of blood, and the supply of watery blood to the cord. It is similar to the weakness of the extremities in aortic regurgitation, or it may be due to peripheral irritation, and in advanced cases from effusion into the spinal canal. There will frequently be found an anæmic murmur at the base of the heart, or even heard over the whole cardiac region and in the vessels of the neck. If the disease still further advances the dropsical stage sets in, there will be effusion into the pleuræ and pericardium, hæmorrhage from the bowels, troublesome diarrhœa, and death, which frequently occurs in an appallingly sudden manner, just as described in the old reports of beri-beri and by Dr. Maclean in his lecture on this disease. If the disease becomes chronic, there is emaciation with disappearance of the subcutaneous fat. Anæmia of varying degrees of intensity, cardiac hypertrophy, and dilatation, with fatty degeneration, dropsy of the extremities, abdomen, &c., with intestinal hæmorrhage. Children suffering from anchylostomiasis for years during the developmental period are small and puny, and at twenty-five years of age look like children of ten or twelve.

27. In chronic cases with atrophy and weakness the latter no doubt depends on peripheral irritation and anæmia of the cord, which is brought about in anchylostomiasis by the quality and quantity of the blood-supply dependent on the disease, and possibly on spasmodic contraction of the vessels caused reflexly or from the fluid effused into the spinal canal.

28. The complications enumerated by Lutz are diarrhœa, intestinal hæmorrhage, malaria, struma—other intestinal parasites, those generally present being the trichocephalus dispar, ascaris, lumbricoides, oxyuris vermicularis, and anguililla—chronic catarrh, pulmonary tuberculosis, epilepsy, arthritic rheumatism, and chronic ulcers, under any of which anchylostomiasis may be, and I have no doubt has been returned. It is the presence of complications and the non-recognition of the effects of the anchylostoma which have hitherto prevented a more accurate knowledge of the disease.

29. The diagnosis of anchylostomiasis can be made with great certainty by attending to the following points:—

(1) The history of the case, with the peculiar anæmia.

(2) The red blood corpuscles are diminished in number: in some cases to one-fourth or one-sixth the normal. The hæmoglobin is said to be reduced in the same ratio. The ratio between white and red corpuscles persists for a long time, but ultimately the former become comparatively more numerous, without, however, any actual increase in their number.

(3) The detection of the ova in the fæces. As the ova of the anchylostoma are, as a rule, uniformly distributed throughout the fæces, they are found with the greatest ease by taking a small portion of the fæces, diluting it, if necessary, with distilled water, and placing it on the microscopic slide,—a quarter-inch object glass is required. The ova of the anchylostoma are easily distinguished from those of the trichocephalus dispar and the ascaris lumbricoides, which are

also frequently present. The ovum is oval, with a very thin shell and often a clear space between the wall (outline of shell) and the contents. It is always found in a state of segmentation, but only in the primary stage, there being no more than three or four segments present. If the ova be kept in a drop of water in a moist atmosphere for from twenty-four to forty-eight hours, the embryo is seen formed within the shell, and may be often observed in the act of passing out of it. Besides the form of the ovum, there is also a distinguishing characteristic, as the ova of the ascaris and trichocephalus have during this time advanced but little in the process of segmentation. The ovum of the trichocephalus dispar is further distinguished by the prominence at the extremities and that of the ascaris by the striated thickness of the shell. The differences in the segmentation of the ova can be seen figured in the plate attached to Lutz's treatise, figs. D and E, and the formation of the embryo in figs. M and N.

30. The prognosis is a matter of much difficulty and uncertainty. In mild cases, when the parasites are expelled, and there is no danger of re-infection by the patient's removal from the place where he contracted the disease, and the anæmia yields to treatment, recovery is secured; but where the disease has not been recognised in its early stage, a fatal result often ensues from the direct effects of the parasites. Where there is anasarca, or intercurrent disease, or where there is hypertrophy with dilatation of the heart and advanced cachexia, the prognosis is very unfavourable; still, with careful treatment, the worst chronic cases often improve. Recovery is to be looked for in the severest acute cases. Relapses are frequent when patients return to their former homes and mode of life, and such cases are difficult to cure, frequently become chronic, and end fatally from the anæmia caused by the parasites or from some intercurrent disease. In no disease is it more necessary to recognise the condition in its early stage and to adopt immediate treatment.

31. On post-mortem examination the anchylostoma may be found either attached to the intestinal wall, "adhering firmly to the mucous membrane," if the examination be made soon after death, and loose in the mucus if made later. The parasites are found in the duodenum and jejunum, and they may be found even in the ileum, or single worms in the stomach or cæcum. Hæmorrhagic spots are also present. Depressions or small lesions are found the size of a millet-seed on the mucous membrane, which may represent the original position of the worm. There is increased mucous secretion. The liver and spleen are, as a rule, normal or atrophied, and the former often in a state of fatty or amyloid degeneration. The kidneys show similar changes. Wucherer describes the pancreas as enlarged. The parenchyma of the heart is flabby and anæmic, and the whole organ may be normal, or dilated, with or without hypertrophy. A high degree of anæmia is always present, visible in the pallor of the skin, muscles, meninges of brain, spinal cord, and organs. Extensive dropsy of the thorax and abdomen with œdema of the brain and spinal canal. The subcutaneous fat is, as a rule, well developed, but in old chronic cases it may be diminished.

32. Lutz makes the following four conclusions:—

- (1) With the presence of the anchylostoma duodenale there are met with in the intestines local lesions, consisting of small and large hæmorrhages in and under the mucosa.
- (2) In a number of cases there were found changes in the mucous membrane of the stomach and bowels, which must be looked on as chronic catarrh with increased mucous secretion.
- (3) As a result of the local processes, there have been observed poverty of blood, which is frequently accompanied by dilatation and hypertrophy of the heart.
- (4) The whole organism suffers from disturbed nutrition. This malnutrition of the whole system manifests itself in the individual organs by atrophic and degenerative changes.

33. It should be always borne in mind, that, curable as the disease is, if taken in hand in time, by removal of the parasites from the intestines, and by the prevention of fresh infection, still in many cases there is little improvement even after the disappearance of the parasites. This occurs in long-neglected cases, where cardiac changes and other complications have supervened; but in recent cases, after removal of the parasites the anæmia is easily cured by suitable treatment: but if the anchylostoma be allowed to remain, no treatment has any effect on the anæmia.

34. The treatment is to be considered under two heads, (1) the expulsion of the parasite; (2) the treatment of the anæmia, and complications, should any exist.

35. The expulsion of the worm is the first object. Several remedies have been tried, but there are only two really reliable, and in practice only one. These are—(1) Thymol (acidum thymolicum), and (2) perfectly fresh pure oil of the male fern. Thymol may be considered a specific. In the Colombo Civil Hospital Dr. Macdonald has obtained excellent results with thymol, and now he uses nothing else. This treatment was introduced by Bozzolo, and he gave it in from 30 to 150 grains in three to six doses in the day. The effect can be watched by counting the worms expelled, and seeing the discontinuance of the ova from the stools. Lutz's treatment is as follows: He prepares the bowels by the administration of a dose of calomel and podophylin, or calomel and senna. This is absolutely necessary to remove the profuse mucous secretion in the intestines, which protects the worms, and prevents the thymol coming in contact with them. The following is the prescription he recommends:—

R/ Calomel ... grs. viii.
 Extract of Senna ... grs. xxx.
 Divide in pil. viii.

S. Two to be given every hour till the bowels move *freely*.

Dr. Macdonald gives the calomel in these doses, but uses the ordinary infusion of senna instead of the extract. The first dose is given two hours after the midday meal,—he allows a

sufficient light nourishment. The bowels are, as a rule, freely moved during the evening, and all action is over by midnight. In the early morning the thymol is given in thirty-grain doses, and repeated at intervals of two hours two or three times. Coffee or soup may be allowed during the intervals, and two hours after the last dose the patient may have his usual meals. After some hours the patient has a fluid stool; if not, a mild aperient is to be administered. The above doses are to be modified for children. Should diarrhœa exist, the senna may be omitted. The thymol may be given in gelatine capsules of fifteen grains each for adults and seven grains for children, the capsules being loosened by pressure before administration. It may be given without any covering, but its taste is unpleasant, and it acts as an irritant, never as a caustic. The objects aimed at in this treatment are—to clear the bowels of mucus, to prevent absorption of the thymol, and to bring it in direct contact with the parasites. The treatment, Lutz states, is perfectly safe, as he has given doses of 150 to 180 grains to children of twelve and thirteen, without any bad effects. For the anæmia which remains after the expulsion of the parasites, iron should be administered, and Lutz considers the *Liquor Ferri Perchl.* the most suitable, in doses of five to ten drops in water three times a day. Good nourishment is essential, and it should be given in the most digestible form—such as eggs, milk, and extract of beef. Dropsy and cardiac symptoms are to be treated on general principles, and Lutz strongly recommends the free use of *digitalis* as being next to anthelmintics, the most effective remedy.

36. The prophylactic measures to be adopted resolve themselves into—

- (1) Removal from the infected area, so as to avoid re-infection.
- (2) The use of pure drinking-water after filtration.
- (3) Good food.
- (4) Good sanitary arrangements; cleanliness; latrines (where none exist), so as to prevent fæces being scattered over the soil, and getting into the drinking-water; the prevention of over-crowding in prisons, schools, and reformatories, with the early detection, removal, and treatment of infected persons.

37. In all obscure cases of anæmia followed by dropsy and the peculiar train of symptoms included under beri-beri, occurring in prisons, barracks, or on board ships, I strongly recommend a search to be made for the *anchoylostoma duodenale*. The disease may not originate in these places, but breaks out when previously-infected persons are exposed to poor food, bad hygienic conditions, and severe work with mental depression.

Summary and Conclusions.

38. That the "wet" or "dropsical" form of beri-beri, or the beri-beri of Ceylon, depends on the presence of the *anchoylostoma duodenale* in the intestinal canal: is, in fact, *anchoylostomiasis*.

39. That while weakness, feebleness, or even numbness are present or follow the Ceylon disease, there are no true nervous symptoms. The paralytic form is not known, nor, so far as I have been able to ascertain, is the Ceylon disease followed by paralysis. The cases end in cure or death, or old chronic cases in atrophy with feebleness. In the beri-beri of other countries paralytic symptoms are present from the beginning or follow the dropsy.

40. That the Ceylon disease may run an acute or chronic course, and that death is often appallingly sudden. The severity of the symptoms depends on the number of the parasites present in the intestines, the state of health, and the food.

41. That residence in an infected centre is necessary before the symptoms become fully developed. During this period the person is acquiring the parasites, and losing blood from their presence, becoming anæmic and finally dropsical if neglected.

42. That the areas in Ceylon where this form of anæmia or beri-beri is prevalent will be found to present the conditions enumerated in paragraph 22, and that the cause will in all cases be the presence of the ova of these parasites in the drinking water.

43. That the disease, if recognised early enough in the dyspeptic or anæmic stages, yields readily to treatment; but if the cases are neglected and dropsy sets in with degenerative changes in the heart and other organs, the prognosis is most unfavourable.

44. That removal from the infected area, with instructions not to return to it, is essential. The best remedy for the expulsion of the *anchoylostoma* is thymol, and for the anæmia iron followed by *digitalis* or *strophanthus*. But no treatment will do good until the parasites are expelled.

W. R. KYNSEY, F.K.Q.C.P.,
Principal Civil Medical Officer
and Inspector-General of Hospitals.

APPENDIX.

ANCHYLOSTOMA DUODENALE AND ANCHYLOSTOMIASIS.

(Translated from the German of DR. ADOLPH LUTZ, by DR. J. D. MACDONALD, of the Ceylon Medical Department.)

ONE of the most important functions of medical research is to separate, out of the mass of observations daily accumulating, certain symptoms occurring constantly among otherwise varying forms of disease, and so constitute out of these unities representing distinct diseases. Even

among nations but little cultivated this practice has obtained, and to this we owe that at least the common diseases have received popular names from their most prominent symptoms, long before scientific research interested itself in the causes which produced them.

No etiological connection bound together this group, but a valuable collection of observations were made, which rational inquiry dared not ignore, although a proper insight into their nature was still wanting.

Science, it is true, cannot exactly follow the same path, but must, as opportunity offers, now follow the inductive, now the deductive method. The disease scabies was known under various names long before its parasitic nature was recognised, whilst, on the other hand, science had discovered the presence of a microscopic round worm in the human muscles, without suspecting that it therein discovered the cause of many enigmatical symptoms of disease. The comprehension of their etiological connection finally permitted the limitation of the diseased process sufficiently exact, and paved the way for prevention and cure.

This has been the case with the disease anchylostomiasis, and its cause the anchylostoma duodenale, which forms the subject of the present paper.

The various symptoms of the disease, and the parasite which caused these, were studied quite independently of each other; but after a long interval the thorough understanding of the connection between them was brought about by the labours of both classes of observers. This knowledge, however, was not shared by all the observers, and after a brief period of interest in the question the matter was allowed to lie over.

Further interest in the matter had to be aroused to complete our knowledge of the subject: and this interest has been aroused during the last ten years, resulting in the greatest advance in the diagnosis and therapeutics of the disease constituting one of the greatest triumphs of medicine. There is yet some danger that the interest in this disease may again flag, and that the advances made may fall into oblivion.

The reason for this is to be sought in the fact that the disease comparatively seldom occurs in those countries most engaged in scientific research, whilst in other regions more or less remote it is a constant scourge.* This also explains why it is that in Germany no comprehensive treatise containing the details scattered throughout the literature of various other nations has yet appeared. The time now seems favourable to take a comprehensive view of the whole subject.

I would scarcely have undertaken such a task, the difficulties of which are great,—far from all scientific help,—if the opportunities had not been granted me to publish the results of long continued observations made on the disease. The point of greatest interest will therefore be the elucidation of the clinical symptoms of anchylostomiasis observed entirely by myself, and an examination into the local causes which give rise to it in the Brazils. The historical-geographical portion, as well as the pathological anatomy, is taken from the literature of the subject, as I had no opportunity of making observations of my own. In the zoological portion I conform to the ordinary text-books; the history of the development of the parasite is founded on personal observation, having at my disposal the publications of the original discoverer. I have endeavoured to do justice to the merits of each individual investigator by name, always excepting the earliest writers, the quotations from whom are merely facts long the common property of science. I sometimes give explicitly what other authors give implicitly, or overlook a quotation: this is entirely due to the difficulties of so scattered a literature. On the contrary, I hope that the description of my own observations, corroborated as they are by those of others, may be of service in advancing our knowledge. The lacunæ in our knowledge I strove to fill up, or where this was not possible, I have pointed them out as subjects for later research. Knowledge of the characteristics of the parasite, of its development and modes of life, is an essential condition to a proper understanding of anchylostomiasis, of its pathogenesis, therapeutics, and prophylaxis. I begin, therefore, my task with a short description of these.

PART I.—ANCHYLOSTOMA DUODENALE.

Nomenclature.—The parasite in question was discovered in the year 1838 by Dubini, in Milan, and was then named ancylostomum duodenale. The first portion of this name, written now more properly anchylostoma, referred to the shape of the mouth; the second to the locality where it was most frequently found. Neither one nor the other name is quite suitable, because the parasite, a strongylus, may be classified under the genus dochmius, which has the same mouth peculiarities. The second portion of the name, “duodenale,” is more suitable, and may be adopted as the name of the species, as it is already popular. The term “anchylostomiasis” may be retained to represent the symptoms caused by the parasite.

Description of the Genus and its place in the System of Classification.—The genus dochmius belong to the order of the Nematodes, which, with the Acanthocephala, form the class Nematelminthes; a more or less lengthened, cylindrical body, without segmentation, is common to both. They possess neither organs of respiration nor of circulation. The nematodes alone possess, either permanently or at least temporarily, a mouth and intestinal tract, whilst the acanthocephala are distinguished by the absence of these, and the possession of a projecting proboscis bearing a circle of hooks. Among the nematodes the family of the Strongylidæ are distinguished by the possession of a bell-shaped bursa-copulatrix by the male sex. In the genus strongylus the bursa consists of a thin membrane, open on the abdominal side, or closed by a thin transverse band, and protected by a number of fan-shaped ribs, each of which forms a papilla at the margin. At the bottom of the bursa lies a conical organ, out of which two spicula project.

* It is undoubtedly a great scourge in Ceylon.—*Trans.*

The group *Dochmius* Dies is thus characterised by Leuckart :—

“Head bent towards the dorsal surface; mouth wide, and provided with a horny capsule, the abdominal margin of which is longer and more prominent than the dorsal margin. At the bottom of the mouth stand, on the abdominal side, two symmetrical teeth, whilst on the dorsal side, on the same level, a conical point projects, inclined obliquely forwards, and reaching almost the opening of the mouth. The abdominal margin of the mouth-capsule is somewhat thickened (jaw-like) at each side of the middle line, and often armed with strong (more or less hook-shaped) teeth. The dorsal margin likewise carries a similar armature. In the circumference of the mouth there are six rib-like papillæ, which, however, do not project outwards.”

Description of the Species.—Leuckart describes our species in the following words :—

“Body cylindrical, somewhat diminished anteriorly in the male, with conical-pointed head and a bulging mouth-capsule; jaw-like thickenings at the upper margin, each provided with two claw-shaped strong hooks; two, but not so strong, tooth-like projections on the opposite margin (dorsal); throat papillæ pointed and conical; bursa with three valves, the breadth being greater than the length; the tail ribs slit at their extremities, each with three short conical projections, of which the internal are only half the length of the external; five side ribs, of which the three middle possess a common stem, whilst the posterior take their origin from the stem of the back ribs; the anterior side ribs are split throughout their whole length; two thin spicula, like fish bones, of some considerable length. The tail end of the female is conical and pointed; vulva behind the middle point of the body; an anterior and posterior uterus, both of which pass into a very long tortuous ovarium.

Macroscopic Characteristics.—The parasites macroscopically offer the following characteristics. Form of body fairly compact, cylindrical; the length exceeds the breadth twenty times; whitish ash-coloured, reddish, or black. The head is plainly seen bent towards the dorsal side. The posterior extremity is not bent—is pointed in the female and broad in the male; length varies from 6 to 15 mm. The smallest female observed by me was 7 mm. in length; the largest among several hundreds 15 mm. Leuckart found the length of the female 10 to 12 mm., rarely 18 mm.; the greatest thickness 1 mm.; I found the male 6 to 8 mm. in length, rarely 10 mm. The growth does not seem to cease at sexual maturity.

Microscopic Characteristics (Anatomy).—On microscopical examination the following peculiarities are noticed: the cuticula plainly ringed; the mouth-capsule resembling a cupping-glass. (The peculiar armature at the entrance of the mouth is only visible after special preparation.) The long stretching œsophagus with thick walls is provided with six serrated chitinous stripes, the bulging stomach into which it opens, and the roomy intestines, lined with epithelium, running a tolerably straight course to the posterior extremity, where it opens.

Besides this, there is observed, on turning over the animal, two minute conical papillæ directed backwards, placed laterally, one on each side of the neck; on the same level as these stand the opening of the œsophagus, and below a *porus excretorius*, in the middle line. Into these open two spindle-shaped organs running from the dorsal surface, the cervical glands. (Leuckart). Leuckart also describes two glands of the head lying in the middle line.

The male organs of generation constitute a system of tubules, the thin extremity of which, intertwined and tortuous, forms the testicles and seminal ducts, whilst the thick tube opening externally is described as the ductus ejaculatorius. Between these lie the seminal vessels, oval or spindle-shaped, placed in the middle of the body and connected with the ductus ejaculatorius by a fine spindle-shaped canal. The seminal fluid, as I found it after a recent coitus in the body of the female, contained round, oval, or pear-shaped corpuscles, as have been observed by various authors in the other nematodes. These corpuscles are apparently capable of amœboid movements. The female genital organs are formed in a manner analogous to that of the male, but attain to twice their development. These organs consist of ovaries, oviducts, the union of which form the anterior and posterior oviducts, which, twisted in all directions, fill up the body; the two-horned uterus, which also serves as the receptaculum seminis, and of a short single vagina, which opens by a transverse slit on the abdominal side of the body below the middle line. The male genital tubes, forming a cloaca with the intestine, open at the posterior extremity upon a small papilla at the bottom of the bursa, which, on copulation, is fixed to the entrance of the vulva by the introduction into the latter of the two long spicula, so that the sperma may pass directly into the vagina. To effect this purpose, the male embraces the body of the female by means of the bursa-copulatrix. The connection is very firm, and may even continue after death. According to Schneider, the nematodes *in copula* are bound together by an adhesive cement; and, in fact, I have repeatedly observed the occurrence of such a sticky substance on the bursa of the male, and found often a pair in copula without the spicula being introduced, so that the union lasts longer than the coitus required. Among several thousands of expelled worms I found about one pair in copula in each hundred. The mode of coitus was first described by Dubini and Bilharz. Bugnion gives a sketch of a pair in copula.

Distinction from other kinds of Worms.—Even on macroscopical examination it is scarcely possible to mistake the anchylostoma for other human parasites. The young of ascarides, which are however seldom met with, are of a much slenderer build. The females of the oxyuris vermicularis are distinguished by their pure white colour and their long, pointed, almost translucent tail, whilst the tail of the comparatively small male is always coiled on itself. The larvæ of insects which develop in the intestines, or accidentally mix with the fæces, are distinguished without much difficulty. At all events, there is never observed in any other of the parasites the peculiarly bent head of the anchylostoma. (I once considered a mass of small, longish bodies, which I found along with a number of anchylostoma, and which showed great similarity to the

latter, as pseudoparasites. On further examination, however, these were found to be the root-bulbs of feathers, due to the cooking of an imperfectly plucked fowl.)

Mode of Life of the Adult Parasite.—What we know partly from analogy, partly from direct observation, of the mode of life of the anchylostoma, may be summarised as follows:—

The adult animal is found in the upper part of the small intestine of man; rarely and only singly are they ever met with in the stomach or large intestine.

According to Bilharz, Saugalli, Roth, &c., the principal seat is not the duodenum, as Dubini asserts, but the upper portion of the jejunum. According to Bilharz, they avoid the *direct* effect of the bile. If an examination is made soon after death, all the parasites are found adhering to the wall of the intestine (their dorsal surface being turned to the mucous membrane, and their bodies lying in the direction of the chyme). To enable them to adhere, they suck up a portion of the mucosa into the mouth-capsule by means of an elastic membrane at the bottom of the capsule (Perroncito, Carita), and fix it there by means of the pharyngeal teeth-like hooks, whilst the two style-like chitinous points at the bottom of the capsule penetrate the mucous membrane.

Through movements of suction (œsophageal muscles?) the blood *streams* into the intestines. According to observations made by Grassi and other investigators, it is probable that the blood is again evacuated more or less unchanged, and that a new supply is at once sucked in. If the worms are expelled, there is always found a number of worms varying with the drug employed, the dilated intestines of which, filled with blood, betray their mode of living, even to the naked eye. In the body, the parasites are often met with, on the contrary, devoid of blood, inasmuch as on the stoppage of the circulation they are no longer able to renew their supply. They also by and by let go their hold of the mucous membrane, and are found free in the intestines. The fact that post-mortem examinations are made so long after death, explains why the presence of the anchylostoma was so long under-valued, and the fundamental difference between these in their mode of living and other human parasites was overlooked.

Grassi has shown that the closely-allied *Dochmius tubæformis* (s. *Balsami*) of the cat is found sometimes quite filled with blood, and adherent, sometimes more or less devoid of blood, and loosely adhering or quite free, according as the animal (cat) is examined immediately after death or twenty-four hours later. Further he asserts, that after the worm is placed in water alive, small masses of blood with the blood corpuscles intact are found in the anus.* Grassi observed further, that an anchylostoma which he applied to the mucous membrane of the gum, took a firm hold of the mucous membrane, and after separation left a red point at the place of attachment. I repeated this experiment with a similar result; only, after the worm once loosened its hold, it would not bite again, and it died before it could be utilised for a new experiment. It would be very desirable to estimate by direct observation the quantity of blood actually withdrawn. Apparently the worm lives on the blood plasma without interference with the blood corpuscles, so that in its intestines rather an absorption occurs, not a digestive process. The parasite becomes as it were an addition to the vascular system of its host, whose blood circulates in it.

On account of the unusual fertility of the worm, the quantity required is not small; and besides, a much larger quantity is lost. Supposing even the daily requirement of each only amounts on an average to one drop, which probably is too small an average, the daily loss caused by five hundred worms would amount to 20 grammes (5 drachms), which, considering the rich supply of nourishment this blood contains, is sufficient in time to cause a pronounced form of anæmia. Five hundred anchylostoma, the intestines of which are empty, weigh 2 grammes, and double this probably when full of blood. Now, supposing this blood is renewed every two hours,—a supposition which has nothing improbable about it,—the loss is seen to be considerable. Whether the parasite takes any other nourishment in addition to the blood (or lymph) is unknown,—at all events it can occur only exceptionally. The discovery of ova in the intestines of the male speaks in favour of the view that it does. (Perroncito.)

The mode of living of the *Dochmius tringonocephalus* of the dog, which does not feed on blood, is also in favour of the view. On the other hand, the occurrence of Charcot's crystals in the intestinal tract is capable of another meaning. They might be deposited from the blood which had been taken up, as has been observed in other blood diseases, *e.g.*, leuchæmia.

As soon as the parasites loosen their hold of the mucous membrane, small hæmorrhages may occur, as usually occurs, after the bite of blood-sucking insects. The highly vascular coat of the intestine must be more predisposed to this than the skin, and possibly the duration of this hæmorrhage may be favoured by the mechanical and chemical peculiarities of the intestine.

Still, I would not attach too high a value to this factor, especially as, after the expulsion of hundreds of the anchylostoma, only a small quantity of blood may be found in the evacuations, and but rarely coagulated blood, or coloured mucus.

If, therefore, intestinal hæmorrhages occur as extensively as those in typhoid fever, it is probable that here also ulceration is the cause. Smaller hæmorrhages occurring in the upper portions of the intestines change under the usual conditions beyond recognition. Whether the adult parasites change their position can only be determined by carefully counting them, and comparing the number of bites (*vide* later on) on post-mortem examination. In favour of this view it may be said that individual worms are expelled by drastics. Apparently, these are surprised in the course of their wanderings, and expelled whilst still alive (as I was able to prove in one case). It is true that only males were surprised in this way, possibly wandering for purposes of copulation.

* I frequently found masses of blood with the corpuscles intact, in the intestines of the worms removed from the human body.—*Trans.*

A regular occurrence of this nature can scarcely be imagined (Leuckart), unless, as a rule, the one sex goes in quest of the other, and apparently this rule, as usual, falls to the male sex.

The discovery of free living worms in the intestines after death speaks in favour of a spontaneous separation from the mucous membrane, when there is no nourishment for them there; and even by expulsion the separation is forcibly effected. An observation which I made of the *Physaloptera semilauceolata* of the *Nasua socialis* may perhaps be of interest here. In the stomach of a recently-killed animal there were found seven females and three males, all deeply imbedded in the tissues.

In addition, there were found a number of recent and old bites exceeding the number of animals present eight or tenfold. This seems to point to a frequent change of place (on an average once in twenty-four hours).

Duration of Life.—The duration of life of the anchylostoma is not yet determined with certainty, notwithstanding that numerous observations speak in favour of several years' duration. Spontaneous expulsion of dead (?) animals was observed by Grassi and others, yet this is neither frequent, nor easily demonstrated, nor of consequence in practice. (In reference to the resistance of the anchylostoma to chemical and thermic influences, we refer to the section on therapeutics.)

Development.—Whilst the contents of the ovarium consist of ova germs, which are grouped round a rhachis, there are found in the oviducts isolated yolks in closely-pressed rows: they already attain the full size, but are somewhat elongated (length $\cdot 05$ mm., breadth $\cdot 028$ mm.—Leuckart). Within the uterus, after impregnation, the ova are surrounded with a translucent capsule. The segmentation begins only after they enter the vagina, by which they are divided into two or four segments, and then expelled. Usually they are divided into from four to eight segments when found in the intestines. Possibly unsegmented ova may be found after the exhibition of drastics, and by abnormally low position of the parasite in the intestine.*

A further development of segmentation only occurs outside the intestines, and goes on, as usual, to the formation of a Morula, prominent upon the one side. The newly-formed embryo has a short cylindrical form, which gradually increases in length, due possibly to the contractions necessitated by the smallness of the shell in which the animal is developed. As soon as the embryo has attained to complete development, it makes this manifest by its movements within the shell. Finally, it bursts its covering, usually in the neighbourhood of one of its poles, and slips out head first, rarely the tail end. (Perroncito.)

Description of the Embryo.—The newly-formed worm is very different from the adult, and shows a typical rhabditis form. The head end is rounded, and behind this rounding is the broadest part. The cylindrical body diminishes in size, at first gradually, then suddenly, forming an awl-like pointed tail. The more slender and flexible posterior portion effectuates the movements, and is therefore seen usually bent in the form of a sickle. A short, narrow mouth-tube, a spindle-shaped pharynx, and at the posterior extremity of the latter a bulging stomach, in which three posteriorly concave chitinous plates, Y shaped, or of an anchor-form, appear, are easily recognised.

To these succeed the intestine lined with darkly granular epithelium, in a zig-zag course. Further may be recognised, somewhat backwards from the middle point and ventral surface, between the intestines and the body wall, a small body ($\cdot 006$ mm. long, $\cdot 004$ mm. broad—Perroncito) which represents the undeveloped genital organs.

Growth of the Embryo.—The growth at first is exclusively in length, so that the worm becomes more slender and flexible, and is able to fold the body up in coils, amounting to from three to four. The intestines are stretched thereby, and become more translucent. After some time growth takes place in the breadth, so that the normal proportion is soon reached. Immediately after emerging from the shell the larva, according to Perroncito, has an average length of $\cdot 02$ mm. and breadth of $\cdot 014$ mm. The fully developed larva measures from $\cdot 55$ to $\cdot 56$ mm. in length and $\cdot 024$ in breadth. In order to attain this size from four to eight days are required, under favourable conditions, so that the daily increase in length is about $\cdot 04$ to $\cdot 08$ mm., and in breadth $\cdot 001$ to $\cdot 002$ mm.

Encapsulation of the Parasite.—During this period of growth the organisation of the larva undergoes scarcely any change, but at its close various remarkable phenomena are observed. Numerous parasites are met with, which seem enclosed in a kind of case or capsule, which has the exact shape of the body, and looks like a second transparent skin. Very often the worm fills this capsule completely, so that the latter is only recognised by the double contour of the worm. At other times the capsule is longer than the parasite, so that it projects either beyond the tail end or head end, or both, very considerably, whilst the larva moves inside. If the worm coils itself, the capsule is wrinkled into very fine folds.‡

The mode of origin of this capsule has not yet been sufficiently investigated. It seemed probable that the capsule was the original skin of the animal, and that the internal layer of it developed into the second skin; and this was the view taken by the earlier authorities who saw in the process only a transition of the skin into the capsule. Perroncito is opposed to this view of it. From my own observations I am in favour of Perroncito's views, that in the process a capsule is really formed enclosing the whole worm. This covering serves the purpose of protecting the worm during a comparatively long period, and is, according to Perroncito, not the old skin, but a secondary product of secretion, and the whole is a process of encysting during life, in which the

* I found unsegmented ova very often after the exhibition of drastics, but as a rule the ova are found in the faeces in two or four segments.—*Trans.*

† In some cases I found both head and tail attempting to pass through the opening. Clearly a mal-presentation.—*Trans.*

‡ In cultivating the parasite from ova, I was, over and over again, enabled to demonstrate this to my class.—*Trans.*

worm forms its own cyst, whilst in the case of other parasitic larvæ (not always, however) the tissues of the host form the capsule. The distension of the capsule takes place under the pressure of the fluid, which is invariably secreted within it.

During the process of development the internal organisation of the parasite undergoes certain remarkable changes. These begin at the commencement of the intestinal tract, which changes into a slender, long œsophagus, a short, slender mouth-tube and a distinct bulging representing the stomach. The chitinous plates of the original stomach disappear completely. According to Perroncito, the position of the future armature of the mouth appears towards the end of this period as brilliant little points. Further are noticed the throat papillæ very distinct and large, occupying the same position as in the adult animal. The rudimentary genital organs appear in the usual position, and remain without undergoing any considerable further development. The exact observation of these changes was rendered very difficult by the fact that the parts were rendered turbid through the existence of granules inside the larva. The one form passes into the other within a very short time, like dissolving views. Whilst these turbid granules are clearing away, or are being collected more regularly into groups, a new circumstance comes under survey, viz., the calcification of the capsule.

Calcification of the Capsule.—This process, which seems essential for the development of the animal, commences by the appearance of clear shining points in the capsule, resembling somewhat globules of fat. These clear spots cannot be dissolved either by fluids which dissolve fat, or, at least in the beginning, by acids. The deposition takes place for a considerable time, longitudinally, in lines along the dorsal and abdominal surfaces, and seems formed by the apposition of minute rod-like plates. In course of time the whole capsule is converted into a rigid case, more or less homogeneous at the extremities, but otherwise forming a mosaic of granules and minute plates. (Perroncito attributes this as due to a disturbance of the deposited material by the movements of the animal.) Probably the newly-formed capsule is principally chitin; at least it appears not only to resist physical influences, but also the effects of alkalies, acids, and solutions of pepsin. Sooner or later, according to my observations, in the course of some months it is possible to dissolve the capsule by even a very dilute acid, and so set the animal free. Very often the latter appears shrunk and motionless in consequence, but it returns again to life on being put into warm water. (Perroncito.) I never succeeded in this myself, although I repeatedly tried the experiment.

At other times, according to Perroncito, the animal is alive and active under the influence of warmth, but finally shrivels up and dies. The same happens when the capsule, either by accident or by the movements of its occupant, bursts, and the worm is set free. Very often the capsule is not dissolved, but becomes again quite hyaline, even in the case of larva over a year old. In this condition, the head-end of it is easily dissolved, and is often apparently burst open by the larva itself.

Further Phases of Development.—As the encapsuled larvæ are not yet in a fit condition to live at large, and besides are most active at the ordinary temperature of the human body, it is improbable that at this period they commence their parasitic life (as Perroncito believes), judging from our experience of the *Dochmius trigonocephalus*, &c. Infection then might take place from the perfectly ripe calcified cyst being dissolved in the secretions of the stomach, and the worm being set free. The uncalcified cyst, on account of its insolubility, would not probably cause infection. At this point direct observation fails us, and we are left to mere hypothesis and analogies.

Probably now the development and the differentiation of the sexes proceed at a rapid pace. In no case can the time exceed a few months, as I can assert from experience in the treatment of young children. According to Leuckart, *Dochmius trigonocephalus* is developed in three weeks. As to the place where this development occurs, we know nothing with certainty, as nowhere in the literature of this subject is mention made of a sexually mature larva. At all events, it seems striking, that such has never been noticed either on post-mortem examination or among the numerous parasites repeatedly expelled in the fæces.

Among several thousands expelled during life, and examined most carefully by myself, I never observed a single worm sexually immature: even an apparently half-grown female of .7 mm. in length was sexually mature and already impregnated. It is true that a portion of the patients had been withdrawn for some time from the sources of infection, whilst others were always exposed; but in no case was a sexually immature worm ever observed.

Even supposing such lived at first in the stomach (as the *Dochmius trigonocephalus*, according to Leuckart), this would scarcely screen them from observation. On the other hand, if the development occurred outside the intestines, then their expulsion would be impossible. As a matter of fact, Griesinger and Bilharz have observed anchylostoma rolled up into a ball in cavities of the mucous membrane. There is no record of the stage of development of these, however, but males and females were recognised, not whether they were sexually mature or not. I quite concur with Leuckart, in opposition to other observers, including Perroncito, in supposing that this was a process of development, and not an error of observation. Still, the question is undetermined, and until it is determined in the case of man, the study of the *Dochmius* of the cat, likewise a blood-sucker, is recommended. My attempts to infect swine by various cultures and at different periods completely failed; nor could I discover parasites in swine from infected localities. I must therefore conclude that this worm is not, like several others, common to man and to swine. Leon Levailant says he discovered it in a *gibbon* (? ape), otherwise its occurrence outside the human race is unknown.

Experiments on monkeys would be of interest.

Conditions of Development.—After having now studied the mode of development of the larva, we must examine the conditions under which this development takes place.

The cultivation of the embryo can be carried out in various ways.* The simplest and most natural way is to take some of the excreta of an infected person, and preserve it in a moist condition, at not too low a temperature. (To keep it moist it may be placed in a porous vessel, which in its turn is kept in water. The vessel should be protected from flies and dust by a stopper of cotton wool.) In the Brazilian Province of São Paulo, at 570 m. over sea-level, I succeeded with my cultures quickest, and best during rainy weather, when the temperature was between 25° to 30° C., and the atmosphere moist. The direct effect of the ray of the sun easily killed my culture. Lower temperatures delay the development, or stop it until the occurrence of more favourable conditions; very seldom stopped it altogether. The fæces selected for use should be well formed, but of soft consistence.

The ova develop in fluid fæces, it is true, but the larvæ die whilst still in the egg, or soon after emerging from it. Neither do they develop well in hard, dry masses of fæces. In both cases the conditions seem to be unfavourable to satisfy their life requirements. According to Perroncito, the excreta after the use of animal food are favourable to development, but they are also easy of development in the excreta after the use of exclusively vegetable food (such as beans, rice, flour, &c.), extensively used in Brazil, provided always these excreta do not contain too much undigested matter.

If the process of decomposition is intense, cultures fail completely. A moderate amount of mould does not influence the development.

The embryos can also be cultivated in moist earth, as Wucherer proved, who employed for cultivation females full of impregnated ova.

Grassi and Parona throw some doubt on the work of Wucherer, but I am not of their opinion. His observations completely agree with what we now know occurs at regular intervals of time, but they have been falsely interpreted. For "skin" we must substitute capsules; for "death of the larva," rigidity of the capsule. Such a quick and numerous appearance of free living nematodes I never saw in my experiments in Brazil.

The most striking feature of Wucherer's work is the circumstance that he did not find the ova. In Brazil their discovery is somewhat difficult, on account of the large quantity of starch granules of beans present in the fæces, beans being used constantly as food, and these formed the principal portion of the undigested residues in the stools. In spite of its incompleteness the work of Wucherer is of great value, and he deserves the credit of being the first, among several hundreds of physicians, to make daily observations of the disease in Brazil, and to recognise its import.

The later stages of development do not require the presence of fæces.

All that is required is mud or moist earth. I deduce that from the fact that in the later stages the cultures died if carried on in pure fæces, although the first stages were very successful. If such substances are taken as may possibly contain the larvæ of other Nematodes, these should be quite eliminated. If movement be taken as a measure of the amount of vitality of the larvæ, it is found that a temperature of about 30° C. is the best at the beginning of the cultivation: they further require a medium of the consistence of thick soup, and rich in nourishment, as they can only take in finely-divided particles, from the smallness of their mouths. As the development advances, a lower temperature is borne with safety, so that the larvæ towards the end of growth can live in more or less pure water at temperatures as low as 12° C. I have preserved such larvæ for weeks in hermetically sealed glass tubes half filled with water. Their development may, however, be greatly retarded, or stopped altogether. On the development of large numbers of infusoria, they die off altogether, not leaving a trace behind. They are probably consumed by the infusoria. When the larva dies its body is converted into bead-like drops or scales, and this change can even be observed in the egg. This change reminds us of the change occurring in the bodies of dead trichinæ in the muscles.

Duration of Development.—The duration of development is extremely variable, and depends on temperature and soil (medium). The minimum is set down at two weeks, whilst under less favourable conditions months may elapse, as after the development of the hyaline capsule the larvæ make no further progress. Development, however, varies within wide limits even under conditions which seem entirely similar. After the great portion are developed, there follow more development at a later period, and many of the ova seem incapable of development. The dimensions of the ova and of the larvæ also vary.†

The following observations were made at a temperature varying from 22° to 28° C., or an average of 24° C. The atmosphere was very moist. Twenty-four hours after I laid aside the fæces eggs were seen in all stages of segmentation, from the very first stage to the complete formation of the embryo: further, several larvæ, which escaped from the shells; the number of these was not considerably increased in 48 hours. After 76 hours I observed on the surface of the fæces several small, round, sluggish larvæ, and a number of long slender ones, exhibiting very lively movements. After 96 hours these increased considerably, but were less active, on account of a lower temperature existing (22° C.). After 150 hours all the larvæ showed the œsophagus more or less modified, but were, with few exceptions, quite motionless: some showed the beginning of the process of encapsuling, whilst others were already surrounded by a beautiful hyaline capsule. In addition, there were eggs still present; others with embryos in a mulberry condition. After 220 hours, at a temperature of 24° C., there were very many encapsuled movable larvæ still; also eggs in the mulberry condition, and others with developed movable embryos. After 270 hours, several larvæ were observed with capsules beautifully calcified.‡

* In our warm climate I found the cultivation an easy process, and never failed to find embryos in all stages of development after a few days' cultivation.—*Trans.*

† I found the development taking place in from three to four days, under favourable conditions.—*Trans.*

‡ All this was corroborated in my experience.—*Trans.*

Physiology of the Larva.—The movements of the worm are strong and incessant when the temperature and medium are suitable.* The head is raised, whilst the body coils itself in all directions, which in media not fluid are mostly horizontal. Sometimes the worm coils itself into the form of a ring, and rolls about or suddenly revolves. On dry smooth surfaces (object glass, *e.g.*) the movements are less active; still, the encapsuled worm is still capable of moving about. On the other hand, the old larvæ showed great activity in water. Irregular as their mode of locomotion is, yet the larvæ can travel considerable distances in a short time. I always found it necessary to follow them constantly on the object glass. These apparently objectless movements lead constantly to one and the same result, viz., an accumulation of the larvæ at the periphery of the faecal mass. This is not always observed in a striking manner, but it may be demonstrated by the following instructive experiment.

In recently-passed fæces the eggs are, as a rule, uniformly distributed throughout the mass, as can easily be proved on microscopical examination. If the fæces be now mixed with some water, the eggs are not found in any quantity in the deposit. After an interval of a few days, however, under the same conditions larvæ are found in large numbers.

If a portion of the fæces be placed upon a sloping surface, so as to allow the fluid to accumulate at its lower margin (*e.g.*, on the side of a wide-mouthed glass bottle, in a sloping position), and be kept in this position for several days at a suitable temperature, &c., keeping the fæces moist with water by means of a syringe, there will be found in the fluid at the under edge of the faecal mass such an accumulation of larvæ that every drop contains hundreds. If the fæces itself be now examined, none are seen. In the inner portions of the mass may still be detected undeveloped eggs, and possibly a few escaped larvæ. The later stages of development go on in the fluid abundantly and rapidly, and are entirely absent here. This process, which I observed constantly in numerous experiments, must occur in nature after downpours of rain. The larvæ do not by any means limit themselves to locality, but pass over considerable stretches of ground by their own movements.

Macroscopic Appearance.—The ova and embryos are not recognisable by the naked eye, but the larvæ, after a short period of development, under a strong light, may be so recognised, as Wucherer already observed. Their movements may be noticed on the object glass with strongly-reflected light falling sideways upon them.

The encapsuled but still movable worm may be studied in all its peculiarities in a watch-glass illuminated from below. On drying, it stretches itself, and then looks like a very fine silvery hair. It has no colour of its own, being quite transparent, and is visible by refracted or reflected light.

Specific Gravity.—The specific gravity of the anchylostoma is greater than that of water in all stages of development. If the larva is placed in water in a glass tube, and watched, the calcified capsule sinks rapidly to the bottom. The movable larvæ sink much more slowly, moving meantime in all directions, and twisting their bodies about constantly: once they reach the bottom they remain there, but still wind their bodies about. By simply inverting the tube this can be observed over and over again. In thick media they remain a considerable time suspended in the fluid. They greedily seize on any matter suspended in the medium, such as slime or algæ, and may be raised to the surface by the formation of gas in these. From what has been said it may be seen that the larvæ can be obtained in large quantities by exercising due care in their culture.

Resistance (offered against drying up).—Before I close this section I must still mention a peculiarity which, for their development, is of importance, *i.e.*, the resistance they offer against drought. They are able to stand being dried up for a considerable time. According to Perroncito, larvæ of different ages may again show signs of life after being dried up for twenty-four hours. After forty-eight hours the shrunken body, on being placed in water again, resumed its original shape, yet with a single exception—life had entirely disappeared.

Although this species is thus placed under less favourable conditions than the embryos of other Nematodes, yet this limited capacity of resistance to drought is a great assistance in the preservation of the species.

Besides this, the calcified cysts apparently protect the animal in this respect, as well as against other injurious materials in the medium.

With the encapsuling and calcification of the capsule, the development of the worm *outside the original host* is complete, at the same time it has lost its power of locomotion. Its transference therefore into an organism, suitable for its further development, must take place mechanically, as is the case with the trichinæ at this stage of their development.

Transference to the Human Body.—Apart from the hundred of accidental circumstances which may carry the larva into the human intestines, there are two principal modes in which it can be effected.

In the first place, accumulations of fæces containing ova, over moist, somewhat uneven ground, favouring the accumulation of water here and there, soon lead to profuse development of larvæ.

These favourable conditions are found whenever latrines are absent. The excrementa lie scattered in large masses near human dwellings, especially in swampy soil frequently trampled on by men and animals, without any outflow of water. This is the peculiar home of the worm. These conditions are often to be met with in Brazil, and other countries where cultivation is in a backward condition, and where men and domestic animals are often crowded together within narrow limits.† In the outskirts of small country towns, these conditions are to be also met with, but to a smaller extent, as their latrines, although of a primitive form, are met with. Conditions of this kind are never met with in large towns.

* Not unlike the movements of the small leeches up-country.—*Trans.*

† Conditions which are very common in Ceylon.—*Trans.*

On the other hand, the same results always occur whenever any temporary activity induce the more or less prolonged accumulation of mud upon any soil favourable for the development of the worm, as in mining operations and brick fields. Under such conditions, where almost all the larvæ develop, the number found over a small area may be enormous, not even to be counted by millions. It is easy to understand how the inhabitants of such localities, in their various habits of life, either from the soil itself or from soiled vessels or clothing, or from portions of the body, especially when they go about barefooted, may easily, by means of fingers or nails, introduce a number of the encapsuled larvæ into their stomachs. This happens specially in the case of work people who take their meals on the spot, and carry their food to their mouths by soiled fingers. On the other hand, infection takes place in the case of young children, still scarcely able to walk, as they often crawl on hands and feet, and carry their hands often in a soiled condition to their mouths. Whoever critically examines the faces of Brazilian children, who, under the favourable influences of climate, play in the open air, clothed only with a small rag of a shirt, will easily understand why a parasite, the stages of development of which are undergone in the soil, *specially* affect this early age.*

A great part of the larvæ do not, however, develop in the place where the eggs are originally deposited. Immediately after emerging from the shells they commence to wander, and by downpours of rain, as occur in the tropics, pass over long tracts of soil.

The lay of the ground favour their movements, as well as the accumulation of the young worms in low localities where water accumulates.

Should the locality have the form of a basin, the sides of which are here and there cultivated, whilst its lowest part is either covered with stagnant, or with water finding its way out with difficulties, there the worm finds conditions favourable for development.

These conditions tending to the accumulation of larvæ in individual localities in enormous quantities, are found in undulating districts, very often in Brazil, and especially in the cultivated portions of Rio de Janeiro and Sao Paulo in a very pronounced manner. If such water be used for drinking purposes, the possibility of infection is always present, especially if the moss at the margin of the pools be disturbed by cattle drinking, and the turbid water be afterwards immediately used by man. Should a stream pass through the centre of such pools, the movable larvæ might be carried away long distances, until they gradually are deposited in shallow places along the margin of the stream, and there undergo further development. In the interior of Brazil streams of this nature are frequent. These are seldom bridged, and travellers either cross them on horseback or on foot. The animals drink freely of the water, and the travellers often quench their thirst from the same source, which cannot be wondered at, considering the great heat and absence of other water. Besides, the inhabitants along the banks of the stream use the same water, and so tend to spread the infection, which very soon appears if any anchylostoma be at all present. A careful observer is therefore in a position to trace the infection along the water-courses in a manner similar to what has been done in typhoid fever. The conditions which I have described exist in many countries. In some countries, as, for example, in Egypt, the periodical overflowing of a river may be of considerable import in the development and spread of the parasite: whether the dried larva-cysts carried about by the wind may cause infection, as pointed out by Perroncito, is doubtful.

Consequences of the presence of the Parasite to the Host.—From what I have said of the mode of living of the adult worm, it will be seen that the invasion of the human organism by a large number of these must be of serious import. As a matter of fact, it has been established by careful observations that the presence of about five hundred anchylostoma produces severe disturbances even in the strongest adult, and that if the individual be unfavourably placed as to diet, &c., a much smaller number will do the same.

These disturbances are of various kinds, but the most prominent and the most striking is the anæmia caused by them. The anæmia produced may be extreme, and is often recognised by the laity themselves on that account, as well as on account of its frequency in certain localities.† The coincidence of chlorosis and of an invasion of anchylostoma has been too often established to raise the question of the connection now, even if it appeared to us much less explicable than it really is.

The idea that the worms are not the cause, but the consequence of the disease, seems, after all our pathological experiences, rather an unintelligible anachronism. To retain such an idea, knowing what we do of its mode of development, its mode of infection, and its mode of living, would be something strange. I may therefore in this place omit the proof that the disease described by me as anchylostomiasis is entirely due to the presence of the parasite anchylostoma, as this will become evident further on.

Before concluding the discussion of the parasite itself, I have another task to fulfil; that is, its geographical distribution, as far as this is known. I will not, however, omit the description of the disease (Anchylostomiasis) itself, and this chapter describing the cause of the disease will form a natural transition to the disease itself.

Historical and Geographical Description of Anchylostoma and Anchylostomiasis.

The first treatise on *Anchylostoma duodenale* dates from the year 1843, but the parasite itself was discovered in 1838. The discoverer, Dubini of Milan, described the worms which he found in twenty per cent. of the cases examined post-mortem. He noticed not only the grayish and reddish points in the intestine, but he also found a number of the parasites adherent, and the

* This also explains why children in Ceylon are so often infected with the parasite.—*Trans.*

† The anæmia produced by the *Anchylostoma* in Ceylon is most characteristic, and is easily distinguished from that of Malaria and other wasting disease. I have never less than from twenty to thirty cases under treatment in my wards in the hospital.—*Trans.*

fact was clear to him that they must have had an injurious effect on the organism, although he did not recognise in what way. The parasite was also found in Milan by Castiglioni, in 1844. It was next observed by Pruner, in 1846. He remarked that the worms affected in particular rachitic and œdematous scrophulous patients. Yet he, like many after him, believed the presence of the parasite was dependent on the pathological conditions, instead of adopting the more rational view that the pathological conditions were due to the parasite. The symptoms of anchylostomiasis *as a whole* were known to him, and were described by him as "cachexie aqueuse."

Bilharz also observed the parasites in Egypt so often that they never failed him in a single case of autopsy. On the contrary, they occurred in *hundreds* and *thousands*. He proved that the worm pierced the mucosa and sucked blood.

Griesinger, who examined the matter along with Bilharz, came to the conclusion that the worm was the direct cause of Egyptian chlorosis—a disease affecting at that time about one-fourth of the entire population. His publications spread the knowledge of the cause, and to some extent was of help in the diagnosis of the disease. On the other hand, I am doubtful whether the very rational treatment adopted by him had been really of any use. At least, the anthelmintics (ol. terebinth and calomel) recommended by him have had no result in the hands of competent observers.* The knowledge of the parasite was further spread by the discovery of the same in Brazil by Wucherer in 1866. Cognisant of the discoveries of Griesinger, he examined the intestines of a patient who died of extreme anæmia, and found there a number of worms, the identity of which with the anchylostoma duodenale was later on confirmed by Schneider. The symptoms otherwise present corresponded with the descriptions of Griesinger.

After him numerous other observers made the same discovery in the bodies of those dead of tropical anæmia, as Rodrigues de Moura, 1866; Fauvray, 1869; Tourinho, 1871; Souza Vaz, 1876.

There are also observations quoted from Faria, Silva-Lima, Santos Pereira Teixeira da Rocha, Marques da Cruz.

Notwithstanding, the knowledge of these relations was but little noted outside the province of Bahia. The old, unintelligible view, which looked upon the worm as the consequence of the disease, still prevailed, and the cause of the disease was attributed to imperfect nourishment, over-exertion, psychological depression, &c. The Professor of Medicine in Rio, Torres Homem, still continued to describe it so in 1883, and in his clinical lectures on *oppilação*, or tropical anæmia, and its treatment, ignored its connection with the anchylostoma, notwithstanding the numerous proofs before him, supporting his view on the occurrence of one case diagnosed, and that correctly, as tropical anæmia, and yet in which on autopsy only five anchylostoma were found. (Further on I shall discuss this case.)

Although the spread of the knowledge of the cause of the disease, notwithstanding even popular descriptions, was still very limited,—a fact to be explained by the rarity of the disease in town and the small number of post-mortem examinations made; yet the treatment, notwithstanding the discoveries of the last year, had even made less progress, and was limited to the old and insufficient remedies, whilst the disease made enormous inroads on the people. How complete the knowledge of the cause and effect was, almost twenty years ago, may be seen from the classical work of Leuckart (*Parasit. Mensch.*, II. Band, 2 Leipzig, 1868), where already the search for the ova is recommended as a means of diagnosis. After the publications of Wucherer, the parasite was also found at Mayotte, by Grenêt and Monastier, in 1867; Cayenne, 1868 (Camuset and Rion de Kérangal); Senegambia, 1882 (Borius); and Japan (Baelz and Schube), as well as in Netherland-India (Stammeshaus). In Abyssinia and India they are also said to occur. (Davaine.)

In the meantime, the knowledge of the anchylostoma had made constant progress in Italy, although the materials for observation there were small, in comparison with other countries. Sangalli, in Pavia, discovered the worm (1866) in one-half of the bodies examined by him, and once in such numbers that he could not help looking upon it as the cause of the deadly disease,—anæmia,—although he blamed neither the direct loss of blood by suction nor the fact that the worm fed on blood, as the cause as a rule.

Sounini and Morelli observed anchylostoma in Florence (1877); Grassi and Parona in Milan (1878); the latter and Ciniselli also in Pavia (1878).

Grassi was the first to detect the ova in the fæces, which, strange to say, Wucherer sought for in vain.

Grassi also found the worm in the stools, and studied its anatomy and mode of development, and advanced our knowledge by the observation of *Dochmius balsami s. tubæformis*. He laid stress on the hæmophagic mode of life of the worm, and its detrimental results.

A number of observations in this respect were made by Bozzolo at the Clinic in Turin, and published by him and his assistant, Graziadei. These were made on bricklayers of the same province (six to seven patients, 1879). Perroncito also observed a case from the province of Turin.

Individual cases were observed, out of Italy, by Kundrath and Heschl, in Vienna, in 1872; by Roth, in Basel, in 1879.

In the first case the infection most probably occurred in Venice; in the latter in Java and Borneo, or Egypt. The medical world was to some extent prepared, when, on the occurrence of a great epidemic in Europe, such materials for observation were at its disposal as had never before existed on that continent. This took place during the construction of the Gotthardt tunnel. All the conditions favourable to the development of the parasite being present, there was suddenly developed a colossal brood, where previously the parasite had never been observed. This gigantic work, which for years gave employment to thousands of labourers, was, as is well known, commenced simultaneously at both ends, Airolo and Göschenen. The labourers at both ends

* Ol. Terebinth. Calomel, &c., were tried by me without any results prior to Dr. Kynsey placing in my hands this treatise.—*Trans.*

were brought mostly from Italy, particularly from Lombardy and Piedmont. Among these labourers there arose, after some time (about the end of 1879), a new disease, particularly characterised by anæmia, often of an extreme type, and which acquired great dimensions, attacking hundreds and thousands.

One of those labourers died in February, 1880, in the Turin hospital, and was examined (post-mortem) by Colomiatti in the presence of several professors and students. There were found in the intestines 1,500 anchylostoma still alive. This discovery attracted the more attention, as the spread of the disease was at the time being discussed. Perroncito observed, along with Concato, yet three other cases of anchylostomiasis among the Gotthardt labourers, and made known the matter through wider circles. Meanwhile, the Turin professors, Bozzolo and Pagliani, undertook the investigation of the epidemic on the spot. They proved that the *tunnel labourers*, almost without exception, passed the ova of the anchylostoma in their stools, whilst this was not the case with those employed elsewhere (outside).

In one case (post-mortem) seventy-seven parasites were found. They still hesitated to blame the worm alone, which was found often in comparatively small numbers, as the cause of the disease, especially as they found the labourers under very bad hygienic conditions. I must make a digression here, in order to remark that, long previous to this time, a disease prevailed among labourers employed in mining, especially among French and Hungarian miners, when overcrowded, the symptoms of which culminated in anæmia in a more or less severe form. Notwithstanding the varied descriptions of this disease, more or less tinged by preconceived opinions, yet there is a common trait in all the cases designated miner's cachexia and miner's anæmia, incapable of being misinterpreted. These diseases had already been the subject of study (Favre, Töth, Schillinger), and their cause was believed to be want of light and defective ventilation. In accordance with these views, some authors (Sonderegger and Lombard) asserted that the Gotthardt epidemic was due to the same causes.

This view of the matter could not be maintained much longer, as the constant occurrence of the disease, with the presence of the parasites, was too remarkable to be overlooked, or ascribed to chance. Besides, the engineers of the tunnel, who were placed under much better hygienic conditions, were not spared; and numerous patients, after being placed under favourable conditions, did not improve, but actually became worse. So Sonderegger himself had to acknowledge that the presence of the parasite *alone* was sufficient to cause the whole train of symptoms.

Soon after ova was found in the dejections of anæmic patients from the Gotthardt tunnel, in Switzerland, as in Basel (Immermann), Rolle (Dumer), Schwitz (Schönbächler), Zurich (Wyss.), and beyond Switzerland in Frieberg (Br. von Bäumler).

The comparison with the published statements of Griesinger and Wucherer contributed more than anything else to the proper understanding of the facts. Finally, the theory acquired fresh strength in the discovery of the anchylostoma in patients (miners) at St. Etienne and Auzin (France), as well as at Kremnitz and Chemnitz (Hungary).

Opinion then changed in regard to the causation of miner's anæmia, inasmuch as it was problematical whether any such existed not identical with anchylostomiasis. The processes were identically the same, and the old opinion had to give way to the more rational of the two. There was finally found a yet more direct method to decide the question, as a remedy efficient in expelling the parasite was discovered after numerous experiments conducted in a systematic and rational manner.

Since that time experience has proved in innumerable cases that this single reliable method has led to a quick and permanent cure of the disease, and that cure consists essentially in the expulsion of the parasite.*

After these observations had made clear the connection between the anchylostoma and certain endemic forms of anæmia, and rendered the diagnosis easy, the number of cases reported in Italy and elsewhere increased.

As for the Gotthardt tunnel epidemic, it seems to have disappeared *in loco* after the completion of the work. The infected labourers were scattered elsewhere, and afforded opportunities of observing the disease in still wider circles; yet these do not seem to have given rise to any fresh epidemic outside Italy. However great the number of patients in this epidemic was, it is small in comparison with the number occurring in countries where the disease is constantly present; and if the experience gained in the former be utilised, the loss of life which occurred there will be small in comparison with the blessing such an experience will carry to millions of the human race †

We see that the knowledge acquired of the anchylostoma and of its signification is the trophy of a comparatively short period, whilst, on the contrary, the results, especially parasitic anæmia, have been long known. Although often unrecognised and misinterpreted, yet they appeared in the severe epidemic form as *morbis sui generis*, and received various local designations everywhere. In the Antilles, where the disease is widely spread, it was called by English, French, and Danish observers "dirt eating," "geophagia," "mal d'estomac," "Malcœur," "cachexie africaine," "cachexie aquense," "anæmic des pays chauds," &c.

Peré Labat, as early as 1748, mentions the great mortality in Guadaloupe from "mal d'estomac," and Bryon Eduards, in 1799, mentions the same concerning the Negroes in Jamaica. Chevalier, in 1752, and Pouppis Deportes, in 1770, report the occurrence of the disease in St. Domingo; and it was further noted in the Antilles by Dazille in 1776 and Bazon in 1778. There are many recent reports from the latter locality on the subject, especially a very good

* This has also been corroborated in my experience in the hospital, where cases which would have formerly been pronounced *hopeless*, make rapid, and let me hope a permanent, recovery after the worms are expelled.—*Trans.*

† This experience has been utilised here, and the author's expectation is being realised among us. I have no doubt very shortly the blessing will be experienced by thousands in Ceylon.—*Trans.*

description under the article Anæmia, given by St. Vel in the "Traité des Maladies des pays chauds." As early as 1648, Piso mentions a disease occurring in Brazil under the term "oppilatio," evidently a corruption of the term "oppilação," a term yet commonly used there for anæmia. Other terms, such as "hypophemia tropical," "amarellão," and "canção," are used, of which the second derives its origin from the pallor of the skin, and the third from the great and constant exhaustion. Among the German colonists it is called "Bleich oder Gelbsucht"; since those days it has been observed and described and in many countries generally recognised. Its connection with anchylostomiasis is easily proved. I have myself found in about 150 fæcal examinations of recent cases, *without exception*, the eggs present in great quantities, and many thousands of anchylostoma expelled.

In Italy, the disease as such was described by Volpato, in 1848, and designated "alotriophagia." Older descriptions come from the southern states of the American Union. Yet, on the whole, there are extraordinary lacunæ in the history of the disease. We do not know how long it has existed in Egypt, where, from immemorial time, it must have found a suitable soil. The reports from the Old World are of comparatively recent dates, although the infection must have long existed there in all probability, and possibly the disease has found its way to America within historical times. In the New World, the slave trade facilitated the spread of the parasite, although the spread was not altogether due to that. It does not appear to me probable that the parasite existed in America before its discovery in 1492. To summarise shortly what has been already stated, and complete it by some additions, it may be stated that the following geographical distribution of the parasite itself, and of the symptoms directly traced to its influence, occur.

In Europe, anchylostomiasis is met with in mining districts: in France and Hungary (Perroncito and others), in Sicily (Grassi), in Sweden (doubtful), in the province of Turin, among the brickmakers (Bozzola). Further, the disease prevailed among the Gotthardt labourers. Among the agricultural population of Italy, rice-cultivators in particular, it appears to be common. We have had communications on the subject from Milan (Dubini, 1838; Castiglioni, 1884; Grassi and Parona, 1878), from Treviso (Volpato, 1848), Pavia (Sangalli, 1866; Grassi and Parona Ciniscelli, 1878), Turin (Bozzolo and Gaziadei, Perroncito, from 1879), Kovarra, Toscana, (Bozzolo, 1880).

In Africa, we have observations in Egypt. Pruner, Bilharz, Griesinger, &c., have observed the parasite from 1847. The disease was observed already earlier than this. Abyssinia (noticed by Davaine), Senegambia (Moulin, Thaly, Borius), Coast of Guinea (Stormont, Clarke), Zanzibar (Lostalet-Bacheé), Mayatte (Monastier).

From Asia reports are but few. Hirsch believes that a communication of Day's from Cochín-China refers to it; Davaine mentions cases in India; L. V. Leens in Borneo. More recent communications come from Japan (Bälz and Scheube), as well as from Dutch India (Stammeshans).

The communications from America are very numerous. The disease was reported as existing in the southern states of the Union, in Louisiana (Chalbert, 1820; Duncan, 1840), in Alabama and Georgia (Lyell, 1849). Numerous reports at various times prove its occurrence in the Large and Small Antilles, as well as in British, French, and Dutch Guiana. Further, we meet with it in North Peru, at Maránon (Castelnan), and in east Bolivia (Salt, 1872). It is very widely spread in Brazil outside the towns, and has been recognised for a long time. The German colonies of Santa Catharina is the most southern point of distribution known to me. I have convinced myself personally of the frequent occurrence of the disease, at the present day, in the provinces of Rio and Sao Paulo. As is seen from the foregoing, the parasite has a wide distribution. If it seems to fail in large stretches of tropical countries, this partly depends on the fact that the disease has not been properly looked for, and mild sporadic cases are easily overlooked, whilst great epidemics are usually attributed to bad hygienic conditions, which are not always present. It seems very improbable that whilst the Appenine peninsula has been infected, that the Pyrenees and Balkan peninsula should be spared; that Morocco, Algiers, Tunis, Tripolis, Syria, Persia, and Arabia should remain free of it, while countries of the same zone were infected, can scarcely be credited. In India and Japan, which countries appear to have an immunity from the disease, the parasite has been recently proved to exist, and in the latter seems to be very common.* Post-mortem examination, and careful inspection of the fæces among the poorer classes of the agricultural population giving negative results, can alone be looked on as evidence of the absence of the parasite, whilst the disease then sets a girdle almost around the earth, it becomes more limited the further we advance from tropical and sub-tropical countries towards the pole. Beyond the latitude 46° N. and 30° S. the disease only occurs under exceptional conditions. This proves its connection with climate. On account of the immense intercourse between the countries of the world in modern times, the spread of the disease wherever favourable conditions exist for its development, is an accomplished, or an almost accomplished fact. Among the numerous Italian road workers and *vagrants* the parasite was not a rarity, and it is most probable that it found its way to Gotthardt through them. Strangers living a long time in infected localities probably carry the parasite home with them, and by the distribution of the ova give rise to local epidemics.

Fortunately, cold climates afford considerable protection, and good hygienic conditions cut short the disease in many localities. It seems to be diminishing in Egypt, and also in Italy (Gotthardt epidemic excepted), especially in Milan. On the contrary, I have repeatedly observed an advance in the province of Sao Paulo, and that was due to the import of slaves from the northern provinces.

* It certainly prevails to an enormous extent in Ceylon, and must have done so for generations.—*Trans.*

From public and private communications since above was written, I make the following remarks :—

The epidemic of the St. Gotthardt tunnel had in fact survived the completion of the work, but had not in its turn given rise to a second epidemic anywhere.

The number of patients treated must have been very large, as E. Parona alone treated 249 in the hospital of Varese; and Fenoglio, from March 3, 1881, to the end of August, 1884, treated 538 cases in the hospital Maggiore Maurisiano. Almost without exception anchylostoma were found in each case, and recovery followed on the expulsion of the parasites.

At the present time (May, 1885) the epidemic may be regarded as completely at an end. The Gotthardt disease gave rise to several publications in the German language, *e.g.*, Schulthess, Monighetti, Sahli, and Baumler. They confirmed in all essentials the discoveries of the Italian investigators, and discovered anchylostoma in all the patients. Schulthess gives, in addition, beautiful plates in his work ("Zeitschrift für wissenschaftliche Zoologie," vol. XXXVII.) of the anatomy of the worm, which cannot, however, be discussed here. They contain numerous details, but do not differ in any essential point from what I have said of the anatomy in this paper.

Sporadic cases of anchylostomiasis were still constantly remarked in the neighbourhood of Turin, especially among the brickmakers.

Brickburners' anæmia, formerly described by Rühle as it existed in Germany, was found on further investigation to be also anchylostomiasis, confirming the supposition made by Hirsch regarding it. Meusche, of Kessenich, near Bonn, published the first case of it, in which the anchylostoma was found. Leichtenstern published thirteen cases of the same kind. These were found in the different brickfields in the neighbourhood of Cologne. Further, Mayer, in Aachen, as well as Masius, Francosse, and Firket, in Liège, proved that the "miners' anæmia" was really anchylostomiasis. The centre of infection was probably in the neighbourhood of Liège, in one case specially at Seraing. The anæmia of the miners of Lyons has been proved to be anchylostomiasis. Bareggi has reported a case of anchylostomiasis occurring in Milan, in which the infection was traced to Venezuela.

Finally, I have to mention that the anchylostoma duodenale has been found by Leuckart in the gorilla.

PART II.—DEFINITION AND DIAGNOSIS OF ANCHYLOSTOMIASIS.

Co-operating Conditions.—By the term anchylostomiasis, we designate the various pathological conditions which arise from the presence of the parasite anchylostoma duodenale in the human intestines. To render our position as to the causation perfectly secure, the following proofs are required :—(1) That a sufficiently large number of the parasites to cause the disease is, or was lately, present in the intestines; and (2) that the symptoms can be traced in an undoubted manner to their presence.

The first can be easily proved, now-a-days, even in the living, in two ways, *viz.*, the parasites can be expelled and collected, or the ova evacuated in the fæces will give us an idea of the number present.

The first method will only give us the minimum number present, as a portion may easily be left behind. Their non-existence is not proved by negative results.

The second method gives us, on the contrary, an approximation of the number of sexually mature females present, but gives us no indication of the males, nor of the sexually immature females. The search for the accidental passage of the parasite in the fæces is too seldom successful to be used as a means of diagnosis.

In the dead body the number present can be easily ascertained, as well as the resulting lesions. On the other hand, many very characteristic symptoms can only be studied during life. The pathological anatomy and the clinical study of undoubted cases make known to us a series of symptoms which, although not singly, are yet characteristic enough in their combination to guide us sufficiently in our examination. In infected localities, a little experience will enable any one to diagnose the disease with tolerable certainty, even from the history and the mere inspection of the patient.*

Notwithstanding this the microscopical examination of the fæces is of the first importance, as it clears away every doubt, and controls the treatment. I shall therefore describe the mode of examination in this place.

The ova of the anchylostoma are *absolutely* characterised by their shape and stage of development. They cannot be mistaken for the ova of other parasites, or for any formed elements which are to be met with in *recent* fæces. (If the fæces are old, stages of development of the anguillula and oxyuris might mislead.) Their distribution in the fæces is tolerably uniform, because they mix with the chyme in the higher portions of the intestines, and are carried down by the peristaltic movements. Notwithstanding this, I once met with a group of twenty ova, closely pressed together and surrounded with a little mucus. To search for them a portion of the former masses of fæces triturated with distilled water is placed in a tall conical glass, allowed to subside, and the deposit examined microscopically.

In order to determine approximately the number present, I recommend the following plan. One part of fæces is uniformly mixed with three parts of water, and of this mixture one

* The mere inspection of the patient is now sufficient in our wards to diagnose a case of anchylostomiasis.
—*Trans.*

decigramme (about three drops) is placed on the slide, and flattened by laying a glass plate over it. This latter plate has a surface area of 25 qcm., and is divided in squares of 1 qcm. each. In each of these squares there appear 4 mm. of the fluid or 1 mm. of the fæces. With a slight increase in the power, the number of eggs present can be counted, and the average number in each milligramme determined. If now the fæces passed during the twenty-four hours be weighed, the number of eggs present can be easily estimated.

On an average the fæces may be estimated at 200 gramme. Now, E. Parona had found in one case, where about 800 worms were present, 200 ova in each centigramme of fæces in the lower bowels; and we may accept as a fact that the number of egg-laying females among them could not be much less than 480. I have examined 3,000 worms after expulsion during treatment, and I have found the ratio between males and females to be as 2 is to 3. According to this the presence of 20 ova in one milligramme would point to the presence of 480 females, and of one ovum per milligramme to 24 females and 16 males. Assuming an average of 150 grammes of fæces passed in the twenty-four hours, this quantity would then contain 150,000 eggs, which, altogether, would weigh about 10 mm., and form the $\frac{1}{15000}$ part of the fæcal mass. Each individual female would, in accordance with this calculation, produce 6,000 eggs in the day, corresponding almost to one-tenth of the whole weight of the body of the parasite and $\frac{1}{360000}$ of the fæcal weight. The presence of 360 females would produce ova amounting to the $\frac{1}{1000}$ part of the dejections; and their average linear distance from each other is less than 1 mm. These numbers are sufficiently exact to give us an idea of the importance of this means of diagnosis, as well as of the conclusions arrived at. Greater accuracy demands that the average daily ovulation of the female should be determined by a number of further observations.

Having determined in this manner approximately the number of parasites present, we find that, in the greatest majority of cases, the presence of several hundreds of the anchylostoma causes a severe general affection, whilst, on the other hand, a small number gives rise to scarcely any, or only mild symptoms of a local character.

Sometimes, however, severe and tolerably characteristic symptoms are coincident with the presence of but few parasites. In such cases we must first eliminate all complications, which in themselves would constitute a cause of anæmia, such as congenital affections, tuberculosis, malignant growths, &c. If none such are present, and if previous intestinal hæmorrhages and chronic diarrhœa can also be excluded, it will be found that we have to do with very old cases, in which the anchylostoma had either been expelled or disappeared in the course of time, inasmuch as the disturbances of the digestive and circulatory organs rendered their continued existence impossible. The cases in which the diagnosis must remain uncertain are rare if the conditions of health and hygiene of the district, as well as the result of treatment, be duly weighed. It is of great importance that the social position and mode of life of the patient be carefully ascertained, as these afford us valuable indications to guide us. Anæmia occurring among miners and brickmakers must always awaken a suspicion of anchylostomiasis, particularly if of a high grade. On the other hand, the same symptoms occurring in a town patient would not waken the same suspicion if he assured us that he was careful as to the water used by him, and that fæces were carefully removed, excluding the possibility of infection from these sources. If a patient, extremely anæmic, assured us that he was in the habit of drinking water from pools and streams, that no latrines existed in his district, and that fæces lay in the immediate neighbourhood of the dwelling-houses and water-supply, we might almost with certainty diagnose the disease as anchylostomiasis. The probability of its being so would still be strengthened, if similar cases of anæmia occurred in the same locality.

The age of the patient is of consequence. I found frequently isolated cases of the disease among very young children, because their habits exposed them to infection, and very few parasites caused decided symptoms. My youngest patient of this class was about one year old. I treated several under two years.

Sex is also of consequence, as a high degree of anæmia in the male is always a suspicious circumstance, inasmuch as men come oftener in contact with the sources of infection. The worm is usually taken into the system at some distance from the dwelling, as along roads, in fields, and where men are generally employed in gangs. Women under the same conditions are even less resistant to infection. Complications from other causes are common in their case, and other previous diseases have often already prepared the way for anæmia.

We cannot say that one race is more predisposed to the disease than another. We find the same parasites producing the same symptoms in the black and white races, and among these, blonde inhabitants of northern latitudes are affected in a similar manner to the dark-haired tribes of the south. In Brazil I had cases of anchylostomiasis among Germans, Italians, Portuguese, as well as among natives (Mulattoes and Negroes). Difference in the frequency of the disease is not due to race characteristics, but to external causes. In a warm and moist climate we have a predisposing cause; in a cold, the reverse. Amongst workers underground the chief factor of danger lies in the natural rise of temperature from position. The Gotthardt epidemic showed this in a striking manner. The physical nature of the ground, as has been already mentioned, is of importance, and deserves consideration, whilst its geological and chemical characteristics are not of any consequence, inasmuch as from a geological point of view anchylostomiasis occurs in the most varied countries. I lay some stress on this fact, as a different opinion prevails in Brazil, founded on erroneous observations. The occurrence of anchylostomiasis, in an endemic or epidemic form, is usual and characteristic, and wherever anæmia occurs in such forms it is almost with certainty due to the parasite. In individual families all stages of the process may be observed: the difference, however, is to be attributed entirely to differences in the time of infection, not to individual resistance to the disease. If the males alone are infected, this fact points to the source of infection being outside the dwelling. Often one member of a family may directly

infect another, of which mode of infection we have undoubted proof. I cured a colonist of the disease some time after he had exchanged from an infected locality, to a place *quite free* from the disease. A child born in the latter place showed symptoms of severe anchylostomiasis a year after, although it had never been much beyond the immediate neighbourhood of the house. The father remained quite free, and there was no other case in the locality. There was here about the house all the conditions favourable to the accumulation of anchylostoma—larvæ—before the father was cured, so that the child crawling about might easily be infected. The drinking water was above suspicion, removing the principal source of danger to adults.

Under favourable conditions even a secondary infection can take place. The patient carries about with him the materials for the development of fresh broods, and constitutes in this manner, not only for others, but also for himself, a new source of infection. He very often is infested with several generations, which originate directly from himself. On this account it is difficult to determine the duration of life of the parasite beyond the time the patient left the place of infection, as a secondary infection is not always to be excluded.

Turning now to the disease anchylostomiasis itself, and beginning with the pathological anatomy, I must acknowledge that the results hitherto obtained are not sufficient explanations of all the clinical symptoms, because, on the one hand, the number of the post-mortem examinations hitherto made are extremely small in comparison with the cases clinically observed, and because even on post-mortem examinations important questions were left undetermined, and because there are, in this disease, many subjective symptoms of great importance, which could be only determined during life.

The post-mortem examinations to be mentioned here refer partly to individuals whose death was caused directly by anchylostomiasis,—as no other cause could be found,—and partly to others in which the presence of the parasite was a complication more or less accidental, and found in small numbers, only giving rise to local symptoms. Further, there are post-mortem examinations referred to, in which the disease had not been recognised and the intestines had not been examined. Under the first class I mention, from the literature of the subject accessible to me,—the observations of Pruner, Griesinger, Bilharz, Wucherer, Felicio dos Santos, Morrelli, Orsi, Grassi, C. Parona, De Maldé, E. Parona, Schönbachler, Graziadei; under the second, Dubini, Sangalli, Heschl and Kundrath, Roth, Bäumler; and under the third Schillinger (Schemnitz).

Besides these, descriptions of the pathological anatomy are found in the works of Wucherer, Leuckart, Bugnion, and Bozzolo. As to the discoveries made in the intestines, we have comparatively old (Bilharz, Griesinger, and Wucherer) and comparatively recent descriptions (Bozzolo, E. Parona, Schönbachler, Roth, and Bäumler). In the first place, the anchylostoma itself was found, sometimes adhering firmly to the mucous membrane, sometimes loose in the mucus, according as the examination was made earlier or later.

Schönbachler found some of them in the pylorus, E. Parona found a great number free, even in the contents of the stomach. Their principal seat is the duodenum and jejunum, but they are also found in the ileum (Roth, Bäumler) even beyond its middle, and, according to Rion de Keragel, even in the cæcum. In such cases the duodenum may be completely free (Roth, Bäumler),—a circumstance which probably depends on medication and antiparasitic substances (*e.g.*, alcohol), which, in concentrated quantities, exert their effects, not only in the stomach, but also in the upper portions of the intestines. The places of adhesion of the worms, according to Roth, are the little gray modules observed, of a diameter of $\cdot 8$ mm. with a reddish centre of $\cdot 3$ mm. diameter, and formed by the accumulation at the spot of white and red blood corpuscles. In addition to these modules, there are also observed punctiform extravasations, also described by other observers. (Grassi and Parona speak of spots of the size of millet seeds with a raised white border and a sunk red centre, in which the mucosa seems to be ruptured.)

Besides this, several authors have described large hæmorrhages in the sub-mucosa, often visible on the peritoneal surface, the diameters of which are variously reckoned (2 to 5 mm., Schönbachler; 6 to 8 mm. by others). Many of these hæmorrhagic spots were found to contain anchylostoma coiled together into a ball, the stages of development of which have not been sufficiently examined: in other spots these were not found. It is possible that in the latter case the worm might have burst its way into the intestines, especially where traces of a perforation were still visible in the sub-mucosa. This encysted anchylostoma is rarely to be met with; but, notwithstanding, it is worthy of note, that they were found by such authorities as Griesinger and Bilharz, who had opportunities to examine bodies in which infection had occurred a short time previously. If this is a question concerning the non-adult worm, as Leuckart believes, the circumstance may serve to explain why it has never been found in bodies which had not been exposed to infection for some time previously. (Roth and Bäumler.)

I am inclined to be of the same opinion as Leuckart, as there is reason to believe that the non-adult form of the worm never inhabits the lumen of the intestines.

Besides these, there were punctiform, spotted, and slate-coloured pigmentations met with, which must be regarded as residual hæmorrhages. In old preparations (preserved in alcohol and in Müller's fluid), which I had an opportunity of examining in Turin, I saw no pigmentation; on the other hand, I observed numerous depressions, the size of a millet seed, on the thickened mucous membrane of both the stomach and the intestines, which might represent the original position of the worm.

The mucous membrane of the stomach is described by Wucherer as thickened, softened, and relaxed. Graziadei found a general dilatation of the stomach.

In a case of Roth's I found gastritis with hæmorrhagic erosions. Grassi and E. Parona noticed grayish spots and vesicles on the mucosa, with profuse mucous secretion and thickening of the walls and general dilatation of the stomach.

As far as the intestines are concerned, various observers noticed an increased mucus secretion often with a slight tinge of blood; large extravasations of blood are rare. (Griesinger.)

Roth found small ulcerations, size of a pin-point, in the duodenum. Wucherer describes the intestinal mucous membrane as thickened. Bäumlér found membranes swollen in the jejunum, and partly so in the ileum. E. Parona observed infiltration of the solitary follicles and of Peyer's patches, as in the commencement of typhoid fever. Roth also found Peyer's patches thickened.

Wucherer saw vesicles of the mucosa and here and there a distinct narrowing of the lumen of the small intestine, allowing only a finger through. Felicio dos Santos is said to have once found the transverse colon narrowed in this manner. Bäumlér found in his case (complication with phthisis pulmonum) amyloid degeneration of the duodenal villi. E. Parona proved the existence of enlargement of the mesenteric glands, as well as Wucherer. The latter found the folds of the small intestines adherent throughout, as well as the transverse colon, by means of a gelatinous exudation.

The spleen is either normal in volume (Orsi, Schillinger) or atrophied (Wucherer, &c.). If it is found enlarged, malaria may be considered a complication. De Malde found it wrinkled with a few maculæ tendineæ, the parenchyma brownish red and softened. Amyloid degeneration is frequently met with.

The liver was either pale (anæmic), normal (Schillinger, Wucherer), or diminished (Wucherer), and undergoing fatty degeneration (de Malde, &c.). The kidneys showed similar changes, being anæmic, undergoing amyloid and fatty degeneration (Bäumlér). Graziadei found the kidneys enlarged through swelling of the cortical substance. Schillinger found three times the parenchyma rough to the touch. The kidneys were once found dry, atrophied, and of a grayish red colour. According to Wucherer the Brazilian physicians found enlargement of the pancreas. The changes in the heart are comparatively uniform. The parenchyma is flabby and relaxed, and very anæmic, the inner layers being specially pale, even yellowish (de Malde).

The whole heart is sometimes of normal size, or is dilated (Wucherer, Orsi), without any hypertrophy of the left ventricle (Bäumlér).

In other cases it is immensely increased in size, and thickened, the left side showing distinct hypertrophy and dilatation. The endocardium and the valves are often normal, sometimes, however, turbid-looking and thickened. Graziadei found them once very thin. No one seems to have examined the state of the papillary muscles. Maculæ tendineæ were found on the visceral and parietal pericardium by Bozzolo. The intima of the aorta showed traces of an endarteritic process, even in young people. As far as the contents of the vascular system are concerned, there were found in the heart soft brownish-red coagula, or a clear reddish watery fluid with a few red and white blood corpuscles.

A high degree of anæmia is almost always present, plainly visible in the pallor of the skin, muscles, meninges, brain, larynx, lungs, and rest of the organs, as well as extensive dropsy, particularly in the form of anasarca, of hydrothorax, hydropericardium, and ascites; besides these, œdema of the brain and lungs are frequent. Further, there is a moderate degree of emaciation, flabbiness of the muscles, and in old cases more or less disappearance of the subcutaneous fat. In most cases subcutaneous fat is well developed, sometimes remarkably so. Graziadei found large accumulations of fat in the anterior mediastinum.

œdema of the meninges and of the brain have been observed to cause death; also intestinal hæmorrhage (Griesinger). In most cases death resulted from œdema of the lungs and cardiac insufficiency.

Tuberculosis of the lung, malaria cachexia, putrid bronchitis, gangrene of the lungs, and other intestinal parasites have been met with as complications.

With these we almost exhaust the discoveries hitherto made in the dead body. Many of these stand isolated, and in accordance with their nature do not, most probably, belong to the disease at all. In others, further observation is most desirable. Unfortunately there are but few among the comparatively few cases examined post-mortem where a thorough examination had been made,—possibly not one *complete* examination. We miss completely the examination of the marrow of the bones as well as that of the eye, both of which are in this disease of great importance. No microscopic examination has been made to determine how much of the pallor of the parenchyma of many of the organs was due to simple anæmia, how much to fatty degeneration. The voluntary and involuntary muscles have not been sufficiently examined.

We know very little of the condition of the glandular elements of the digestive tract, or of the mesenteric glands. The examination was often satisfied with the discovery of amyloid degeneration, whilst otherwise it seemed to have been limited in extent. Sufficient attention has not been bestowed on the process of development of the worm, nor where the non-adult worm is to be met with. All these deficiencies and lacunæ must be borne in mind in future research, and it is not too much to assert that, under favourable conditions, the careful anatomical examination of one single pure case would give us more information than has been given by all the post-mortem examinations hitherto made. Such an examination is to be earnestly desired, as we expect and hope that the occasions for such autopsies will become fewer and fewer.

Meanwhile, what has been actually discovered enables us to come to a number of important conclusions, the following in particular:—

- (1) With the presence of the *ancholostoma duodenale*, there are met with in the intestines local lesions consisting of small and large hæmorrhages in and under the mucosa.
- (2) In a number of cases there were found changes in the mucous membrane of the stomach and bowels, which must be looked on as chronic catarrh with increased mucous secretion.

- (3) As a result of the local processes, there has been observed poverty of blood, which is frequently accompanied by dilatation and hypertrophy of the heart.
- (4) The whole organism suffers from disturbed nutrition. This mal-nutrition of the whole system manifests itself in the individual organs by atrophic and degenerative process.

We now leave the region of pathological anatomy and turn to the clinical symptoms.

The examination of a patient suffering from anchylostomiasis is to be carefully conducted, and both the objective and the subjective symptoms are to be recorded.

The latter appear, as a rule, earlier, are more constant, and are therefore of great diagnostic importance. According to their nature, they either point to digestive, or circulatory disturbances, or to mal-nutrition of the whole system. They generally rise in this order, followed or accompanied by symptoms more or less easy of recognition, which gradually rise in intensity as the disease itself advances.

The digestive organs suffer, as a rule, very early, and must on that account be carefully examined in localities where the anchylostoma prevails. Occasionally, indigestion alone leads the patient to the physician, and it is most essential that the cause should be recognised, in order to effect a speedy cure. It is only in rare cases that symptoms of dyspepsia fail altogether, as for instance, in forty well-marked cases at various stages examined by myself, I found them absent *only once*, and the number of parasites in that case was small. In some cases the symptoms may be so mild that the patient does not refer to them unless questioned on the matter.

The most frequent of the localised symptoms is a painful sensation in *scrobiculo cordis*. I found this in 32 of the cases quoted above (= 80 per cent.), and this pain was complained of by the patients themselves in 27 cases (= 67 per cent.). The pain is increased on pressure. In 5 cases pressure was necessary to elicit the pain at all. In two cases the feeling of pain was slight and intermittent. Accompanying this symptom there is generally a constant distension of the abdomen at the same spot (28 out of 40, = 70 per cent.). After meals there are feelings of weight and of over-indulgence in food, with frequent eructation of gas. In several cases a more or less degree of pyrosis betrayed the presence of abnormal processes in the contents of the stomach. Vomiting is further a very frequent symptom, occurring in almost one-half of the cases; on the other hand, no periodicity can be traced in the act. Now and again (2 out of 40) there were small quantities of blood in the vomited matter; in individual cases, on the contrary, the quantity of red blood or of coffee ground masses was considerable. The vomit contains otherwise large masses of mucus and any food previously partaken of. Vomiting occurs on an empty as well as on a full stomach. The ova of the anchylostoma have been found in the vomit. In a simultaneous dilatation of the stomach I found also *sarcinæ ventriculi*.

The contents of the stomach have not been examined chemically as yet, but it is probable that there is a diminution in the muriatic acid.

That the volume of the stomach is greatly increased, can occasionally be shown by physical examination. In a few cases a real dilatation exists, betraying its presence by the usual symptoms.

Further, violent cardialgia is occasionally complained of, felt more in the back,—a circumstance which I also observed in carcinoma of the cardiac end and the smaller curvature of the stomach.

The appetite is variable, in rare cases it is quite normal, but mostly it is quantitatively and qualitatively altered. Very frequently a ravenous appetite is present, amounting to complete bulimia. There are also cases in which it is diminished almost to complete anorexia: the latter condition is frequently accompanied by constant nausea. This condition is found generally in the later and extreme stages. In the beginning of the disease the appetite is increased, as a rule.—Between these extremes there lies an interval of time, in which the appetite varies from extreme ravenousness to complete failure.

The disturbances of digestion are frequently accompanied by a slight catarrhal stomatitis, the tongue being coated with a whitish slimy layer. In one case the stomatitis was intense, accompanied by *fætor ex ore*, for which no other cause could be assigned. This symptom disappeared on expulsion of the parasite.

Another symptom which has been sometimes observed is salivation, and that to some extent.

Qualitative alterations of the appetite with the prevalence of certain more or less strange desires come with tolerable frequency under observation.

Adults, otherwise quite rational, cannot often resist the desire to eat unripe fruit, uncooked rice, &c., whilst they reject ordinary food. The appetite for acid substances is frequent. There was no inclination for alcohol, at least among temperate Brazilians. The most of the patients assert that alcohol in any form does not agree with them. Still the symptoms may require the exhibition of brandy, in which it gives relief. That form of appetite termed allotriophagy, by which the patient eats a variety of unsuitable articles, such as clay, wool, paper, feathers, &c., is much rarer. Still this form has been observed by various authorities, who lay stress on it (e.g., Wuchurer, St. Vel. Volpato). I myself have only met with one form of it, viz., geophagy (earth-eating). This peculiar symptom is frequently observed among children (white as well as black) affected with the parasite. At the period of puberty, or arrival at years of discretion, and more limited freedom, the habit is usually given up. I have never observed the habit among white adults; occasionally, on the contrary, among the blacks, although less seldom than among children. As a rule, the most of the patients are inclined to conceal the habit: some say they feel the inclination, but never give way to it; others assert they satisfy it by merely smelling the earth.

That earth-eating is not only a habit, but also a real passion, is seen in the case of slaves

and children, who cannot be restrained either by commands or punishments. St. Vel relates the case of a black child who, even with his strength failing in death, endeavoured to gratify the miserable craving.*

I have not been able to satisfy myself that in geophagy there is any particular form of earth chosen, clay and black mould being consumed without distinction. The foot-paths and clay-walls supply very often the material. Some patients lick bricks and bite pieces out of them. That such a habit should conduce to the introduction of fresh parasites is easily understood, but it cannot be granted that geophagy is the primary, anchylostomiasis the secondary disease. The first is rather a symptom of the second, and almost pathognomonic.

Alterations and peculiarities of taste also occur in other diseases, as in hysteria and especially in chlorosis and pregnancy. Geophagy may be one of these, only this symptom is much too rare to alter in any way the practical and important rule, founded on varied experience, viz., that wherever geophagy prevails in localities infested with the anchylostoma, the symptom is in the first place to be regarded as indicative of the presence of the parasite in the intestines. The parasite is only to be regarded as the indirect cause, the anæmic condition as the direct cause of the craving. As far as the geophagy of entire races is concerned (*vide* Humboldt's "Travels") it seems this depends on other conditions, at least in a portion of the cases. The geophagy is limited to certain kinds of earth, and is not accompanied by any symptoms of disease. It is always interesting to know that earthy substances are not quite so disagreeable to the races of "nature" as they are to our refined palates. Also it would be worth while determining whether this peculiar kind of nourishment does not favour infection with parasites, and whether amongst many races only infected individuals eat earth, which in its turn would favour the idea of the presence of anchylostomiasis.

It is most probable that in geophagy hunger plays an important part, as the patients are not always in a position to gratify the craving at all times. The idea of alteration of taste is not always to be overlooked, at least geophagy in other diseases accompanied by ravenous appetite, as for instance diabetes, which even occurs in children, has not, according to my knowledge, been observed.

Next to symptoms of dyspepsia, the most frequent functional disturbance is chronic constipation. This symptom is rarely absent in cases of ordinary intensity and duration, whilst mild and incipient cases show in this respect quite an ordinary function. This constipation is very obstinate, and not easily overcome by drugs, and leads very often to fæcal accumulations, which patients often find distressing, and the removal of which gives great relief.

Diarrhœa is much less seldom than constipation, and only occurs on the whole in one-third of the cases. Yet only acute attacks occur, and these otherwise common enough. The diarrhœa is of special interest when it occurs frequently, with intervals of constipation. The irregular intestinal function, diarrhœa alternating with constipation, is often observed in this disease. Long continued and intense chronic diarrhœa is extremely rare, and only occur in advanced cases. If some authors assert this as common, as for instance in the Gotthardt epidemic, the reason is that these came across very severe cases. For the organism diarrhœa is accompanied by severe consequences, inasmuch as it runs its course with loss of appetite, whilst chronic constipation is accompanied by an increase in this respect. The fæces, macroscopically, offer nothing characteristic. This is specially the case in the first stages of the disease. Later on they are either dry, or fluid, especially through mixture of undigested food, of mucus, and of blood. The discovery of large quantities of undigested food is the more striking, when a rather slow passage through the intestines must be supposed, as is really the case. In such a case we must suppose the bowels incapable of exhausting the nourishment from the food. Mucus is not only found covering the fæces, but it also occurs in larger and small masses throughout it, and we are really obliged to suppose an increase of the mucous secretion in the upper parts of the intestines.

Blood is either mixed in small quantities with the mucus, or the solid or fluid stools look dark like coffee-grounds, or large quantities of fluid blood may be evacuated, as in the abdominal hæmorrhages of typhoid fever. Hæmorrhages may be easily overlooked, but they betray themselves when they occur repeatedly, or in large quantities, by the rapidly advancing anæmia. According to most authorities hæmorrhage is a rare occurrence; yet, according to my experience in a fair number of cases, running a chronic course, but usually at long intervals. They are seldom observed in hospitals, on account of the short stay of the patient there. Patients who use latrines seldom notice the blood in the stools. It is the reverse with those who use the open field, who, either spontaneously, or on being questioned, report the passage of blood in their stools.

Seven of the forty patients already referred to asserted that they passed blood during their entire illness, lasting most probably for several years. In three cases I found traces of blood: in one black, solid, or fluid evacuation; in another coffee-grounds, and in the last a real intestinal hæmorrhage had occurred, with the evacuation of fluid blood. In some cases the hæmorrhage was referred to hæmorrhoids, but none such could be found to exist.

Small quantities of blood effused into the upper portion of the intestines are not macroscopically, and sometimes not even microscopically, discernible. Whether the presence of blood can be proved by chemical reagents, remains a matter for future investigation. I have still to mention another peculiarity, viz., the discovery of microscopic crystals of a characteristic form in the fæces. Perroncito was the first to observe these. In his treatise on the disease, he considers their occurrence as constant in anchylostomiasis. Bäumlér, who at an earlier date found them in the colon, spoke of them as Charcot's crystals. Later on they were noticed by other observers.

* A common occurrence among labourers on the coffee estates of Ceylon.—*Trans.*

I myself found them in one of my earliest cases. They lay in large numbers in the midst of small masses of transparent mucus.

Their resemblance to Charcot's crystals struck me forcibly, and I convinced myself of their analogous action towards reagents. As the observations of others were not known to me, I examined other cases, but could not convince myself they were of constant occurrence. Their presence in the bronchial secretion would speak in favour of their connection with catarrhal processes. On the other hand, they are also met with in leukæmic blood. In addition to the functional disturbances already described, there is yet a symptom pointing to disease of the intestines, viz., pain along its course. There are two regions in which this symptom frequently appears, viz., right and left from the pit of the stomach, and immediately below the transverse line of liver dulness. The pains in these localities are described as piercing or griping pains, seldom as burning. In some cases it is only a dull pain, in others very intense. The patient very often complains of the pain, but it can always be elicited by pressure. Both sides of the abdomen are sensitive, as a rule, but if the pain is limited to one side, it is generally the right. This localised pain has something very characteristic to me, because it occurs not only in more than one-half of the cases appearing early in the disease, but also because, according to my experience, it is so seldom to be met with in other diseases, and such cases are easily excluded. Only insufficient examination or defective anatomical knowledge can lead to the seat of the pain being assigned to the liver, as happened constantly in Brazil. Meteorism is usually present over the painful spots, which gradually blend with that of the epigastrium.

In severe cases the extent of the pain may be great, spreading over other portions of the abdomen,—e.g., over the ileo-cæcal and umbilical regions. These regions are painful on pressure, or what is more common, the whole of the lower part of the abdomen is painful subjectively, and to touch. These cases usually suffer from chronic diarrhœa.

As examples of the frequency of this symptom the following cases may be quoted:—

Among the forty cases already referred to, the patients complained of abdominal pain in the right side in twenty-six cases, of which six were mild and transient and three elicited only on pressure. Twenty-two patients complained of pain in the left side, of which five were mild and four elicited on pressure. Pain of the ileo-cæcal region was found in one case; of the umbilical region in one case.

In twelve cases the whole abdomen was painful, one of which only on pressure.

In conclusion, I shall here mention a complication, or result, not hitherto described. It was found by me four times in 250 cases, and consists in a peritonitis circumscripta, with only mild general symptoms. Vomiting and meteorism may be entirely wanting, and the rise of temperature be inconsiderable. The peritonitis does cause a *free* exudation, and there are traces of such between the folds of the intestines, which bind the convolutions together at the seat of inflammation. By suitable treatment all the symptoms disappear in the course of a few weeks, by which it may be distinguished from a very similar disease, viz., tubercular peritonitis. Adhesions may remain in the former, however, permanently.

In one of the cases, such a local peritonitis was accompanied by a properitoneal phlegmonous infiltration above the symphysis pubis, which, however, resolved without any suppuration. If we now look for the pathological processes which give rise to these symptoms, in view of the many observations made, inclusive of the life-history of the parasite and of the pathological anatomy, we come to the following results:—We must refer the pain in the scrobiculus cordis to the stomach, and specially to its lower part. The pathological process is indeed the same, which we so often observe in feverish or anæmic cases, where the digestive powers of the stomach are quantitatively or qualitatively altered.

The German physician in such a case speaks of "catarrh of the stomach," whilst the French use the very suitable term "embarras gastrique" (gastric embarrassment) to express the same idea. Here there is no question of a lesion, but simply of functional disturbance, which rapidly disappears after treatment. This happens in our cases, inasmuch as after purgative and anthelmintic remedies, the symptoms disappear. In such cases we find in the dead body only slight changes in the stomach, or none at all. If we inquire into the cause of this condition, we must refer it, in the first place, to anomalies of gastric secretion. It is most probable that in consequence of loss of blood the secretion is already altered quantitatively or qualitatively before the anæmia appears. It is also possible that the peristalsis of the bowels may suffer in consequence. On the other hand, at this period of the disease the patient takes his usual quantity of food, or possibly more than usual. The digestion under such conditions cannot be *complete*, and the gases evolved and acid products of decomposition give rise to the disagreeable symptoms complained of. In course of time these symptoms become intensified, and are not easily relieved. These are the cases where the appetite suffers, and the patients vomit slimy masses of mucus, even whilst fasting.

Here we have chronic gastric catarrh, the presence of which can be detected on the post-mortem table. How much of these changes is to be attributed to the presence of the parasite must be left undetermined, as we know so little of their presence in the stomach.

Experience of other parasites, as the round worm, teaches us that the stomach is quite as intolerant of the parasites as the rest of the digestive tract. If they are present, they certainly must aggravate the symptoms. Piercing pain in the stomach, accompanied by traces of blood in the vomited matter, make their presence there probable, although we must not lose sight of the possibility of hæmorrhagic erosions. On the other hand, the presence of the anchylostoma itself, or of its ova in the vomit, would make the diagnosis quite sure, if regurgitation from the duodenum could be excluded. Severe cardialgia points to the existence of an ulcer, specially should the pain be unusually localised, as in the back. Hæmatemesis renders the diagnosis almost certain. Although hæmorrhagic erosions and ulceration are either accidental complications

or dependent on the anæmia, yet there is still the possibility that they might have originated from injuries inflicted by the worm on the mucous membrane.

Passing now to the other epigastric pains, we may refer that, in the left abdominal region, at least partly, also to the stomach. On the other hand, that on the right side can only be referred to the portion of bowels lying underneath. We cannot refer it to the colon, as otherwise the symptoms would be found in its course, and besides, other symptoms would be present. We cannot refer it to the more movable portion of the small intestine, the position of which is neither constant nor fixed like the pain. The duodenum alone, and the upper portion of the jejunum, could give rise to such a pain, and this also explains why it is in some cases only elicited on pressure. A similar pain has been noticed in *ulcus duodenale*. A large experience has taught me that the pain has a direct connection with the presence and activity of the worm, as it very quickly disappears after the use of suitable anthelmintics, often even before the worms are expelled *per anum*. If it should persist, we must conclude that some worms are still left *in situ*, and this may be proved from the appearance of the eggs still in the *fæces*. A few are quite sufficient to maintain the pain.

In this explanation, there is still to be determined why the upper portion of the intestines should be the most painful. If we relinquish the idea that here is, by preference, the habitat of the parasite, and the place where it accumulates most, then there is only left for us either to suppose a hyper-sensibility of the part, or some change of the intestinal fluid irritating to the mucosa.

The fact that even mere purgation eases the pain might be quoted in support of the latter view.

Meantime, as we have seen, other parts may show the same symptoms, and this is not at all rare, as far as the small intestine at least is concerned.

The constipation is explained partly by the fact that large quantities of indigestible materials are taken with the food,—at least this is the rule in Brazil,—partly because in the chyme the bile materials on which the increased peristalsis mainly depends are present in comparatively small quantities. There may be other causes depending on the anæmia itself. Large masses of mucus and undigested articles of food, possibly also the presence of Charcot's crystals, point to a special form of chronic intestinal catarrh.

Frequent intermittent or continued diarrhœa point to an advanced stage of the disease with possibly amyloid degeneration of the mucosa, as well as follicular ulceration. In several cases we were obliged to found our diagnosis on the presence of ulcers. (*A priori*, it does not seem at all improbable that ulcers should be developed from the bites of the parasites, and from submucous hæmorrhages, still the peptic effects of the gastric juice must not be overlooked.) The profuse intestinal hæmorrhages observed clinically, in which the hæmorrhagic diathesis was not present, speak in favour of this. In one case pain was complained of on the right of the stomach, which became intense a few hours after each meal. The diagnosis of the duodenal ulcer made, was, later on, confirmed by symptoms of dilatation of the stomach. Further, the swelling of the lymphatic glands and adhesive peritonitis observed by Wucherer, and which is the pathological discovery of the process diagnosed by me *intra vitam*, prove that an inflammation of the intestine occurs, which may involve the serosa; further, that the inflammation, instead of leading to the adhesion alone, may also cause perforation, has been made apparent in at least individual cases. A Negro infected with *anchylostoma*, but still capable of work, was suddenly seized with extremely violent pain in the abdomen, and showed signs of collapse. On first examination I could discover no distension with gas over the liver, but I discovered it two hours later on, distinctly pronounced. The case, which I unfortunately only observed for a short time, terminated in recovery.

As far as the adnexa of the digestive tract is concerned, we have no clinical facts before us which speak of any independent disease there. The liver on percussion may be found slightly enlarged or diminished, and in combination with other symptoms, amyloid degeneration, congestion, or atrophy may be present, as a portion of the general process. On the other hand, I must lay stress on the fact that I never found pain over the hepatic dulness, nor ever noticed icterus.

The latter fact is of interest, because it speaks in favour of the rare occurrence of the catarrhal process at the orifice of the ductus choledochus, giving colour to the idea that the parasite avoids the bile. I have never found the bile-colouring matter absent from the stools, of which Heller (in V. Ziemsen's Handbook) speaks; and I believe the production and secretion of bile is never *seriously* interfered with.

I will now consider the very interesting, but very complicated, circulatory symptoms. There are two subjective cardiac symptoms frequently met with, *i.e.*, palpitation and pain. Palpitation was present in four-fifths of my cases, and is almost without exception present in the advanced stages of the disease.

This symptom is only observed at first after exertion, but later on slight movements, or even mental emotion brings on the symptom, and in many cases it is observed in a state of complete rest. In 83 per cent. of the cases the palpitation was accompanied by a characteristic persistent sensation of pain, felt over the whole cardiac area, and described sometimes as a dull pressure, sometimes as piercing burning pain. The shooting pains characteristic of angina pectoris or aneurism were not usually observed. On this account, and on account of their frequency, they have something characteristic, and have given rise to the very suitable term "*Malcœur*" (*Mal de Cœur*). If we examine the patient after exertion, such as ascending a stair, we cannot but be convinced that these subjective sensations are not without cause. We find that the cardiac action is strong and fast, and we infer from that that the heart can only perform its function by violent efforts. These efforts cannot persist long without producing exhaustion of the organ, which is the cause of the subjective sensation of pain. I classify this pain with the pain felt in the muscles after violent walking, riding, rowing, &c., often felt only on the following day. If we

now allow the patient to rest himself thoroughly and examine the heart by inspection, percussion, and auscultation, we may find no peculiar symptom whatever. These are, however, cases of no great severity or of short duration.

In other cases, however, we find distinct and several changes. On inspection, whilst the patient sits up, the cardiac impulse is easily observed. The impulse may be normal in every respect, but the rule is that its area is enlarged, and that the chest wall bulges out over the place, or we may find the impulse removed considerably outwards to the left, and downwards to the sixth intercostal space, and rarely lower than this. In some cases, especially in children, the whole cardiac area may bulge outward, the impulse being observed extending over the most of it. We may already recognise by inspection increased action of the heart. Sometimes it is so fast that the stroke is more of a vibration than a pulsation.

In a few cases we noticed epigastric pulsation. By palpation we discover that the impulse is strong, its area enlarged, and that it causes vibration of the chest wall distinctly felt by the hand. The latter symptom must be referred to the closure of the valves. In other cases there may be no symptoms discovered on palpation. On percussion we discover that the cardiac dulness is increased, especially to the left, and downwards. Now, keeping in view the fact that the right margin of the dulness is often removed beyond the centre of the sternum, and that the impulse is felt in the sixth intercostal space, we must conclude that the heart is considerably enlarged. In very many cases, however, the cardiac dulness is normal.

On auscultation we find the cardiac sounds altered in three directions, viz., in their frequency, intensity, and their acoustic properties. We shall discuss the frequency of the action when speaking of the pulse. The first cardiac sound is either of normal strength, or very much increased in intensity, sometimes to such a pitch that it may be heard at a distance from the patient. On the other hand, when the action of the heart is fast and irregular, and the contractions are weak, as is the case in the most advanced stages of the disease, the first sound is very weak. In a considerable number of cases the sound will be found indistinct, having the character of a blowing sound, not unlike a valvular murmur. This blowing sound is heard sometimes *only* at the apex, sometimes *only* at the base. In addition, a more or less indistinct systolic murmur is heard in other places. This murmur may, however, be heard over the whole cardiac area, and nowhere else. The second heart sound may be likewise intensified, remain normal, or become very weak, in a similar manner and from the same causes. If the systolic blowing sound is developed, the second sound may be altogether inaudible or only heard over the aorta. It is, however, often intensified, and accentuated especially over the pulmonalis. According to Leuckart and Heller, it may sometimes be heard at a distance from the patient. I found it audible at a distance only in connection with the first. It is very exceptional for it to be replaced by a murmur.

The pulse may be altered in various ways. Its frequency is seldom normal: it is most commonly increased. The frequency may be very great even in a state of rest; in other cases, the pulse only rises after exertion, but the rise is very considerable. The average of thirty-six cases of different degrees and ages, in a state of rest, was ninety-eight pulsations per minute. The rhythm of the pulse may also be disturbed. Intermittency is a frequent phenomenon, often during convalescence. This intermittency is noted both in the heart and in the arteries, and occurs after every ten or fifteen pulsations. It is not uncommon for the patient to observe it himself, and it gives rise to a painful sensation. On the other hand, the pulse may be irregular, the pulsation being now weak, now strong, but with that it is always fast. It is well to count the cardiac pulsations, as almost the one-half may not be discernible at the wrist. The character of the pulse may be altered. It may be weak, quick, thready, and compressible. In other cases the pulse is high, but of short duration (on account of its great frequency), a large volume of blood being suddenly passed from the dilated ventricle into the arteries. The finger paced over the artery experiences a sudden sharp impulse, and it is considerably raised: but, notwithstanding, the pulse is not hard, but, on the contrary, easily compressed. This quick heaving and soft pulse is very frequent, and for certain stages of the disease very characteristic. In some cases the pulse is dicrotic. (The above remarks refer only to the pulse in a state of rest. On exertion it always becomes fuller, and at the same time harder.)

The full, fast arterial wave become apparent in the distinctly visible arterial pulsation, especially in the carotid. This pulsation is often enough felt by the patient himself. On auscultation there is often heard over the large arteries a systolic blowing sound, and in some cases this sound is heard even in the smaller branches, and is, besides, conducted to considerable distances. I had a case in which the sound was heard, no matter on what part of the head the stethoscope was placed, and another case in which it was heard over the whole hepatic dulness.

Sometimes a blowing sound is heard in the arteries, whilst the heart sounds are normal; but, as a rule, the sound is heard over the heart and over the arteries at the same time. Turning to the veins, on inspection, considerable swelling of the jugular is noticed in many cases; undulation, rarely pulsation, may also be detected. On auscultation in the erect position, blood murmur is heard in half the cases. This murmur is heard on both sides of the middle line, as a rule, but when limited to one side, it may occur on either. Sometimes it is very intense, of a blowing character, and may be heard distinctly in the second intercostal space on both sides, and may, on auscultation of the heart, give rise to the idea of organic disease. On palpation of the veins the murmur is felt as a continuous fremitus.

These vascular murmurs, arterial as well as venous, may be noticed by the patient himself, and I have convinced myself from long observation that the noises in the ears complained of by such patients are due to these murmurs. Whenever noises in the ears exist, there exist also blood murmurs. Taking the intensity of these phenomena into consideration, it is easily understood how the patients themselves become conscious of them. The symptoms on the part of the heart and large vessels are here described as they occur in the majority of cases. The great variety of

these explain to us why the various authors who describe the disease, from experience of only few cases, vary so much in their descriptions, often contradict each other, and enter so little into the details of the symptoms otherwise so very interesting.

Without entering here in detail into an explanation of the causation of these symptoms, I may, however, select four groups from which the objective phenomena may be easily understood. Usually these groups are connected with each other in a very complicated manner.

The first group includes those cases in which the organs of circulation are normal, but in which there are increased frequency of the pulse, and increased irritability of the heart.

The second group includes cases in which symptoms of dilatation and hypertrophy, especially of the left side of the heart, exist, and in which sometimes the one and sometimes the other is prominent. These symptoms are manifest in the increased cardiac dullness, the heaving cardiac impulse extending to the left beyond the normal, the arching forwards of the thoracic wall, the loud heart sounds, the strong arterial pulsation, the full pulse, &c.

The third group includes those cases in which we have symptoms of valvular insufficiency in one or both auricles; ventricular openings, according as there is a systolic murmur, initial in character, with a pronounced second pulmonary sound, and a cardiac dullness extending to the right, or a prolonged blowing murmur with the disappearance of the second sounds altogether. The pulse presents all the characteristics of valvular disease, but is on the whole faster.

The fourth group includes those cases in which there is evidence of parenchymatous degeneration of the heart—intermittent or irregular, small, fast pulse, weak cardiac sounds, and imperceptible impulse.

Turning our attention now to the smaller vessels and capillaries, their degree of fullness and the nature of their contents are of interest, as these determine the colour of the skin and mucous membranes.

The most striking symptom observed here is the general pallor. In the mildest cases this may be overlooked, as it appears only after a more or less prolonged rest, whilst these same patients after bodily exertion or mental excitement may show mucous membrane of the normal colour, tolerably red cheeks, ears, &c. The parts where the pallor is best observed are the lips, the mouth and palate, the conjunctiva, and the nails. These must be observed in succession, and as a whole, otherwise mistakes may occur. The conjunctival sac is the most suitable for the observation of small degrees of pallor, as here the small vessels can be recognised singly; but it must be remembered that in individuals the vascularity of the conjunctiva varies at different times, even in health, and that slight irritants may cause a rich flow of blood in the part.

Changes of temperature effect alterations readily in the circulation of the lips and nails, whilst high tension of the blood vessels on the inner surface of the lips may easily lead to a wrong conclusion. Still, with careful observation, it is not difficult to estimate the effects of decreased as well as of diminished supply to these parts. In the course of the disease the uniformly injected mucous membranes, as that of the lips, become paler and paler, whilst in the conjunctiva the vessels ordinarily visible to the naked eye gradually disappear, and with them the red appearance of the membrane.

The conjunctiva bulbi first shows the pallor, which gradually spreads until the whole conjunctiva becomes of a milky, or yellowish-white, colour. In the lips, the limitation of skin and mucous membrane is no longer distinctly recognised: the soft and hard palate and the tissues under the tongue now only show the larger vessels against the pale ground. In advanced stages of the diseases all the mucous membranes accessible to inspection acquire a uniformly pale colour. In fair people it becomes quite white. The alæ of the nose and the ears acquire a waxy look, almost translucent, the nails become snowy white, as well as the scleræ, unless, as in dark individuals, the choroid pigment gives them a bluish appearance.

Patients finally acquire completely the colour of a dead body, and they are to be distinguished from the latter during sleep only by the movements of respiration.

The skin of pigmented races becomes lighter in colour under the influence of anæmia. Negroes acquire a gray or ashy-gray colour, and the skin at the same time becomes dry and loses its polish. Yet the variations in this respect are so numerous, that it is as well to depend upon the colour of the conjunctiva, the mucous membranes, and the nails alone.

Whilst individuals poor in pigment, appear white, pigmented persons, on the other hand show, especially in parts exposed to the sun, a yellowish or dirty brown colouration, resembling the skin in cancer cachexia or intermittent fever. In many cases the skin pigment appears increased. Not only ephelides, but also large chloasma are seen even in men. Often the whole cheek is covered with a large splash of colour, and the whole skin seems at the same time to be strongly pigmented. The yellowish colour of the skin goes under the name of amarellao (jaundice) in the province of São Paulo.

As for the retina we know that the vessels, especially the arteries, are diminished in size, and that the papilla is whiter. Examination in this direction is yet required. Another symptom deserves notice besides the pallor, *i.e.*, cyanosis. This symptom occurs only in extreme anæmia, and on that account has a peculiar characteristic. The mucous membranes and nails become then quite pale, but with a violet tinge. The venules visible on the former are likewise more violet than blue, but tolerably well filled. The pale rosy red colour becomes more or less livid. If a little blood be removed from the finger for examination, it may be seen by the naked eye to be paler than usual. In the most advanced cases a weakly-coloured fluid is only obtained. After standing, this blood separates into a transparent serum, in which small reddish specks may be seen with the naked eye. These are made up of blood corpuscles, which have formed themselves into rouleaux, and adhere to each other. There can be no doubt as to their immense reduction in number. As a matter of fact, all the experiments undertaken in this respect, both by counting the number of corpuscles and by other means, prove that the red

blood corpuscles are constantly and greatly diminished in number. In various patients they were reduced to a quarter and to one-sixth the normal, and in one case of Bareggi they were reduced to two-sevenths. As a rule, the reduction is one-tenth. The hæmaglobin, as far as I can learn from the literature of the subject, seems to diminish in the same ratio, so that no peculiar oligochromæmia occurs with the oligocythæmia. The ratio between the white and red corpuscles seems to persist for a long time, but ultimately the former become comparatively more numerous, without, however, any actual increase in their number, the actual number present being in fact considerably under the normal. No striking or characteristic changes in the sense of mikrocytose, or poikilocytose,* occur in the blood corpuscles in anchylostomiasis, but there is here a field for further study.

Some authors describe flakes of pigment as met with in the blood, and I also have seen such, but in my cases a complication, viz., malaria, existed. As for the volume of the blood and of its individual constituents, further and prolonged examination is still required to determine the changes these undergo. The property of coagulability is retained even in the most advanced stages of the anæmia.

I must still mention one symptom connected with the circulation before leaving the subject—*i.e.*, the occurrence of dropsy. This symptom occurs in a large number of the cases to a more or less degree, and serves as an index of the gravity of the case.

The most frequent forms of this dropsy are œdema of the eyelids and of the cheeks, as well as anasarca of the extremities. Œdema of the face appears early, and gives the patient a peculiarly characteristic appearance. In the more advanced form the impression of the teeth is visible on the mucous membrane of the cheeks. Œdema of the eyelids occurs at the same time as that of the cheeks, and both eyelids and cheeks appear more swollen in the early morning. Œdema of the extremities appears principally on the dorsum of the hands and feet. Later on the calves of the legs become œdematous, then the abdominal walls, and finally the skin of the back and of the arms.

The œdema remains as a rule moderate in amount, but in severe cases it may acquire great dimensions. In such cases the cavities of the body become dropsical, as the abdomen and thorax (ascites and hydrothorax). In rare cases symptoms supervene pointing to œdema of the brain.

I must mention here yet a rare symptom, and one not hitherto pointed out, and which I look upon as localised dropsy, *i.e.*, chemosis conjunctivæ without any eye affection. This symptom occurred in three out of 250 cases seen by me. It affected specially the fold, and was constantly accompanied by œdema elsewhere. The remaining symptoms are all more or less the direct result of the anæmia itself. To this class belong the giddiness of which the patients so frequently complain, especially when they bend down, and which is accompanied by dimness of vision. Further, the patients complain of being wearied and sleepy. They are, as a rule, apathetic, &c., and inclined to shiver. To these may be added formication, numbness, &c., in the extremities.

There is no change in the organs of respiration. The breathing keeps pace with the heart's action, and is more or less increased. The slightest exertion increases the frequency of the respiration, to a degree of dyspnœa, usually accompanied by palpitation.

The temperature in mild cases remains normal: in severe cases it is somewhat abnormal, on an average about one-tenth of a degree. Authors mention, however, the occurrence of occasional rises of temperature, as in pernicious anæmia. This fever may be looked upon as anæmic fever, only when inflammatory processes in the bowels or lungs can be excluded.

These feverish attacks, which occur most frequently during the night, account for the perspiration and thirst of which the patients occasionally complain. Otherwise the skin is dry as the sebaceous follicles, and sweat glands by normal temperature act but feebly.

The quantity, colour, and specific gravity of the urine remain apparently normal. Albumen is met with only exceptionally, and then in very small quantities, but is usually absent even in the severest cases. Should the circulation begin to fail, the urine becomes small in quantity and dark in colour, as in valvular disease of the heart, where the compensation begins to give way.

A high degree of anæmia leads, in men, to impotency, in women to amenorrhœa. Conception only takes place in mild forms, and pregnancy is always accompanied by danger. If carried to maturity, the children are poor and atrophic.

If children suffer from anchylostomiasis for years, during the developmental period, this development is retarded, so much so that at twenty-five years of age they look like children of ten or twelve.

The period of puberty is considerably delayed by several years. The development of tone is retarded, and the whole type remains that of a child. Although the disease in mild as well as in severe cases causes no disturbance of the general nutrition, yet long duration and advanced stages cause malnutrition, so that the patient begins to look emaciated. The panniculus adiposus begins to disappear, but only to a moderate degree, so long as the appetite is good, unless persistent diarrhœa sets in. Some sensations of pain are still to be mentioned, which are to be considered less as the symptoms of a local affection than as the result of the general condition. Of these, the headaches, of which most patients complain, take the first place. These headaches have nothing characteristic either in respect of locality, intensity, or duration. They are not to be explained in any other way than that they are the result of the anæmic condition.

It is otherwise with certain forms of pain, occurring now here, now there, in the trunk and extremities, and which have been described, erroneously as I believe, by some authors as neuralgias

* I have left these words as they stand in the original. Their derivation explains their meaning. Mikrocytose is derived from μικρός κύτος; poikilocytose from ποικίλος κύτος.—*Trans.*

On careful examination these pains are found to be situated in the muscles, especially the muscles of the extremities, and the lumbar and intercostal muscles. They occur after any exertion, and are transient in character, even in high degrees of the disease. I consider them, therefore, as mere expressions of exhaustion. In two extreme cases I found the bones painful on palpation and percussion. This symptom occurs also in pernicious anæmia.

With this I conclude the description of the symptoms peculiar to the disease. In this respect, however, much remains yet to be done. On the whole, these agree with the pathological changes, and give us some insight into this many-sided disease.

The symptoms of anchlostomiasis have been discussed one by one, and we may now attempt to explain their origin and mode of onset. It must be clearly understood that the disease varies extraordinarily in the duration of its development, the degree to which it may attain, and the extent of its effects, whilst the organism attacked shows varying degrees of resistance according to age, constitution, and other conditions, chiefly the state of nutrition. On this account the course is always irregular atypical, and it requires a careful observer to distinguish the more accidental variations from the results of suitable treatment. In general, we may divide the disease into two forms, one more or less acute, and the other more or less chronic.

The term "acute" is certainly to be applied here, not in the same sense as in the infectious diseases. Acute cases are those in which the disease has run through its several stages in the course of some months, without, during that time, becoming stationary at any one period or showing any distinct remissions. Chronic cases, on the other hand, are cases in which the disease has extended over several years (sometimes from ten to twenty years). In such cases the disease frequently shows remissions and exacerbations, and occasionally becomes stationary.

The Gotthardt tunnel epidemic ran a tolerably acute course; some cases were very acute. E. Parona mentions a case in which the patient acquired 1,250 anchylostoma within two months. Many of these cases, it is true, became afterwards chronic.

Among the natives of the locality, on the other hand, the disease on an average runs a chronic course. Twenty cases are exactly recorded, in which the average duration from the first appearance of grave symptoms was four years. From this may be explained many symptoms which I frequently observed, but which were rare in the Gotthardt epidemic.

Should the patient on exposure to infection be slow in acquiring the disease, the number of the anchylostoma may, for a considerable time, be limited, and their presence give rise to no symptom whatever. I have often found in the fæces of children the ova of anchylostoma, whilst searching for those of the ascaris, without any suspicion of the presence of the former. This discovery was rare in adults. In other case the presence of the anchylostoma was suspected from the local symptoms alone, whilst as yet no general symptoms were observable. As the disease advanced the local symptoms became more pronounced. Yet there are cases in which the patients complained of nothing locally, even in advanced stages of the disease. Should the patient be weakened by other causes, the general symptoms appear comparatively early, and which are not due to the parasite alone. It may be said that adults, in the absence of any complication, and in whom the disease runs a tolerably quick and uniform course, do not begin to show symptoms until the number of anchylostoma passes into the hundreds, so that when pronounced general symptoms are present three to five hundred parasites may be set down as present in the duodenum.

In several cases I have not found them over a thousand present, but in the Gotthardt epidemic two and even three thousand were found. Of the general symptoms, the first to appear are palpitation and a feeling of weariness, often comparatively early before any trace of anæmia is observable. Yet these symptoms must be referred to impoverished blood, as can be proved by careful examination of the latter. Inspection alone detects changes in the blood only when these have already attained to a high degree. The constituents of the blood principally affected are the red blood corpuscles, the regeneration of which first ceases to keep pace with the constant small losses occurring in the duodenum. Although there is no direct proof, yet clinical facts speak in favour of the regeneration of the plasma occurring much more easily, and remaining much longer in a satisfactory condition. We have, therefore, to do in the first place with pure oligocythæmia or oligochromocythæmia.

(The average duration of life of each individual blood corpuscle is lowered, and it may be reasonably inferred from that that the hæmoglobin is diminished in quantity, and that a comparative oligochromæmia must exist. There is no satisfactory proof of this as yet; on the contrary, the observations hitherto made speak against the occurrence of higher degrees.)

So long as the disease remains at this stage, it has the greatest resemblance to chlorosis, on which account it has received the name Egyptian, or Tropical, chlorosis; and as in chlorosis, in spite of the extreme discoloration, mostly neither deep-lying lesions nor threatening symptoms are present, so also in this disease the pallor may become extreme without the patient becoming bedridden.

It is true that every exertion of the patient causes palpitation, dyspnœa, and lassitude. Giddiness and fainting-fits have been observed, but, with the exception of the gastric symptoms, the patient scarcely suffers, and his nutrition continues fairly satisfactory.

Should the blood losses still continue, the regeneration of the blood plasma begins finally to suffer (principally in consequence of diminished absorption), and a certain degree of hydræmia appears. The latter is betrayed by the occurrence of œdema, without the occurrence of any cardiac anomaly, except increased action.

In cases running a more chronic course, striking changes are frequently met with in the heart, as hypertrophy and dilatation. A causation for the development of these changes seems to me to be found in the fact that individuals so affected were strong, and the anæmia developed itself slowly, attaining even a moderate degree after a comparatively long period, and allowing

the patient to go about his daily duties. It is of course understood that the nourishment of the patient kept pace with the increasing requirements.

I have most frequently found these changes in strong adults, with a moderate degree of anæmia, and in boys, but never in small children.

These symptoms are, at all events, the most striking symptoms of anchylostomiasis, and seem scarcely in unison with the facts hitherto observed. Causatively we can connect them at all events with the existing anæmic (or oligocythæmic) condition.

The latter is the result of successive small blood losses; and we are forced to the new but striking conclusion, that through these in fact hypertrophy is caused. On closer examination, however, these results lose somewhat, and cannot be reconciled with other well-known facts. This symptom seems to me to belong in the category of the so-called spontaneous cardiac hypertrophies, which occurs in mountain-climbers and in men engaged in heavy employments. Under the influence of strong exertion the heart must perform increased labour to satisfy the claims made on the blood circulation, and this finds expression in the strength and frequency of the contractions. This seldom occurs in the normal heart with a normal blood circulation, as slight hindrances scarcely cause increased activity; but, on the other hand, under pathological conditions even slight exertions are followed by the same results as heavy exertions in the normal state. The blood need not lose its capacity to nourish the tissues, although its corpuscles are numerically diminished, but to attain the same effects with diminished corpuscles all the reserve power of the heart must be brought into play.

The patient who continues to perform his ordinary work finds himself constantly in the position of a man who makes constant demands on the circulation, and it is this increased effort which, as daily experience teaches, leads to hypertrophy and dilatation.

The inefficient closure of the valve, which is met with in almost the half of the more pronounced cases, is quite another symptom, and may occur in the apparently normal as well as in the hypertrophied heart. It belongs usually to a later stage. Its mildest grades are well enough known in other anæmic conditions, and in chlorosis the higher grades have been sometimes observed. In the former cases, when only a slight blowing sound is present, the effects on the circulation is scarcely noticeable. It is otherwise in those cases in which the murmurs are scarcely to be distinguished in quality from those of valvular inefficiency. Here the same secondary changes are observed as in valvular defects, only modified to a more or less extent by the existing anæmia. For instance, the cyanotic coloration is never so pronounced as when the blood is normal. On the other hand, the hypertrophy of the left ventricle and of the right half of the heart is developed often in a typical manner. The pulse assumes the same peculiarities as in mitral deficiency, and in time dropsy supervenes, when the anæmia is not so pronounced as to account for this symptom. The course and termination are the same as in genuine valvular diseases, and death may result from cardiac insufficiency, hæmorrhagic infarcts, or dropsy.

On the other hand, the affection is not only amenable to the same treatment, but also, the cause being once removed, complete recovery is possible. This recovery as well as the results of pathological anatomy prove that there is no loss of substance in the valves. There remain to us only two ways in which to explain the defective closure of the valve. The first and the more rational supposes a deficient contraction of the papillary muscles to exist in consequence of fatty or some other degeneration, and that in consequence the valves are not properly adjusted, but allow regurgitation into the auricle. The second supposes that in consequence of dilatation the valves are no longer able to close the orifice. This may indeed be the case in secondary tricuspid insufficiency. The symptoms of cardiac degeneration and insufficiency may appear without any previous functional valvular insufficiency.

The causes seem to be advanced age, long duration, a high degree of anæmia, or the rapid occurrence of the highest degrees of same. Very often the premature appearance of the arcus senilis points to the existence of a similar process in the heart. With or without the existence of valvular insufficiency, a regular cardiac cachexia may set in accompanied by extreme emaciation and various functional disorders.

The gastric catarrh, occurring constantly in the advanced stages of the disease, and leading in its train loss of appetite, diarrhœa, and imperfect absorption, helps to bring about emaciation. This symptom, as well as the chronic pulmonary catarrh which occasionally exists, and the still rarer albuminuria, are partly the results of passive engorgement of the tissues in question.

We may now, after what has been said, decide anchylostomiasis into a number of forms and stages for the purposes of realising at once the condition of individual cases. Such a division has of course something artificial about it, as transition stages always exists.

I.—STAGE OF PURELY LOCAL SYMPTOMS.

(a) ACUTE FORM.*

(b) CHRONIC FORM.*

II.—STAGE OF SIMPLE ANÆMIA, OR OLIGOCYTHÆMIA. (CHLOROTIC STAGE).

(a) ACUTE FORM.

(b) CHRONIC FORM.

1.—*Slight Degree.*

Conjunctival vessels still visible. Nails and lips pale red. Pulse increased in frequency. No blowing murmurs over cardiac area.

Anæmia which has not reached the highest degree. In many cases distinct cardiac hypertrophy and dilatation; in other cases disordered valve closure, seldom both combined. Moderate increase of frequency of pulse.

2.—*Higher Degree.*

Conjunctiva devoid of vessels. Nails whitish. Lips pale. Pulse frequency very much increased. No blowing murmurs.

* The symptoms are in both forms the same. The presence of the disease is only betrayed by pain and disordered digestion. There is no pallor, and the pulse is normal.

III.—DROPSICAL STAGE.

(a) ACUTE FORM.

A high degree of anæmia. Pulse small, much increased in frequency. No blowing murmurs. Œdema of a hydræmic character.

(b) CHRONIC FORM.

Symptoms of cardiac defects with disturbed compensation, or of fatty degeneration. Distinct symptoms of cyanosis. Dropsy of engorgement. Anæmia of varying intensity. Disordered nutrition.

It depends on numerous conditions which stages of the disease are developed, and in what manner these succeed each other. *Ceteris paribus*, the number of parasites present give the indication. These may develop slowly or quickly, or almost remain stationary, the number thrown off being exactly replaced. Finally, the parasites may gradually or quickly diminish in numbers.

Should a constant increase occur, the disease will run with a corresponding speed through all the stages of the acute or chronic form, and finally end in death. Should, on the other hand, the parasites gradually diminish in numbers, the disease will gradually disappear, and may cease in its manifestations before all the parasites are dead. This often occurs when the patient removes from the infected locality;—hence the much-praised effects of “change of air” mentioned by many authors. It were more correct to designate it “change of water and employment.” The same results are obtained under good hygienic conditions.

Such spontaneous cures have been observed by various authors, and numerous examples have occurred in my own experience in Brazil.

Inexact observers always ascribe these cases to some mode of treatment, although such treatment in very many cases has otherwise proved ineffectual.

Such a process of recovery is however very slow, and may take many months, nay even years. Spontaneous cure may not, however, take place at all even after the parasites have all disappeared. This is specially true of the chronic cases of the disease, when the cardiac cachexia has set in, and the patient is already advanced in life. The cardiac degeneration and the chronic gastric catarrh have then become an independent disease, which, on account of disordered circulation and nutrition, prevent recovery. Such cases, in which the patients finally succumb to the disease, may on post-mortem examination show few or no parasites at all. Such cases are by no means rare, and have mostly contributed to make the etiological connection between the parasite and the disease obscure.

It is therefore the more necessary to emphasise the occurrence of a cachexia as the residuum of an anchylostomiasis, which has run its course, as authors have only spoken of it hitherto indefinitely. It is characterised by the fact that there is never a question of simple anæmia, but that disordered nutrition and circulation are constantly present, and are often the most prominent symptoms.

Should the number of parasites remain approximately the same, the stage of the disease may remain the same for a considerable time; still there is always a slow tendency for the worse, as soon as the first stages are passed, because the losses occur in an organism less and less able to tolerate them. On this account, after a comparatively sudden infection, notwithstanding removal from the infected locality, an increase of the symptoms has been observed for a considerable time, as, for instance, was the case in the Gotthardt epidemic. Here the number of the parasites may be considered as unchanged, inasmuch as the infection was probably caused by young and active worms.

From what has been said, it follows that it is impossible from the stage of the disease to make any estimation of the number of parasites, especially if the disease has already existed for some time. Besides the various resistances, which diminish with increasing years, as well as the varying conditions of nutrition, there is yet a cause which has a prominent position in the disease, and that is the complications which are seldom long absent.

The complications observed in anchylostomiasis may be brought under four categories:—

- (1) They are directly connected with the cause.
- (2) They originate under the influences of the same hygienic conditions.
- (3) Their development is favoured by the existing disease.
- (4) Their coincidence with anchylostomiasis is purely accidental.

Should important functions suffer under the influence of these complications, the disease becomes worse. Should the complication be curable and of short duration, the disease may gradually return again to its original state, which here is tantamount to complete convalescence.

The changed conditions make, however, very often the restoration of the *statu quo ante* impossible, and the result is an increase of the symptoms of the disease.

In severe and incurable affections the existing anchylostomiasis may be a secondary disease, or both may be so combined, forming a complete whole, that either the one or the other may elude the observer.

It is of the utmost consequence here to recognise the anchylostomiasis, as it is usually easily cured, and leave the field clear for the treatment of the other.

The first group of complications has been already partly mentioned with the symptoms, such as dilatation of the stomach and circumscribed peritonitis. I emphasise only two here, on account of their frequency and their injurious effects, viz., diarrhœa and enteric hæmorrhage. Both increase the anæmia. Severe enterorrhagia does this in the most rapid manner, so that on any sudden increase of the anæmia this fact must be kept in view. Should the process cease spontaneously, or in consequence of suitable treatment, the anæmic condition rapidly improves.

Even favourable results are obtained with indifferent treatment. The experienced physician knows that these sudden changes form a part of the disease, and he looks on the treatment

which is followed by complete and permanent recovery, as the only successful and suitable treatment.

Malaria is another complication frequently met with. Both diseases are connected with water or moist soil, and very often the same district contains the germs of both diseases.

Anchylostomiasis has been, in consequence, often mistaken for malaria cachexia, although neither the symptoms nor the local distribution correspond. In Brazil I had occasion to treat successfully with quinine some cases of intermittent fever in patients suffering at the same time from anchylostomiasis. Should such patients be seen during the acme of the fever, pallor, otherwise very marked, may escape notice.

The frequency of coincidence of the two diseases was not striking, considering the wide distribution of malaria.

Struma is a much more frequent complication. Apart from the occurrence of anchylostomiasis in a strumous individual, it often seemed to occur in an endemic form in the same localities.

Complications with other intestinal parasites are frequently observed. These complications were frequent in Italy by the presence of the ascaris, trichocephalus, and the rhabdomena (*anguillula*) of man. I observed the same thing in Brazil, where in fifty cases of anchylostoma only ten were found free from other parasites. In the remaining forty cases trichocephalus were found in eighteen, rhabdomena *strongyloides* in twenty-five, and ascaris in thirty.

The whole four were found present in six cases. The ascaris and trichocephalus were numerically much smaller than the anchylostoma. This does not apply to the rhabdomena.

The two last complications are usually of no consequence to the patient, and are as amenable to treatment as if these alone were present.

Further observations are required to describe exactly the third group of complications. I mention a few, which probably belong to the group. In the first place, a frequent catarrh of the respiratory organs, with a tendency to chronicity; it might be regarded as the result of disordered circulation, and be placed under the first category. In the second place, I mention pulmonary tuberculosis, the frequent occurrence of which in anchylostomiasis has been noted by several authors. The anæmia is most probably here the predisposing cause. In one very pronounced case of my own, the lung process came to a standstill after the expulsion of the parasite, and apparent recovery took place.

Further, I frequently observed attacks of epilepsy occurring in anchylostomiasis, and it seems to me the latter predisposes to the former. By expulsion of the worms and removal of the anæmia the attacks became less and less rare, yet there was no definite cure. I also soon lost sight of the patients.

In some cases ulcers, chronic in character, and with a tendency to spread, healed up rapidly after expulsion of the worm, followed by suitable internal remedies.

The fourth group of complications extends over the whole field of pathology. Of interest, however, are specially the processes which are distinguished by frequency, similarity with the disease itself, or by running a modified course. Hitherto, few of those have been observed, as sero-fibrinous pleuritis in Turin, with three cases of death (Bozzolo), and among the Gotthardt labourers frequently anthracosis pulmonum, and a limited number of cases of pellagra.

From my own observations I can mention two cases of arthritis rheumatica, the one acute and easily cured, the other more chronic and accompanied by changes in the heart, which were more probably to be ascribed to the complication than to the disease itself. In another case, carcinoma of the uterus existed with the anchylostomiasis, which alone sufficiently accounted for the anæmia.

The patient, a negress, complained of nothing locally, and the cancer was only found when the anæmia would not yield to ordinary treatment.

Of other hæmorrhages which naturally influence directly the course of the disease, I have often observed epistaxis in a young person with cardiac hypertrophy. Besides this, I have never noticed an increased tendency to hæmorrhage. St. Vel asserts that in operations many ligatures are required, but this may be explained by existing cardiac hypertrophy. In an amputation below the elbow I found the hæmorrhage extremely small in a young person suffering from anchylostomiasis. In this case a high degree of anæmia existed, with a small fast pulse, but no heart enlargement. The case ran its course without fever, notwithstanding which small necroses appeared along the margins of the wound, which cicatrised very slowly.

We may now discuss the differential diagnosis of anchylostomiasis shortly, as so much has already been said. It is true that there are many pathological processes which have the greatest resemblance to the several forms and stages of this disease, yet a careful examination will almost make a mistake impossible. If it be only a question of purely local symptoms, then the microscopical examination of the fæces must decide the point; the presence or absence of the ascaris *lumbricoides* can be shown at the same time, as the latter, when very numerous, cause similar symptoms. The history of the case will exclude chronic gastric catarrh (especially alcoholismus), ulcer, and carcinoma ventriculi, &c. When valvular insufficiency is present, the diagnosis between functional insufficiency and defective valves may be difficult. Should the pulmonary and aortic valves be normal in a case with a high degree of anæmia, and should there be no history of polyarthritis rheumatica in particular, the assumption is in favour of functional disorder. Recovery decides the matter finally.

Chlorosis and anchylostomiasis of an average degree have the greatest resemblance to each other, but have quite a different distribution. The former is rare in tropical climates (especially in Brazil), affects the more highly-cultivated localities and towns especially, and in these again females during the period of development, whilst anchylostomiasis affects the working

country population—brickmakers, miners, without reference to age or sex—and is promoted by a warm climate and bad hygienic conditions, further occurs in an endemic form, which is never the case with chlorosis.

Should these conditions, as well as the local symptoms, be insufficient to diagnose the case, then recourse must be had to the examination of the fæces for specimens of ova.

Anæmia from exhaustion and lactation may occur as a complication. The latter may be estimated from the number of parasites found, the history, and the further course. As advanced anchylostomiasis in the main comes under the idea of pernicious anæmia, it is very easily mistaken for some of the forms of the latter. As in the former changes occur in the blood corpuscles, and hæmorrhages in the retina have been proved to exist (Grassi), it is scarcely possible to make a correct diagnosis, except that the ova are found in the fæces, and the conditions of distributions exist. Pernicious non-parasitic anæmia is a rare disease, occurring in but few in the same locality, and limited in its distribution, and is rarely met with in countries where anchylostomiasis prevails.

Leukæmia is easily differentiated by the specific blood changes, or the enlargement of the spleen, or of the lymphatic glands.

Malaria cachexia may be diagnosed from the history, the enlargement of the liver and spleen, melanæmia, and the absence, as a rule, of dropsy.

Latent malignant tumours and centres of suppuration, tubercular affections, chronic poisoning, and cachexias of various kinds, may, in individual cases, present the same symptoms as anchylostomiasis. These are to be decided, like the preceding, by the absence of the parasite. The history as regards residence and mode of life is of the highest importance. Even the presence of but a few parasites decides the question. Where the above diseases and anchylostomiasis are combined, it is not possible to define the effects of each singly. The result of treatment gives the best indication.

The prognosis of anchylostomiasis depends, as already mentioned, on external conditions. By repeated infection recovery cannot take place, and although a rapid course is rare, yet many patients, after a longer or shorter duration, succumb directly to the disease.

Others fall into a state of chronic marasmus, and are usually carried off by some inter-current disease before the patient attains to any great age.

If the patient is withdrawn from infection without the cause of the disease being treated, the prognosis is always uncertain in severe cases; relapses, and even a fatal termination, are still possible. Even in mild cases the recovery is slow. In time, and by the disappearance of the parasite, the prognosis becomes better, yet secondary cachexia is common in severe cases.

If the patient be removed, for good, from the infected locality, and complete elimination of the parasite takes place, the prognosis becomes then very favourable. Mild, and even average cases, then recover with certainty, and tolerably fast. The prognosis of the severest cases becomes good, *quoad vitam*, if they survive the first few weeks. Complete recovery is doubtful in severe and old cases; still, to be looked for with certainty in the severest *acute* form.

The secondary cachexia is amenable to treatment, but recovery is slow even in the most favourable cases.

The following figures serve to illustrate what has been said.

After the discovery and use of proper remedies to expel the worm, E. Parona, in Varese, had only good results among 249 cases treated in hospital, and Fenoglio, in Turin, among 538 cases.

On the other hand, in Graziadei, in Turin (1880-82) had 12 deaths among 290 of the Gotthardt labourers treated in hospital. Of these, 5 were complicated with tuberculosis or pleuritis. The mortality diminished from year to year, absolutely and relatively, according as the diagnosis and treatment of the disease became better understood.

In two and a half years I myself saw about 250 patients, of whom one-half were dropsical. Of these about 150 cases were treated, and 5 cases of death were reported to me; but of these 5, 3 were not treated at all for this disease, but fell victims, one to intestinal hæmorrhage, one to phthisis, and the third to a mild attack complicated with syphilis.

The two others were girls. One of these died unexpectedly and suddenly with symptoms of hæmorrhage or embolism of the brain, whilst under treatment, after an interval of several days. The other was a girl of fifteen years of age, who came under treatment with extreme anæmia, livid mucous membranes, general dropsy, and bloody expectoration, which last was referred to a hæmorrhagic infarct. The circulation was extremely feeble, and there was a constant tendency to œdema of the lungs. The number of anchylostoma present was estimated at over 1000.

Treatment was undertaken with great caution on account of the wretched condition of the patient. After several hundred anchylostoma were passed, the patient seemed to be improving under the constant use of stimulants, when suddenly large masses of blood appeared in the sputum, and soon after death took place from pulmonary œdema. I was once called to a patient who had been in a deep comatose condition for several hours. This had probably lasted for some time, as the bladder was enormously distended. The patient recovered consciousness, and lived yet for several hours. The history, in combination with excessive anæmia and general dropsy, left no doubt as to the cause. The immediate cause of death in this case was cerebral œdema.

We now finally come to the—

Therapeutics of Anchylostomiasis.

After having recognised in the anchylostoma the cause of Egyptian, or tropical chlorosis, and of the anæmia of the Gotthardt labourers, of brickmakers, and miners, and of the disease "cachexie aqueuse on Africaine," or whatever name it is known by, we must now discuss the

first therapeutic indication in the treatment of the disease. If this is completely successful, then in the mildest cases our task is fulfilled. Much oftener, however, new indications will arise from the results of the disease, the treatment of which may become the principal treatment, especially when we have to do with secondary cachexia.

It is only since the Gotthardt epidemic that regular treatment was adopted for the expulsion of the parasite, and to this we owe the discovery of two drugs upon which we may thoroughly depend. A series of other remedies have been tried in vain, but between these two categories lie a third series, with which partial success had been obtained, but the effects of which are too limited and unreliable to find use in a rational plan of treatment.

The first remedy which successfully expelled the parasite was the Ext. Fil. Mar. Ether, a drug long known in the treatment of tape-worm, and which had also proved effective in expelling the trichocephalus. It was first employed unsuccessfully by Bozzalo, Grassi, and E. Parona, but Perroncito recommended it again anew, his recommendation being based on the effects of the drug on the larva and on clinical observation. Soon afterwards E. Parona announced that with a dose of $4\frac{1}{2}$ drachms of the extract he expelled 230 worms.*

Eight other cases followed in 1881, in which this drug proved effective in large doses. In the same year, later on, he published yet other 18 cases in which small doses frequently repeated caused the complete disappearance of the ova from the fæces: on an average a total quantity of $3\frac{1}{2}$ drachms was required, where the average parasites expelled amounted to 450. According to later communications Parona had treated 249 Gotthardt patients in Varese, with the extract of the male fern, successfully.

Perroncito, who in the meantime had continued his researches, published in 1881 a series of corresponding results. Dr. Campiglio and Dr. Schönbächler, in Schwytz, made corroborative observations; besides, numerous communications to the same effect appeared in Italy, Switzerland, and Germany. Brilliant as the results obtained by this drug were, still there were a number of disadvantages in its employment. The first of these was the great inconstancy of the preparation, so well known from its use in the treatment of tape-worm, and lately emphasised in numerous publications. Whether the drug was originally ineffective, or became so on keeping, must be left undetermined. The latter should be obviated by glass-stoppered bottles, cool situation, and by the addition of ether. At all events, we must accept the reports of non-success as well as of success, especially as the former almost equal in number the latter.

The difference seems to be less in the doses and mode of exhibiting it than in the quality of the drug. E. Parona, into whose hands an ineffective specimen fell, gives, in a little brochure, the following characteristics of an extract very effective according to his own experience:—"The fluid is thick, of a green colour, and with a fairly bitter aromatic taste, recalling the taste of iris-root, and an ethereal odour."

A cubic centimeter of the extract weighs one gramme. If five grammes be made into an emulsion with six grammes of gum-acacia in thirty grammes of distilled water, the mixture acquires the colour of coffee and milk mixture, and the extract does not again separate on standing. Bad preparations are lighter, more fluid, of a dirty green colour, nauseating taste, and smell of turpentine. The extract separates from a mixture made as above, and floats on the surface.

I myself have examined about half a dozen preparations, some of which were prepared in Brazil; and others of particularly good quality came from Europe. All, however, approached rather the latter than the former description, and, as a matter of fact, proved unsatisfactory or problematical in their effects.

Although we therefore advise, in the preparation of this drug, the rules to be followed as laid down in the Pharmacopœia, yet we are not satisfied as to the point of view from which these are authoritatively laid down. A more exact study, and, if possible, a purer preparation of the effective constituents, are urgently required to assure to this drug a due recognition and more extensive use.†

Whether the effects of the various preparations stand in the same proportion in the treatment of tænia, as in anchylostoma, has not yet been shown, although probable.

A further disadvantage of this drug is the nauseating taste, acknowledged even by the unprejudiced, and which is characteristic of the best, although to a less degree, as well as of the worst preparations. This may cause nausea, vomiting, and unconquerable repugnance to a repetition of the dose. The emulsion of it with various corrections, as the aqua fœnicula, only partially removes the evil. Success in this respect is better attained by giving the extract in gelatine capsules (pills and trochisci are less suitable); yet nausea and vomiting may still occur from the irritant effects on the stomach, but are much rarer. On the other hand, the patient complains of eructations and of a bad taste; this may perhaps be obviated by the use of coated pills, or boli. Much graver symptoms have, however, been repeatedly observed. In some cases icterus (probably of hæmatogenous origin) occurred, and in other cases amaurosis. Besides, giddiness, diarrhœa, rise of temperature, and burning pain on passing urine have been noted. Many of those symptoms may also otherwise occur in this disease. A case of temporary amaurosis occurred in my own experience in connection with this drug, which was yet not accidental.

Besides this, great caution is required not to give the patient any cause to complain, as he is very apt to attribute to the remedy symptoms due to the disease itself. Notwithstanding, severe symptoms occur only when large doses of the drug are given and the patient is low. As

* A very large dose, and one not to be recommended. The extract of male fern in large doses has certainly an irritant effect on the bowels, which in weakened individuals may cause death.—*Trans.*

† I have obtained a very pure extract from two firms in Colombo, with which I had some success.—*Trans.*

we may obtain, according to E. Parona, the same results by means of small doses, although much slower, such mode of treatment is recommended in severe cases. Strong remedies are more dangerous for such patients than even the continued loss of blood through the parasite. Cases in which the parasite must be immediately expelled are not frequent, and always of uncertain prognosis; besides, it is to be hoped that these will become rarer in time. It seems that, except in the worst cases, two and a half drachms may be given at once, or in two doses with an interval of two hours. By this procedure less indeed of the drug will be absorbed than by a greater sub-division, as in large doses it causes local irritation and diarrhœa, and is in a great measure carried off in the fœces, which then acquires its peculiar odour. At all events, it is better, in the case of a remedy with such irritating properties, and which, besides, is said to affect the deeper parts of the intestines, to limit the absorption as much as possible.*

Whether the drug be given pure or diluted, is indifferent. A mild aperient is given the preceding day. Patients should fast the same evening, and the remedy should be taken on an empty stomach next morning, as in the treatment of tape-worm.

In case of failure the treatment may be repeated a few days later.

A further repetition is said, in case the drug is good, to be unnecessary as a rule. In the cure with small doses, from one-half to one drachm are given daily on an empty stomach. A special diet is not necessary: only the bowels should move regularly.

A good preparation has the advantage of surer success by a tolerably easy mode of use, and even small children may be induced to take it, although with difficulty.

The second remedy with which the parasite was completely expelled, is thymol (*acidum thymolicum*). This was first used by Bozzolo, but again abandoned, because the desired effect was not produced. Later on he resumed the use of the drug, giving it in the following manner. The thymol was powdered, and in from three to six doses, a total quantity of from 30 to 150 grains being given in the day.

Some time after taking the medicine a little diluted brandy was given to the patient. By this mode of treatment he was able as early as the beginning of 1881 to report six cases, in which the remedy, without exception, expelled numerous anchylostoma. Soon after this he published a case in which, after the first dose of thymol, 650 worms passed, and the ova disappeared from the stools; besides, male and female trichocephali were also expelled in two cases.

Later on, the cure was so formulated that on the preceding day an aperient was given, and nourishment limited as much as possible. Next day the patient received on the whole 180 grains in six doses, at intervals of two hours, with a little wine or diluted brandy after each dose. This process was repeated after an interval of a few days, and as often as necessary.

In 1882 Graziadei, Bozzolo's assistant, was able to publish forty-five cases, in which, by means of thymol, the ova had disappeared from the fœces. Of these, twenty-nine were exclusively treated with large doses of thymol.

I myself adopted this mode of treatment as soon as I heard of it, and obtained results agreeing in all particulars with those of Graziadei.

In all cases where the treatment could be continued long enough a complete elimination of the parasites was effected. Only whilst this result was often obtained after the first—frequently after the second dose of 3 drachms—I was obliged in other cases to repeat the dose four or five times, almost exhausting thus the patience of the patients, and the more so as non-success had already followed other remedies. The severe diet which I then considered necessary forced some to resistance by sheer hunger. Besides, the whole treatment proved too complicated, and the more so as the patients belonged to the lowest ranks of society, and could neither read nor write. As also a certain degree of apathy and want of energy is peculiar to the disease, there was always the danger that the prescription would not be carried out properly, or not at all, endangering the success of the treatment and bringing discredit on the method.

It then became necessary to find a surer and less complicated mode of treatment, and I placed the following questions before myself:—

1. Which of the given prescriptions can be omitted without endangering the result, or can be replaced by something more suitable?
2. Upon what do the greater or less results depend?
3. How is the cure to be effected at the cheapest rate possible with good results?

The following are the results of my experiments undertaken to solve the above, and which, on account of insufficient control over the patients, extended over two years. Many of these conclusions, the correctness of which I can vouch for, have in other publications found confirmation:—

1. It did not seem necessary, nor particularly desirable, to favour the solution of the thymol by giving alcoholic fluids after each dose, as increased absorption increased only the subjective symptoms, not the therapeutic effects. The effect of the thymol depended on each individual particle in the form of pulp, or rather suspended in fluid, than dissolved, coming into direct contact with the parasite.

3. Some absorption always takes place, probably in the form of the more easily soluble salts, but a great portion passes through, and in successful cases is not met with in the fœces in such quantities, and is so well distributed that it prevents further development of the ova.

4. There is no reason to suppose that the effect takes place from any portion which has been absorbed.

* A valuable addition to our knowledge of the physiological effects of the extract of male fern. But too little stress is laid on this in our textbooks on *Materia Medica*, in the handling of such a dangerous drug.—*Trans.*

5. The anchylostoma are not only rendered torpid, but killed, and an aperient is not therefore required after the thymol.

6. The certainty and intensity of the effects do not stand in direct proportion to the size of the dose, but depend on other conditions.

7. In successful cases the whole intestine is freed from the parasite.

After establishing these points, it was necessary to inquire into the causes which led to the frequent failures. The supposition that the obstruction lay in the chyme, met with in the intestine, was given up as untenable, because, on the one hand, the drug must be as uniformly mixed with this chyme as the latter is uniformly mixed with the ova; on the other hand, it may be easily imagined, that after an aperient and a fast of from ten to twelve hours the duodenum is quite empty, and the jejunum itself at least comparatively so. From this and other reasons gases were also excluded. To blame the low position in the intestine was also out of the question, as sufficient thymol was always present in the stools, and neither large doses nor increased or diminished peristalsis led to a sure result. From this the shorter or longer stay of the drug in the intestine could not be blamed as the cause of failure. These causes may be of some importance in individual cases. One further supposition, however, occurred to me. If, under otherwise similar conditions, thymol proves deadly sometimes to all the anchylostoma, sometimes to the majority of them, and at other times only few or none at all are killed, then must those so spared enjoy something which protects them.

It was probable that this protection lay in the profuse mucous secretion of the intestine itself, and which, by its tough consistence, prevented the drug coming in contact with the worm. The following clinical facts favoured this view:—

1. The complete elimination of the worm followed the exhibition of the doses in mild and recent cases invariably. In such cases it may be supposed that but little alteration had yet taken place in the mucosa. On the other hand, failures occurred in severe and chronic cases.

3. Other observers as well as myself have noticed large masses of mucus in the fæces.

4. Pathological anatomy has proved the existence of chronic intestinal catarrh with increased production of mucus.

Cures easily and completely effected might be due to the fact that the intestine produced mucus only in small quantity, or that the mucus was removed by previous remedies, and that the drug proper had then free access to the parasite. Unsuccessful results might be due to opposite conditions, and the fact that the male, a smaller worm than the female, as well as the delicate rhabdonema (*anguillula*) appeared in the stools in comparatively small numbers, or not at all, add weight to the supposition.

Similar results were obtained with the ext. filicis, but it is probable that the best preparations of the latter drug are better calculated to mix with the mucous secretion.

From these considerations I slowly elaborated a mode of treatment, comparatively simple and easy for the patient. I gave the patients, first, a saline purgative with the addition of bicarbonate of soda or common salt. This was given about 2 o'clock in the afternoon, in order to move the bowels before bedtime. Next morning the patient received, on an empty stomach, from forty-five to ninety grains of thymol, in divided doses of fifteen grains each every hour. Before going to sleep the same night he received a Seidlitz powder, not with a view to purge, but only to empty the upper portion of the bowels.

The thymol was again repeated next morning, and this was continued for two or three days. Food was allowed during the day, and the effects of the thymol were never formidable to the patient. The appetite remained unimpaired, so that the treatment was suitable for even severe cases, in which heroic treatment is not advisable. A series of successful cases resulted from this mode of treatment, but there were still failures. In fact, the effect on the intestinal mucus was not satisfactory. The stools after the saline were mostly fluid, without any visible mucus, and the worms passed were mostly gorged with blood.

The exhibition of smaller doses over a longer period had already been tried by Graziadei, with indifferent success. Experiments instituted by myself on the same lines resulted in the same way. I now tried with various other purgatives to prepare the intestines. In the course of these experiments I discovered that a peculiar sluggishness of the bowels existed.

I found that doses of upwards of fifteen grains of gamboge only produced slight purgation in from six to ten hours. I gave the following to a patient:—

R/ Ol. Croton : ... m. x.
Ol. Ricin : ... oz. iii.

M.

S. Tablespoonful to be given every two hours till the bowels are moved.

The patient finished the whole and complained of the insufficiency of the result.

I tried calomel and podophyllin, either alone or in combination with jalap and aloes, and a little Ext. Bellad. Large doses of podophyllin were necessary to ensure success, and these readily produced vomiting and abdominal colic, and colomal caused stomatitis if more than seven or eight grains were given; and even with these doses the bowels were still but slowly moved. I succeeded best with senna, which, by uniform doses, proved a prompt and reliable purgative.

The stools produced by the calomel and podophyllin with or without additions, were not of a watery consistence, but rather thick, and like an emulsion often of an intense yellowish-brown colour, and contained large masses of mucus coloured by bile. If these stools continue after the thymol is given, the expelled worms are found in all parts of the fluid, and are easily recognised. The intestinal canals of the parasites are invariably empty; the worms themselves are of a whitish or grayish colour, bent or even coiled up. They are sometimes enclosed in little masses of mucus.

It is not a matter of chance that this effect was produced by substances which are known as cholagogues.

In these patients, in whom rather a diminished than an increased bile secretion were to be expected, there is apparently an increased quantity of bile in the fæces. Whether really increased production takes place, is not determined; but there is no doubt the contents of the upper portions of the bowels are moved downwards more quickly and effectually.

It seems as if the solution of the mucous masses was rendered more complete by a more complete contact with the bile. Whether the bile itself has a deleterious effect on the worm by contact, could only be ascertained by experiments on the living worm; and I had none such at my disposal.

By preparing the bowels with calomel and podophyllin or senna, as stated above, there were found, after the exhibition of the thymol, so many anchylostoma, and among them so many males, that there could be no doubt as to the thoroughness of the effects.

As a matter of fact, in a number of cases after the first dose of thymol the ova completely disappeared from the fæces. This was the more striking, as I only used small doses, from 45 to 90 grains subdivided into two or three doses.

Once, after one dose, I counted 12 ascarides, 460 anchylostoma, and 9 trichocephali. Another time, a Mulatto, fourteen years of age, passed 2 ascarides, 370 anchylostoma, and a single threadworm (female). He remarked that he was too tired to pass more. In the course of the observation it was often necessary to repeat the process to obtain a complete elimination. I now contented myself with using on an average in each case about two drachms altogether, whereas formerly I considered four times that quantity necessary.

The average quantity would have been still smaller could I have watched over all the cases myself. I have sought to simplify the mode of cure still further by giving the calomel the same morning two hours before the thymol, but I was not satisfied with the results. I shall here sketch shortly the method which I found most reliable. Two hours after the patient has taken his mid-day meal, the following should be given:—

Calomel, gr. vii.

Ext. Sennæ gr. xxx.

Divide in pil. vi.

S. Two to be taken every hour.

Should the bowels show symptoms of being freely moved before the last dose is given, that dose need not be given. Should, on the other hand, the effects be unsatisfactory, more senna may be given. During the evening sufficient nourishment may be allowed, but the food should be light, easy of digestion, and such as leaves little residue. Usually, in the early part of the evening the bowels are freely moved, and the purgation is usually over before midnight, so that the patient enjoys several hours of undisturbed rest. In the early morning he receives the thymol, in 30-grain doses, repeated at intervals of two hours, two or three times. Coffee or soup may be allowed during the intervals. Two hours after the last dose the patient can have his usual meals. After some hours the patient has a sparse fluid stool; if not, a mild aperient may be given if examination of the stools be desired.

Weak patients should be allowed to rest until after the first meal, because the fasting and purgation favour fainting fits. For children the doses are to be modified according to the age, but the calomel can be given in comparatively high doses. Should diarrhœa already exist, the senna may be omitted. I am now in the habit of giving the thymol in gelatine capsules of 15 grains each. The powdered drug should not be pressed, as otherwise it may pass in a mass through the intestines; if in capsules, the powder should be loosened by pressure, &c., before a capsule is administered.*

Adults can swallow these capsules very easily with a little water, especially if they are softened shortly before.

For children I order capsules of 7½ grains each; thymol cannot well be given in pills on account of its acrid and burning taste.

As an unpleasant effect of thymol, may be mentioned a burning sensation in the stomach and in the urethra on passing urine; even in the anus the same can be felt, especially when hæmorrhoids are present.

Excitement, giddiness, confusion of ideas, and fainting fits are (so far as these can be referred to the medicine, not to the disease) only observed when large doses are given, and active absorption has taken place. The urine then becomes olive-green, and this coloration increases on standing, as in carbolic acid poisoning. Albuminuria, even of a slight nature, is seldom observed, and of no consequence.

In carrying out this method, which has for its object the limiting of absorption and the avoiding of long fasts as much as possible, I hear no complaints now, or only complaints of eructations and of a slight burning pain in the stomach.

By the earlier methods there were more complaints, yet of nothing serious, if I except one case of fainting, which occurred in a thirteen-year old negress. The treatment of Bozzola was adopted, and the girl had long fasts. This, in combination with the purging, had more to do with the fainting fit than the thymol. I gave several times doses of 150 to 180 grains to children of twelve and thirteen, and never saw any bad effects.

A patient of Graziadei took six drachms in twenty-four hours, and felt no bad effects.

A strong inclination to vomit must be mentioned as contra-indicating the drug. This tendency must first be corrected by suitable diet and medicine, and finally by washing out the stomach. Thymol itself rarely causes vomiting if given properly covered, perhaps one per cent. of

* In the Colombo hospital the thymol is given (finely powdered) in water, and this answers very well.—*Trans.*

the cases ; still it is very unpleasant, as in broken masses it causes a burning sensation in the œsophagus, mouth, &c., and if it enters the larynx may cause laryngitis.

Its effects are, however, only that of an irritant, not of a caustic, and no injurious effects are caused when the thymol is given without any covering. Graziadei gave 180 grains in powder without any bad effects, and I have done the same. The result was only a slight burning sensation, lasting several days, and a temporary difficulty of swallowing. In many cases it might be given by the stomach tube, and in one case with dilatation of the stomach I injected a dose with the stomach pump.

If we now compare the two methods of treatment, as to complete success, there is something unsatisfactory in both. In the case of Ext. Fil. this is caused by the quality of the preparation, and it is difficult to procure it good. Thymol, a chemically definite substance, may be obtained in a pure state, the difficulty in the case being the mode of administering it.* Bad taste is common to both, and prevents the use of thymol altogether in solution. On the other hand, the male fern irritates the stomach more. Other disagreeable effects seem also to accompany the latter, whilst the mode of administering it is simpler ; and it may also be given to small children. The quantity required and the cost, in my mode of treatment, is less. Which method gives the best results, time alone can tell. Thymol seems to be more applicable for general use ; in difficult cases both may be tried. Fenoglio used them both at the same time, but this method, notwithstanding good final results, is not to be recommended, because large quantities were, on an average, necessary, making too great claims on the patience of the sufferer.

We may therefore lay down the following types of treatment :—

A.—Treatment with Extractum Filicis (of good quality).

(1) Use of large doses— $2\frac{1}{2}$ to 5 drachms (Perroncito). Simple, quick, and effective, but a method to be employed with caution.

(2) Use of repeated small doses (Parona). Slow, but sure, without bad effect, and suitable for dispensaries.

B.—Treatment with Thymol.

(3) Use of large doses—150 to 180 grains per day. Previous preparation by purgatives (Bozzolo). Somewhat detailed, slow, and not absolutely certain. Not suitable for open dispensaries.

(4) Use of repeated moderate doses, taken in the early morning. Previous preparation by salines (Lutz). Also somewhat slow, and not absolutely certain. Better adapted for open dispensaries.

(5) Use of one moderate dose. Previous preparation of bowels by calomel without any other purgative (Lutz). Quick according to present experience, certain, and without bad effects.

(6) Use of smaller doses without any particular preparation (Graziadei). Uncertain.

C.—Combined Method.

(7) Use of thymol and Ext. Filicis together (Fenoglio). Slow, but tolerably certain, yet unnecessarily complicated.

It still remains to mention other drugs the use of which has been observed as followed by the expulsion of the anchylostoma, but which in their effects are too uncertain to use in any method of treatment. Santonine is to be mentioned in the first place. Success followed its use in a few cases, but it completely failed in very numerous instances. Grassi and Parona noted the passing away of a few parasites by the use of calomel, jalap, and santonine combined. Parona once saw 65 worms expelled by this method, of which one-half were males. In one quite exceptional case, after the use of $2\frac{1}{2}$ grains of santonine and 3 grains of calomel, 440 anchylostoma were passed.

It is a striking circumstance that in all the successful cases calomel was also prescribed, and it serves as a proof that this drug, in itself devoid of anthelmintic properties, yet increases the effects of other anthelmintics. Yet this combination is thoroughly uncertain, and has never given me satisfaction, although modified in many ways. Apparently, santonine acts only after long contact and in concentrated form. Santonine, according to Perroncito does not kill the larvæ.

Still more uncertain are the effects of gamboge and other drastics. As far as I can gather from the literature of the subject, only a few males were ever expelled by their use. Probably these were surprised on their wandering expeditions, and mechanically expelled without the drug affecting them in any way. At least I have used all the drastics, and after careful examination I only found one male, and that alive.

After the use of Ext. Tanacetæ, in combination with senna and flores cinæ, as well as calomel and jalap, Parona saw from six to twelve expelled. It seems that alcoholic liquors under certain circumstances expel the anchylostoma. By moderate doses I have never seen any good result, and I consider this drug as valueless. On the other hand, other observers noted a great diminution in the ova after great excesses. It can be easily imagined that in the stomach and duodenum worms would be affected when these parts were swept with solutions of alcohol. I have still to mention some remedies used in Brazil. These are the milky juice of the carica dodecaphylla (Taracatia) and ficus doliaria, as well as a substance, doliarin, obtained from the latter by Dr. Peekalt in Rio-de-Janeiro. The milky juice is given in doses of from three to six teaspoonfuls in water, and act in this quantity as a strong purgative. It is a most remarkable fact that none of the Brazilian practitioners ever saw an anchylostoma pass, although, for instance, Wucherer, who knew them well, searched the fæces for them, and that the diarrhœic character of the latter must have made the search easy. The same thing happened to me in one case after the use of the milky juice of ficus doliaria.

* I tried the thymol in solution on *myself*, and I am satisfied that no patient could stand it. I now give it, finely powdered, shaken up with water, and patients never object to it.—*Trans.*

Further, I had an opportunity of examining the fæces of three patients after the use of *carica dodecaphylla*, and with great benefit, as I was informed. All three showed a high degree of anæmia, and in their dejections were found a corresponding number of ova. Further, I was informed by colleagues, who had some experience of this drug, that they were never able to satisfy themselves of its specific effects, and that even in favourable cases relapses occurred after its use. From other sources I had more favourable accounts of it, and its effects on the round worm was pointed out to me. Whether the latter is reliable remains undetermined, but in this respect, as St. Vel assures us, the juice of *carica papaya* is very useful.

Direct experiment only affords me a negative result, as I could keep the larvæ of the *anchoylostoma* in both juices for hours together without bad effects. This native remedy cannot, therefore, be recommended, and no doubt a great deal of the success attributed to it was really due to spontaneous recovery, aided by better attendance and rest. At all events, chronic cases and fatal terminations occur very frequently in districts where both trees abound. (*Ficus doliaria*, especially, is widely distributed.)

To make these remedies widely known is a duty undertaken by the authors of all the popular works on medicine; and these are found in every one's hands. Although we do not deny that *anchoylostoma* may be expelled by these juices, yet their effect cannot be compared in any way with the methods already mentioned; besides, they cannot be procured at all times of the year. They have one recommendation, viz., taste, which is not unpleasant, but their drastic effects on weak patients is considerable.

As far as *doliarin* is concerned, the expulsion occasionally of *anchoylostoma* has been observed after the use of the preparations "*Pós de Dolearina com ferro*" was brought into the market by its discoverer.

Bozzolo saw 16 *anchoylostoma* expelled after the use of the drug. Bäumler noted 30 in four stools. Although by continued use the number of ova diminished in the stools, yet numerous parasites were found on post-mortem section made later on. The original preparation failed in many hands; although I proceeded according to the prescribed course, no worms were passed. The patient, much weakened by the treatment, complained of the drastic effects, and refused to take any more.

On receiving 180 grains of thymol, he passed 500 parasites, and recovered completely (Bozzolo's method). I did not use this substance afterwards, but had occasion to treat repeatedly patients who had taken it for a considerable time without any results. Even in favourable cases the treatment by these substances must take a long time, as so few *anchoylostoma* are expelled after each dose before they are all expelled. Whether the *anchoylostoma* were expelled living or dead, is not said, and nothing is mentioned as to the proportion between the males and females.

From what has been said, it is seen that there is a series of drugs, by the use of which individual *anchoylostoma* can be expelled, and large numbers only in rare instances. Only in two cases was there complete elimination obtained.

The probability of still increasing the number of drugs, and so obtaining a simpler, cheaper, and more agreeable remedy, is not great. A considerable number has been already tried without any results.

Grassi and Parona tried *Kamala*, *Valeriana silvestris*, turpentine in large doses, either alone or with calomel; Bozzolo, besides, tried benzin, glycerin, picric acid, carbolic acid, arsenic, corrosive sublimate, and chloral in large doses; Bäumler tried pomegranate, *ol. chenopodii*, *ambrosiodes*, &c.; I myself have tried several of these drugs with negative results, as well as the following: *ol. caryoph. menthæ*, *eucalypti*, *naphthalin*, and common salt in large doses.

Too much importance need not be laid on these failures however, as even thymol and *ext. fil.* had but poor results to commence with. Some of the preparations mentioned alter very readily, and in their altered condition vary in their effects. Others, like the ethereal oils, were only hitherto given in very small doses, which may perhaps be increased without bad effects. Much also depends on the mode of administering the drug, as we have seen in the case of others. Many substances might be effective if brought quickly into the intestines, which might be done by means of coated pills and capsules.

In general, we can only hope for success from drugs which are to all intents and purposes insoluble, and incapable of absorption, and can spread over wide areas of the intestines, and are, besides, characterised by intense odour and taste, and chemically belong to a group the other members of which have anthelmintic properties. Previous preparation of the intestine must always be kept in view. For the guidance of others I may give here the most important results of a series of experiments undertaken by Perroncito as to the effects of various drugs on the *anchoylostoma* larvæ.

The results obtained do not, without further modification, apply to the fully-matured worm in the intestines, as these are probably less resistant than the encysted larvæ, and, on the other hand, more so than the embryo just escaped from the ovum, the chitinous skin of which must more readily allow diffusion. In addition, the difference in the nutrition and the nature of the media are of moment. Many of the substances cannot also be used internally. It were therefore desirable that further experiments be made in this direction on living, fully-developed parasites, and at a suitable temperature.

1. A five-per-cent. solution of caustic potash kills the encysted larvæ in less than half an hour.

2. Solutions of common salt (nine to twelve per cent.) kill the larvæ tolerably quick; only the fully encysted larvæ resist a solution of sixteen per cent. for twenty-five minutes.

3. In a two-per-cent. solution of corrosive sublimate the young larvæ die in less than fourteen minutes; the encysted were still alive after forty hours.

4. In a ten-per-cent. solution of bromide of potash the larvæ were still alive after thirty minutes.
5. In a five-per-cent. solution of chloral hydrate the larvæ of various stages were still alive after three hours.
- 6, 7, 8. The sulphate, bisulphate, and phosphate of soda in strong solutions (seven to eight per cent.) inflicted no injury on the larvæ.
9. In pure glycerine the larvæ gave still signs of life after the lapse of forty minutes. (The young larvæ died quickly, even in a weak solution.—Lutz.)
10. In aethyl-alcohol larvæ of various stages died in five minutes; in strong wine they died within an hour and twenty minutes.
11. Turpentine vapour was tolerated over six hours.
12. An infusion of kamala had no effect.
13. Santonate of soda did not kill the mature larva.
14. Concentrated sulphuric and muriatic acids, on the contrary, at once. In a forty-per-cent. solution of sulphuric acid they died within three minutes; in a twenty-per-cent. solution, within fifteen or sixteen minutes.
15. A one-per-cent. solution of thymol killed the larvæ in one minute; a half-per-cent. solution the immature in eight or ten minutes. Water which was allowed to stand over thymol for some time, and had a distinct taste and smell of the drug, showed itself effective. (Lutz.)
16. In a good specimen of Ext. Fil. Liq. they died quickly. Doubtful or bad preparations no effect. (Lutz.)*
17. In the scarcely diluted milky-juice of *Ficus doliaria* and *Carica dodecaphylla* the young larvæ remained over an hour still living. (Lutz.)
18. Ol. absinth. menth. caryoph. chenop. ambros.
19. Naphthalin showed itself, suspended in water, as without effect. (Lutz.)
20. A temperature of 50° C. killed the embryo in the various stages of development in less than five minutes.

After having shown that the parasites could be expelled by the first-mentioned anthelmintic, there still remained the question whether the parasites were really the cause of the disease, and whether with their removal the symptoms came to an end. This question must be looked on as already decided, as every observer is agreed that the most rapid and the most striking recoveries were made by those from whom complete expulsion had taken place.† Should no secondary cachexia exist, and it does not exist, in consequence of a disease existing only for a short time, or in children even after a disease of several years' duration, a high degree of anæmia may disappear in an astonishingly short time (three to five weeks), a quicker recovery than takes place in anæmia caused by hæmorrhage. Even when the conditions are not quite favourable the anæmia disappears in two, or at the least three months, as has been proved by examination of the blood.

I have still to mention a few drugs, which are not anthelmintics, but which have a reputation in anchylostomiasis. Their use can naturally be only symptomatic or palliative, and I shall therefore mention them in connection with individual symptoms and complications.

The most striking symptoms of our disease is anæmia, which can only be cured gradually within a certain time. It may be asked (1) whether this symptom can be removed without removing the cause; and (2) whether on removal of the cause the anæmia can be cured in a much shorter time. The latter is attempted in various ways, and the following agents are employed: drugs, diatetic treatment, and transfusion.

Among the drugs, iron takes the first place, already used in all kinds of anæmia, although it has shown specific effects only in chlorosis. The improvement noted after its use in other forms of anæmia, and especially in the anæmia resulting from hæmorrhage, has not been so striking.

Now, anchylostomiasis is very like chlorosis in its external appearance, and it was therefore resolved to give iron a trial in the former, especially at the time when the cause was unknown, or could not be removed, and when the treatment was merely symptomatic. As a matter of fact, this remedy was in use everywhere. Notwithstanding this it is difficult to estimate its advantages clearly, as other factors in the treatment have also to be taken into account. At all events, iron alone cannot prevent relapse and fatal terminations—rather these were observed in spite of a free use of iron.

This, *a priori*, is not to be expected otherwise, as the anæmia depends principally upon losses of blood, which cannot be replaced by ever so rich a supply of blood constituents; and we cannot expect it to influence the disordered digestion for the better. As far as its favourable effects on the blood corpuscles are concerned, we have no proof that these in one disease suffer individually, or that their normal function can be increased by drugs.

On the other hand, improvement frequently takes place in chronic, almost stationary cases, by the use of iron, rest, and good diet, whilst on these being discontinued the patient relapses, so that it is not justifiable to refuse to the iron some share in the improvement. Probably also much depends on the form in which the iron is given. In the province of Sao Paulo the impure sulphate of iron is used by the people at large. In spite of its impurity, and of the large quantities in which it is taken, it is well borne, and the results are good. Another favourite remedy with the people is iron filings boiled with lemon or citron juice.

* I tried the effects of Ext. Fil. Liq. obtained from Messrs. N. S. Campbell & Co. of Colombo, on the larvæ, and they died very quickly in it. The drug was very pure.—*Trans.*

† Very rapid recoveries are made in the Colombo hospital after the expulsion of the parasites.—*Trans.*

that which is daily observed in cardiac disease, when the compensation begins to give way. Only in anchylostomiasis is a definite cure possible. I once saw intense general dropsy with fast, irregular pulse occurring in a negro suffering from a very pronounced form of secondary cachexia, the result of anchylostomiasis of ten years standing, after the expulsion of only a few parasites three times in the course of the last year. Each time the pulse became regular under the use of digitalis, and remained so a long time, whilst the dropsy suddenly disappeared. He did not again come under observation, as he gradually got perfectly well. I have almost always used digitalis in the form of pulvis foliorum, in pills of $2\frac{1}{4}$ grains each from four to six times a day. The drug in this form was not only completely effective, but also preferred by the patient to the infusion. I begin with large doses, diminishing them as the effects are produced, and stop them when complete, examining the pulse twice daily. Whenever possible, well-known preparations should be used; with new preparations caution is constantly required. Should no effects be produced, the quality of the drug should be at once examined.

In many cases it is necessary to commence by the exhibition of digitalis, in others the drug is used after the expulsion of the parasite. Should the cure last over several days, digitalis may also be given during the period. I will still here mention two series of drugs which came into use through the absence of a specific treatment. The first consists in the so-called stomachics and bitters, of which some are domestic remedies, yet they have had less results than the other domestic remedies, and may now be quite dispensed with; the second series consists of purgatives, amongst which the drastics are specially used.

It is not to be denied that a temporary improvement of digestion and of local pains often followed their use. They, apparently, acted beneficially by expelling masses of mucus and accumulated fæces, yet, as already said, their use requires caution: the sluggish bowel peculiar to the disease during its acme requires the use of purgatives after the expulsion of the parasite is completed. Saline purgatives in moderate doses are the best remedies in this condition. With suitable diet this symptom also disappears—disease itself tends to recovery. Following the directions which have already been given, it is rare that other drugs will be required. Muriatic acid, or Carlsbad salts may be often prescribed with advantage. If diarrhœa is present, this should be stopped after the parasite is expelled by opium or astringent remedies. Narcotics are seldom required to alleviate pains. Having discussed the various methods and remedies, we may review shortly the whole treatment. Successful as the treatment of anchylostomiasis is, yet it is by no means simple, and success essentially depends upon strict adherence to the directions. It is therefore very desirable that the treatment of the severest cases should take place in hospitals, or under the personal supervision of the physician; and even for the milder cases this is at least necessary until the parasites are completely expelled, because, unfortunately, we have to do mostly with patients who cannot obtain otherwise either nourishment or nursing. One is too often forced to an ambulance form of treatment, and we must, therefore, have regard to this, but we must first show how this can be best done for the patient himself.

A clue to the diagnosis is mostly possible at the first glance, and gains in all probability on learning the history. The examination of the individual organs brings further confirmation. For the purpose of recording the history of the disease, the scheme annexed to this monograph may be used. If the state is put down weekly, the smallest changes in the condition of the disease may be easily judged, and valuable statistical material is acquired for the solution of many questions still unresolved. The examination is only complete when it includes examination of the fæces. By the microscopical examination of the latter one becomes convinced that the anchylostoma ova pass in corresponding numbers, and recognises at the same time the presence of other worms. A small number of ova points to some complication, which should be looked for; besides, it may indicate a disease of long duration or little resistance on the part of the patient; or, lastly, to having already undergone treatment. A large number of ova point to the opposite conditions, but besides the number, the amount of food taken, as well as the volume and condition as to water of the fæces, must not be left out of consideration.

It is therefore better to examine the natural stool than that passed after an aperient. Before beginning the treatment, any nausea, disorders of circulation with considerable dropsy, as well as constipation, must be treated in a suitable manner.

The evening meal preceding the exhibition of the thymol should be light, easy of digestion, nourishing without leaving much residue behind. Some hours before that the preparatory medicine should be given. The anthelmintic is given next morning early on an empty stomach. Coffee and soup are allowed during the cure, but the patient had better keep his bed. One hour after the last dose is taken the ordinary meal may be allowed, after which mild cases may be allowed to go about; if the bowels are not moved for some hours after, a mild aperient may be given. Fluids, too, are desirable in the interest of the examination. The first stools which pass after the use of anthelmintics are preserved. They are distinguished by the odour of thymol, which almost covers the fæcal odour. After previous dilution, when this appears necessary, the fæces are placed in small portions in flat white plates, or are allowed to flow slowly over an inclined surface. In this manner the worms may be easily counted. From their number in connection with the results of the examination, the final result may be already anticipated. When the treatment is successful the patients, according to their own statements, feel greatly relieved.* After the process is completed, a few days may be allowed to elapse, during which the treatment may be merely diatetic and symptomatic. Diarrhœa should be controlled, and any increase of dropsy be treated by digitalis. In the absence of any other indication, iron may be prescribed. After the lapse of a few days a microscopic examination of the normal fæces should be made. If no ova are found, the symptomatic treatment may be continued so long as it appears necessary.

* In my experience patients feel greatly relieved after the dose of thymol, and long for a repetition of it.—*Trans.*

Mild cases may be allowed to go with an injunction to present themselves for inspection once a week. Even at the first inspection, new, or rather increased, vessels are seen in the conjunctival sac, the pulse begins to fall towards the normal, and later on all this becomes more plain. The appetite improves rapidly, and all the abnormal sounds and murmurs disappear, but slowly. The intermittency of the pulse disappears very slowly. In many cases the general condition is already markedly improved within the first two weeks, so much so that the patient, if he strongly urges it, may be allowed to resume his ordinary occupation, on condition that he should stop on the first feeling of exhaustion. The cure can only be considered complete when the patient feels perfectly well and fit for work, and the colour of the skin and mucous membrane becomes normal, which mostly requires from three to eight weeks. If microscopic examination show that only a few females are still left in the intestines, these may certainly be left, but the cure will be slow in consequence. Generally then, in comparison, more males are left, as these, on account of their size, are more difficult to expel. If the parasites are not approximately expelled in the proportion of two males to three females, then most probably a portion of the former are left behind, but they are less injurious than the females. In cases where the cure is not radical, numerous females are also left behind. In that case the process should be repeated in the course of one week, and this should be continued as long as ova pass in the fæces. By my mode of treatment I have never been obliged to repeat the process more than once.

In ambulance practice one can only judge of the case from previous examination of the fæces. The drugs are given with due instructions, and examination of fæces follow in a week's time; according to what the examination reveals, the dose is either repeated or other treatment adopted. If examination of the fæces is not practicable, one must judge by the feelings of the patient, and repeat the dose or not.

It is not recommended to continue repeating the process only until no more worms pass, as the patients cannot always find the small animals; and further, when the directions are not properly carried out, anchylostoma may still exist in the intestines although the anthelmintic may carry none away. After the cure is completed the patient should still be examined once or twice after long intervals. The task of the physician must then be considered at an end, when he has informed the patient, further, of the conditions of infection, and has given directions how to prevent further introduction of the parasites.

We have still to say a few words about the prophylaxis of anchylostomiasis.

Two cardinal questions face us here:—

- (1) How can the spread of the anchylostoma and their larvæ be prevented?
- (2) How is their introduction into the human intestines to be prevented?

As an answer to the first question, a knowledge of the cause of the disease, and of the methods adopted to cure it, should be made as well known as possible. Every infected individual becomes a source of danger to his immediate surroundings, which can only be obviated by the expulsion of the parasites. A methodical treatment of every case of infection must, even under the worst hygienic conditions, lead to the stamping out of the disease. Still this goal is not so easily attained, as the presence of a small number of anchylostoma is only detected by the microscope, whilst it is generally only those infected with great numbers that come for treatment.

Our method of treatment is not yet so agreeable that we can try it without more ado in every suspicious case. If we possessed a remedy against the anchylostoma, such as we have in santonine against the ascaris, then it could be administered periodically as the existing circumstances pointed to infection. Another indication, in the first question, is much more easily met, the preventing of fæces being left scattered over the soil by the erection of suitable latrines.

Self-evident as this is from a hygienic point of view, and general as these are in civilised countries, yet all the epidemics which have yet occurred of the disease have been undoubtedly due to a want of regard for these.

The larvæ do not seem to develop in the contents of latrines, because, apparently, the latter are too fluid.

There has never as yet been any case which could be traced to any latrines, or to their contents when used as dung. This proves that the mode of disposing of their contents hitherto in use is in this respect without danger. Should it be desirable to sterilise the excrements, heat is the best for the purpose. Crude carbolic acid or the stronger mineral acids are less effective. In order to prevent the introduction of the parasite into the stomach, caution is required in the use of the drinking-water. Running water taken immediately at the well or spring is the best, or the water of draw-wells to which rain water from the surface has no access. But even in all possibility, infected water, if not directly swallowed, but allowed to stand till impurities settle to the bottom, is without danger, provided the deposited matters are avoided.

Filtration offers full security against infection. Porous stone or carbon filters may be used; a piece of paper, or even a few folds of cloth, are all that is required to remove the larvæ from the water, so that there is no necessity to boil the water to sterilise it. Where the condition of the drinking-water is patent, as in most countries affected with the anchylostoma, it is as well, from other reasons as well, to use for drinking purposes only water which has been boiled.

The attempt to prove the presence of the anchylostoma in the water or mud is without any practical value, as a negative result proves nothing, and a discovery of larvæ valueless, because the larvæ of other parasites may resemble ours very closely.

After many attempts I only succeeded once in finding in the mud of an undoubtedly infected water two living nematode larvæ, which corresponded in every respect with those of the anchylostoma reared by myself. A later examination of the same water remained without result.

Infection by the hands, through clay or mud, &c., adhering to them, as often is the case with brickmakers, miners, and children, can be avoided by cleanliness. Eating with unwashed

hands should also be prohibited. In mines and brickfields the infection of the locality can be guarded against if the fæces are properly disposed of.

As can be inferred from what has been said, the development of the disease only takes place under bad hygienic conditions, and it behoves us in every case of anchylostomiasis to search into the cause, and do our utmost to remove it.

APPENDIX.

The first part of this work was completed in Brazil before the end of the year 1884, and the second at least roughly sketched out. As the publication was considerably delayed, it was possible for me to examine the large number of works on the same subject which the year 1885 brought to me. I had also an opportunity, during my travels through Europe, to become acquainted with many of the authors, and to confer with them both by word of mouth and in writing. I then became aware of many gaps in my description, which I now endeavour to fill up from personal information and from the literature of the subject. As to the propagation of the anchylostoma, I have to add that this was observed by Grassi and Parona in an individual from Navarre (Piedmont). Further, Grassi found the same amongst the brickmakers of Lombardy, likewise in Sicily amongst country people, not miners, who came from swampy districts. This author emphasises the occurrence of the disease in Italy in swampy districts. Leichtenstern has collected already up to June, 1885, forty-seven cases amongst the brickmakers in the neighbourhood of Köln. I heard also that amongst miners in the neighbourhood of Aachen new cases have been discovered. Further, the communication of a friendly colleague makes it probable that anchylostomiasis occurs also among the miners of Saxony—at least there severe anæmia has been noted amongst the miners. It is indeed time to have all mines examined systematically for the presence of anchylostomiasis. To the history of development of the anchylostoma I have still to add from observations made by Professor Leichtenstern, and kindly shown to me, that with the stage of the formation of the cyst, the free life of the anchylostoma does not end, which I, without anticipating further communication from this observer, quote here with his permission. I further infer that the period of the so-called encystment is only to be understood as a stage in the development of the skin, which Leuckart and Grassi had also the goodness to point out to me. It is worthy of note how long the larvæ retain the old skin under certain conditions, and how large the same appears in comparison with its contents. The throwing off of this covering, which I often observed, but considered pathological, is explained now as a physiological process; whilst, on the other hand, sketches as those in figures V, W, X, must correspond to processes of degeneration after death. I can now explain why an attempt at infection, undertaken upon myself with encysted larvæ, failed. Further, I believe, supposing further stages existed, that what has been said on the condition of infection is not affected thereby.

Further, Grassi, on post-mortem examination of a case in which about 3,000 parasites were found, made the discovery of encysted specimens in the submucosa. These were smaller (three to six millemetres), and much more delicate than the mature specimens; six of them were females with somewhat developed ovaries and oviducts, as well as an empty uterus. The constant occurrence of an encysted stage of development in the submucosa may now be looked on as certain. The cases are thus explained, mentioned by Leichtenstern, in which, after all the ova had disappeared, after some time these again appeared in the fæces. In these cases, in which fresh infection was possible, encysted larvæ must have been left, and became capable of further propagation after passing into the lumen of the canal.

It is therefore advisable to repeat the process after some time in view of this eventuality, as I did. In doing this, however, I had only cause in very few cases to suspect that single worms were developed later on.

The most of the patients had been withdrawn from conditions of infection for a considerable time.

Grassi, in the same case, in the examination of the fæces, found a young nematode of .002 mm. with a capsule-like mouth, which resembled a larva of the dochmius trigonocephalus, as described by Leuckart, and may be regarded as the first parasitic stage of the anchylostoma. It is to be hoped that the other stages in the history of development may soon be discovered. I will further mention that Grassi is of opinion that the dochmius trigonocephalus of the dog is hæmatophag, and that dochmius balsami is not identical with dochmius tubæformis. To the pathological, anatomical, and chemical state of the anchylostoma I have further to add that the spontaneous evacuation of the worms was not observed by Grassi, but by Parona. The first found in one case of hæmatæmesis numerous ova in the vomited matters. On autopsy made later on the left ventricle was found thickened with a slight amount of fatty degeneration of the cardiac muscles, more intense degeneration in the capillary muscles. In the same case hæmorrhages were discovered in the retina, already detected during life. The examination of the blood during life showed a number of blood corpuscles of various degrees of size, all abnormal. In this case the medulla of the bones was also examined. (Grassi "Intorno ad un caso d'Anchylostomiasis.")

Further, Leichtenstern—"Börner's deutsch med. Wochenschr,"—Nos. 28 to 30, 1884, corroborated the fact that, even with good preparations of Ext. Fil., relapses occur, which does not accord with my experience with thymol. I would therefore urge in using male-fern that previous preparation be carefully made, and eventually the method recommended by me be employed.

Bern, September 1, 1885.

SCHEME FOR THE EXAMINATION OF PATIENTS SUFFERING FROM ANCHYLOSTOMIASIS.

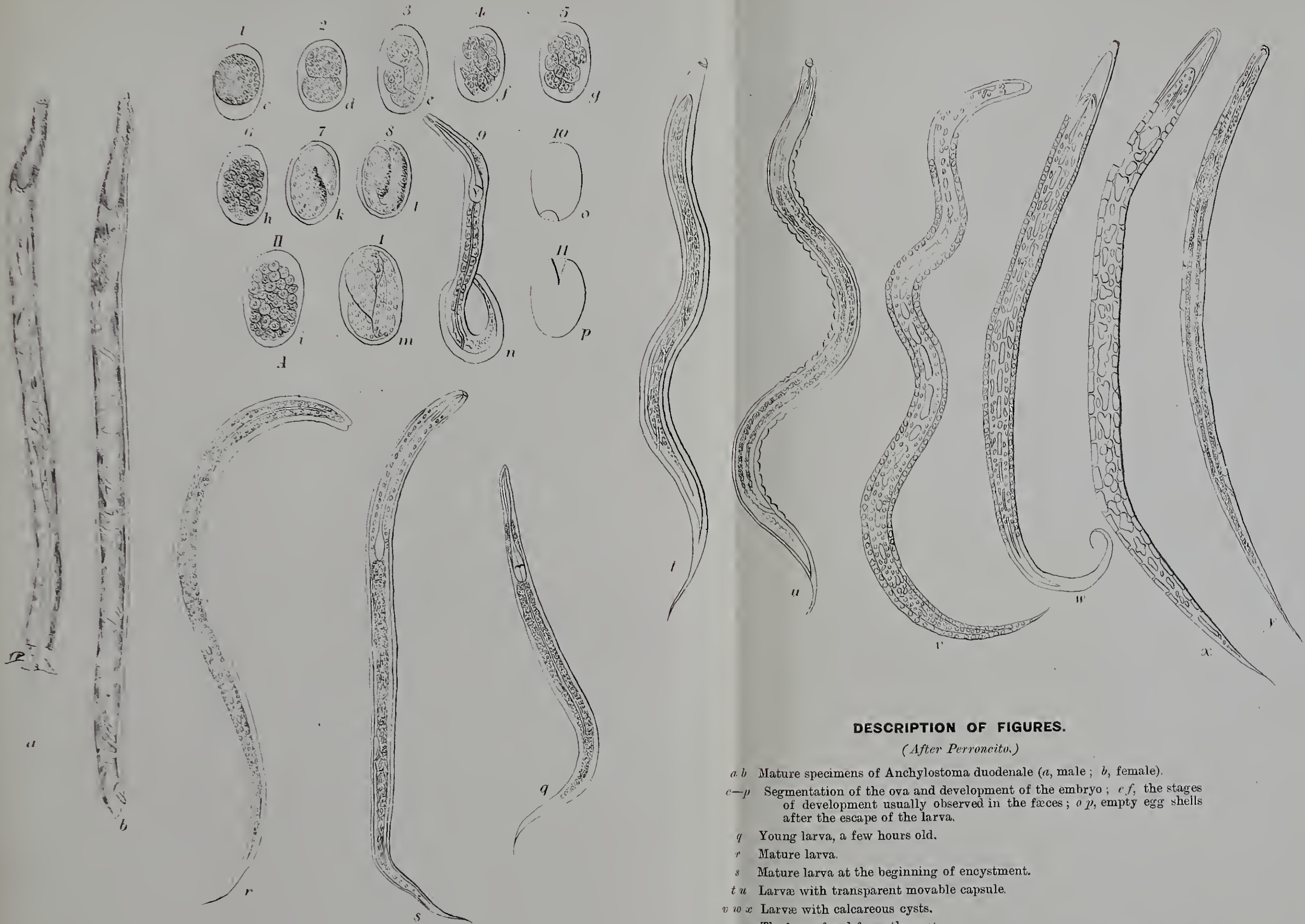
Name of Patient.....	Form of Disease, and stage.....	Date.....
1. Personal:—		
(a)	(b) Early course and treatment	
(b) Age	(c) Place of residence at time of infection	
(c) Occupation	(d) Employment there	
(d) Race	(e) Condition of drinking-water	
(e) Nationality	(f) Fæcal matter, how disposed of	
(f) Other remarks	(g) Occurrence of analogous diseases in the neighbourhood	
2. History: etiological and hygienic conditions:—	(h) Latest place of residence, occupation, and hygienic conditions	
(a) Time and mode of commencement	(i) Other remarks	

3. Examination of the digestive organs :—
 - (a) State of the tongue
 - (b) Saliva
 - (c) Eructations
 - (d) Vomiting
 - (e) Increased appetite (bulimia)
 - (f) Diminished appetite (anoxæmia)
 - (g) Changed appetite (geophagy and allotriophagy)
 - (h) Meteorismus
 - (i) Diarrhœa
 - (k) Constipation
 - (l) Hæmatemesis
 - (m) Intestinal hæmorrhage
 - (n) Other remarks
4. Examination of the heart, arteries, and veins :—
 - (a) Cardiac area
 - (b) Intensity of heart's action
5. Examination of the skin, mucous membranes, and eye :—
 - (a) Vascular condition and colour of the cheeks, ears, nasal alæ, nails, &c.
 - (b) Pigmentation of skin
 - (c) Vascular condition of conjunctiva bulbi and of the conjunctival sac
 - (d) Sclera and conjunctiva scleræ
 - (e) Cornea
 - (f) Retina
 - (g) Vascular state and colour of lips, tongue, and palate
 - (h) Other remarks
6. Dropsy :—
 - (a) Œdema of eye-lids and cheeks
 - (b) Œdema of extremities
 - (c) Chemosis conjunctivæ
 - (d) Hydrothorax, hydropericardium, and ascites. Cerebral œdema
 - (e) Other remarks
7. Examination of respiration :—
 - (a) Frequency and character of the respiration at rest and in motion
 - (b) Other remarks
 - (c) Impulse
 - (d) First cardiac sound
 - (e) Second cardiac sound
 - (f) Fremitus (epigastric pulsation)
 - (g) Other remarks
 - (h) Frequency, state, and rhythm of pulse
 - (i) Arterial pulsation, sounds, and murmurs
 - (h) Blowing murmurs
 - (l) Venous pulse and undulation
 - (m) Other remarks
8. Disorders of the special organs of sense, of sensation, and of the secretions :—
 - (a) Noises in the ears
 - (b) Colour, vision, and darkening of the field of view (temporary)
 - (c) Amblyopia and amaurosis
 - (d) Formication and numbness of the extremities
 - (e) Other remarks
 - (f) Perspiration
 - (g) Other remarks
9. Organs of generation :—
 - (a) Whether normal
 - (b) Menstruation
 - (c) Pregnancy and lactation
 - (d) Other remarks
10. Localisation of pain :—
 - (a) Palpitation
 - (b) Pain in cardiac region
 - (c) Pain in scrobiculo cordis
 - (d) Pain in right and left hypochondriac regions
 - (e) Pain in other parts of abdomen
 - (f) Headache
 - (g) Intercostal pains
 - (h) Lumbar pains
 - (i) Pains in extremities
 - (k) Pains in the bones
 - (l) Other remarks
11. General disorders :—
 - (a) Increase of temperature
 - (b) Diminution of temperature
 - (c) Sensation of cold
 - (d) Weariness
 - (e) Thirst
 - (f) Dyspnœa
 - (g) Sleep
 - (h) Sleeplessness
 - (i) Giddiness
 - (k) Fainting fits
 - (l) Other remarks
12. Examination of the blood :—
 - (a) Number of blood corpuscles
 - (b) Hæmaglobin (quantity)
 - (c) Abnormal elements
 - (d) Other remarks
13. Examination of the urine :—
 - (a) Quantity
 - (b) Specific gravity
 - (c) Colour
 - (d) Albumen
 - (e) Other remarks
14. Examination of the fœces :—
 - (a) Increased mucus
 - (b) Passing of undigested materials
 - (c) Anchylostoma ova
 - (d) Charcot's crystals
 - (e) Blood
 - (f) Quantity (daily)
 - (g) Consistence
 - (h) Colour
 - (i) Other remarks
15. General examination of development :—
 - (a) Development of skeleton
 - (b) Muscles
 - (c) Panniculus adiposus
 - (d) Retarded growth
 - (e) Retarded puberty
 - (f) Other remarks
16. Results and complications :—
 - (a) Pulmonary œdema
 - (b) Hæmorrhagic infarct
 - (c) Cerebral apoplexy and embolism
 - (d) Epileptic and hysteric attacks
 - (e) Other parasites
 - (f) Struma
 - (g) Malaria
 - (h) Laryngitis. Acute and chronic bronchitis
 - (i) Tuberculosis
 - (k) Ulceration
 - (l) Hæmorrhages (epistaxis, metrorrhagia)
 - (m) Injuries
 - (n) Other remarks
17. Therapeutics :—
 - (a) Drugs used
 - (b) Number of anchylostoma expelled
 - (c) Duration of treatment
 - (d) Other remarks
18. Termination of the disease :—
 - (a) Complete recovery
 - (b) Remaining disorders, &c.
 - (c) Passing into other diseases
 - (d) Death, cause of same. Post-mortem examination
 - (e) Other remarks
19. Later observations :—
 - (a) Further history of the patient
 - (b) Continuation of the focus of infection (instruction thereby)
 - (c) Other remarks

ANCHYLOSTOMA DUODENALE.*

(Translated from the German of DR. SCHULTHESS, by DR. J. D. MACDONALD, of the Ceylon Medical Department.)

ABOUT five years ago there was quite a flood of medical literature on the occurrence of the anchylostoma duodenale among the workers of the St. Gotthardt tunnel, and on the anæmia caused by the parasite.



DESCRIPTION OF FIGURES.

(After Perroncito.)

- a b* Mature specimens of *Anchylostoma duodenale* (*a*, male ; *b*, female).
- c-p* Segmentation of the ova and development of the embryo ; *e f*, the stages of development usually observed in the faces ; *o p*, empty egg shells after the escape of the larva.
- q* Young larva, a few hours old.
- r* Mature larva.
- s* Mature larva at the beginning of encystment.
- t u* Larvæ with transparent movable capsule.
- v w x* Larvæ with calcareous cysts.
- y* The larva freed from the cyst.



This literature merely established the fact that the worm in question caused anæmia among a large number of the workmen, and a large mortality, and that this anæmia and high mortality was due to the presence of the worm alone. It, on the other hand, established little or nothing at all in regard to the development of the worm, or to the description of the disease as a whole. Since that time contributions have appeared from time to time from the mining districts and brickfields of France, Austria, and England, which have kept alive the interest at one time aroused in the minds of practical physicians by the St. Gotthardt outbreak. Some of the St. Gotthardt patients, about fifteen, as far as I remember, were treated in Zurich in the year 1881. I had then, being assistant at the time of Professor Wyss, an opportunity of examining this parasite. The results of my researches were published in 1881 and 1882.

Once familiar with the subject, I followed with interest such contributions as appeared from time to time by others, the more so as I myself differed from earlier observers as far as the anatomical relations of this nematode was concerned. Unfortunately, at the time very few took any interest in the anatomy of the worm, and so I had few opportunities of controlling my own observations by comparison with those of others.

The books on medicine and helminthology which I examined had nothing new to offer me, and very often repeated over again views already, as I believed, proved to be erroneous by recent researches. I may therefore be permitted to make some remarks on the subject. As to the statements concerning the geographical distribution of the parasites, the following passage occurs in Brass's "Text-book on Human Parasites," page 63:—"This worm is principally met with in southern lands, especially in Egypt, Brazil, Italy, and Switzerland. Lately it was found among the workmen engaged in the St. Gotthardt. It seems to be spreading gradually towards the north."

In the first place, I must protest against any such supposition as that Switzerland possesses a "southern climate," and ranks with Egypt as the home of the anchylostoma in consequence. Herr Brass may satisfy himself from earlier contributions—*e. g.*, Buignon—that before the St. Gotthardt outbreak anchylostoma duodenale was never observed in Switzerland. I have no doubt that every one at all acquainted with the subject will agree with me in contradicting the above statement, inasmuch as it is calculated to give false ideas concerning the (gradual) spread of the parasite.

The characteristic peculiarities of the localities where the parasite is met with, such as badly drained land, dirty habits of the inhabitants with regard to food and drink, are sufficiently well known.

It seems to be worthy of remark that amongst these localities some, especially mines, have a high temperature, whilst others, such as brickfields, have a low.

Leichtenstern, in his latest observations, asserts that it is possible that the epidemics amongst the brickfields may have originated from the mines. According to Leichtenstern the infection is not constant amongst the brickfields, and the attacks, which now and again occur, are to be attributed apparently to infection from the mines. It is to be expected that the observations of Leichtenstern, so valuable in this respect, will give us further conclusions on the influence of this factor in the spread of the disease in the near future. It is as yet doubtful whether the parasite, without renewed infection, can persist in any place where the temperature is low; further, in recent literature on the subject there occur statements as to the size and form of the anchylostomum duodenale.

Leichtenstern has made a number of observations in this direction. He comes to the same conclusion as I myself, although, as far as I know, my work was at the time unknown to him. I am quite satisfied that the statement made as to the length of the worm, *viz.*, that the male is under all circumstances smaller than the female, is not correct: it is more in accordance with facts to make the lower measurements of length for both sexes equal.

Leichtenstern gives the following measurements of length:—

Male	7.0 to 17.2 mm.; average 8.3 mm.
Female	7.0 to 16.5 mm.; average 11.48 mm.

My own measurements give the following results:—

Male	6.0 to 11.6 mm.
Female	6.0 to 15 mm.

At the same time I found that the female met with in the stools appeared usually bent backwards, forming a slight curve, whilst the males, on the other hand, appeared with the lower part of the body sharply curved, or coiled up, or perfectly straight.

Leichtenstern made the same observations, and they are worthy of record as distinguishing at once between the males and the females. I repeat this, inasmuch as Brass asserts that the male appears bent in the middle. I had a further opportunity of observing that the length and the thickness of the animal differed in this respect, that the one patient passed on an average larger worms than the other.

Leichtenstern—who, so far as is known to me, is the only one, except myself, who made the same observation—connects it with the age of the worm. It is possible that the age may play a part; but I would remark here that length does not indicate age so much as the large and strongly developed coils of the ovary. I do not at all agree with Leichtenstern when he represents the female as the blood-sucker (*κατ. εζοχήν*), and its darker colour as due to the larger quantity of blood taken up by it. In the numerous examinations made by myself personally of the stools, I have found the intestines of the male oftener filled with blood than that of the female. At all events, it may appear plausible that the female, on account of stronger development, may require more nourishment. I never had an opportunity of observing the entire animal of the colour of blood, if I understand Leichtenstern rightly to mean that; the intestines alone were coloured.

If totally coloured, then the blood colour must have diffused into the fluids of the other cavities. The darker colour of the female, which I have likewise referred to as a distinction between the sexes, depends, as I have already explained, on greater development. A question very much discussed is the relative number of the two sexes, which Bilharz puts down as one male to three females. Numbers originating from post-mortem examinations are but little known; we therefore depend mostly on numbers obtained from worms expelled. I cannot be certain that these numbers, which I obtained from the patients treated by me, have any great value.

The diluted stools were poured out in quantities easy of inspection upon plates, and submitted to my own inspection, so that none of the parasites escaped detection. Of other observers, only Lutz, Leichtenstern, and Trossat counted the worms passed in the stools after anthelmintics, giving males and females. Trossat only gives one case, and limited the examination to the first three or four stools after the anthelmintic. In this enumeration another question arose, viz., whether the males passed constantly in the later stools, and why? It has been already observed by different authors, that after the exhibition of medicine the males were always late in passing. Various hypotheses have been set up to explain this fact. I give in the following tables figures found in the literature on the subject, and valuable in this connection:—

Roth, Bâte (*s. b.* Bugnion [4] page 11) counted on post-mortem examination—

No.	Males.	Females.	Proportion.
1 ...	35 ...	47 ...	1 : 1·34

E. Parona (9) counted in the stools:—

2 ...	131 ...	460 ...	1 : 1·95
-------	---------	---------	----------

Leichtenstern (5) counted in the stools:—

No.	Males.	Females.	Proportion.
3 ...	235 ...	460 ...	1 : 1·95
4 ...	38 ...	131 ...	1 : 3·44
5 ...	10 ...	35 ...	1 : 3·50
6 ...	83 ...	223 ...	1 : 2·68

W. Schulthess (2):—

7 ...	188 ...	459 ...	1 : 2·4
8 ...	13 ...	51 ...	1 : 3·9
9 ...	10 ...	125 ...	1 : 12·5
10 ...	8 ...	222 ...	1 : 27·0
11 ...	1 ...	152 ...	1 : 152
12 ...	0 ...	142 ...	0 : 142
13 ...	0 ...	250 ...	0 : 250

E. Parona (9):—

14 ...	5 ...	95 ...	1 : 19
15 ...	25 ...	150 ...	1 : 6

Adolf Lutz (7):—

16 ...	— ...	— ...	1 : 5·5
--------	-------	-------	---------

These tables show that the females are found in larger quantities than the males, both on post-mortem examination and after the use of purgatives. The proportion between males and females varies from 1 : 1·34 to 0 : 250.

I remember quite well that during the Gotthardt epidemic it was at first difficult to discover males. What is the value of the above numbers in determining the relations of the sexes? In order to decide that, I must first speak of the peculiar so-called tenacity of the male against anthelmintics, which E. Parona discovered. It has been noted in the numerous examinations made that the males passed, as the above figures show, never appeared in the first stools. I cannot give numbers, unfortunately, from my own experience like E. Parona, who gives the following:—

Stool.	Males.	Females.
1st ...	8 ...	104
2nd ...	16 ...	19
3rd ...	107 ...	66

Leichtenstern gives the following:—

1st ...	10 ...	124
2nd ...	28 ...	7

I find only one observation in the literature of the subject which does not correspond with this. Bäumler found in one case, which he treated with various anthelmintics, first, seventeen males on different days, and a few females later on.

Leichtenstern is of opinion that the males resist anthelmintics more than the females, apparently because, on account of their smaller size, they are better able to conceal themselves. I am not of this opinion. In the first place, Bäumler's statement is against it, and, further, a post-mortem examination made by Bäumler and Schottelius in 1885 supports my view. The patient had been treated twice with doliarin, which, the first time, carried off a large number of worms, the second time a smaller number. On section, traces of the parasites were found in the duodenum, in the jejunum, and ileum, and here, and there, anchylostoma; in other words, the upper portion of the intestine was free from worms, the lower portion still infested. Unfortunately in this case the sex was not noted. Amongst the parasites left behind, there must at least have been some females, as the stools contained eggs. If this experience is to endorse the clinical observations quoted above, we must consider that the unexpelled parasites were mostly males.

Further, we must consider that the males do not appear in the stools simultaneously with the females, because they, at least at times, do not occupy the same place in the intestines. In favour of this view the following fact speaks, viz., that the males wander from place to place, as was ascertained by A. Lutz. He succeeded often in expelling single worms by drastics. They were mostly males, and once he found one of them alive. This proved that the parasite was only carried away mechanically, from its being loose in the intestine and not firmly adhering to it. Analogies with the other nematodes also favour this view. From the life-history of the oxyuris we know that the males are found principally in the immediate neighbourhood of the ileo-cæcal valve, whilst the females lie scattered in the cæcum and large intestines. From physiological reasons we may suppose that this separation occurs at times also amongst the anchylostoma, and this is rendered more probable by clinical experience of a number of cases in which, after a single dose of medicine, a large number were expelled, including, if we accept the proportion between the sexes, all the males. On the other hand, I cannot altogether accept Leichtenstern's view. The difference in size between the sexes is not sufficiently great to account for the one being able to hide itself. Unless further observations teach otherwise, we must accept that the so-called tenacity must be due to position alone. It is to be regretted that we have no post-mortem examinations which give, in addition to the number and position of the worms, also the position of the two sexes. Several sections, of course, would be required to establish with certainty, or to overthrow the above supposition.

As far as the first question is concerned—*i.e.*, the constancy or inconstancy of the proportions between the males and the females—we learn from the experiments hitherto made that results obtained by the expulsion of the parasite are very unreliable. It is only when several cures have been carried out throughout that the numbers acquire value. For this purpose cases must be chosen not long after infection has occurred. Spontaneous expulsion of individual parasites, death of others, and so on, render the numbers of less value. The observations of Lutz deserve consideration on this account. He found the ratio between males and females to be as 1 : 1.5. Leichtenstern in one case found the ratio to be as 1 : 3.44 ; another, with males more numerous, the ratio being as 1 : 1.95 ; and, further, a case observed by myself six weeks after the patient was removed from the Gotthardt tunnel, the ratio being as 1 : 2.4. In considering these numbers we must conclude that the number of the males is more numerous than was hitherto believed : proportions may vary sometimes. The males may be said to form from one-fourth to two-fifths of the whole number. The case mentioned by Roth shows relatively the greatest number of males. But the patient, in this case, had wandered about a long time after apparent infection, and had been treated in several hospitals, and cannot be accepted as normal. It may appear striking that in our cases there were so few males present.

From the experience of Leichtenstern we must conclude that repeated and re-repeated cures would have expelled more worms and certainly mostly males. That may be true for individual cases, but not for all. In one case, after the worms were once expelled by a strong dose of malefern two other strong doses were given without any result. I have tried to explain this by attributing a shorter period of life to the males than to the females ; only the case of Roth, which, as indicated above is exceptional, is opposed to this view. In support of the view that it was exceptional, I can quote the following facts, that the patient in question had left the Gotthardt tunnel eight months before, whilst the patient in whom the greatest number of males were found had left the tunnel six weeks only before the cure was commenced. From the literature of the subject I may still quote that all inquirers into the subject living in countries where the worm is endemic, or who, like Leichtenstern, have had an opportunity to treat patients soon after they left the place of infection, always speak of a comparatively large number of males. If due attention be not paid to the last-mentioned fact, the supposition of Leichtenstern, that three females must at least be present for one male, may not find any great support in further cases. A definite decision concerning these suppositions can only be expected from post-mortem examinations.

As far as microscopic anatomy is concerned, but few works of modern times give any assistance. In the text-books even of the most recent dates, Leuckart's description, more or less altered, is still met with. The hooked teeth are sometimes described as outside, sometimes as inside the margin of the mouth, whilst the projection on the dorsal half of the border of the mouth becomes in some works two pyramidal teeth. The schematic picture in Brass corresponding to this idea, and representing the head of the animal, is distinguished by great want of clearness. The author could have had no clear conception of the parasite present in his mind, and much less can any one not acquainted with the subject gain an idea of the animal by contemplating this picture. Even as little can his sketch of the bursa copulatrix satisfy, especially a zoologist. It is well known that among other characteristics the ribs of the bursa serve to distinguish genera and species.

The termination of the posterior rib with its bifurcation resembles, according to Brass, rather a fir tree than the delicately-formed object so easily recognised under the microscope. In this place I must refer to the work of my French colleague Fabre (13) (Commentary). There is a table given by him with copies of sketches from the works of Bugnion and my own works. Although Bugnion's sketches are duly acknowledged, I must remark that of the three sketches taken from my work, viz., a representation of the tail end of the female and a lateral and an abdominal view of the head, no mention is made of the author.

In Trossat (8) I find several pages of text descriptive of the anatomy of the worm, and two plates.

Unfortunately, in view of text and plates, I must express my astonishment that the author was not able to make better use of materials ready to his hand, whilst, as is evident from the work itself, he is not acquainted with the appearance under the microscope.

It would occupy too much time to mention individually points easily proved to be erroneous, and contradict them, but a few examples may be quoted.

Because Trossat had found no pure blood in the intestines of the worms examined by him, he believed that the digestive powers of the animal were slow, that it required but little blood, and that, accordingly, it was not dangerous as far as anæmia was concerned. He deduced his conclusion from but a small number of cases, or from an imperfect examination of the stools. Let him teach himself otherwise from Grassi and Lutz. The stripes on the skin are, according to Trossat, often limited at the sides, sometimes occupy the whole periphery. It is here apparently a question of a variety. Of the existence of the mouth-capsule Trossat knows nothing.

"A hyaline membrane acts as a cupping-glass, and masses of muscular fibres give the necessary support to the head." "The delicate teeth on the dorsal margin of the mouth are placed in the bottom of the mouth." The author has evidently read something of triangular plates which occur there, and as he could not find them the teeth were made to serve the purpose, which, unfortunately for him, are also of a triangular shape. Trossat has further found a sphincter separating the mouth from the œsophagus, again a gross deception. The appearance was caused by the movements of the chitinous œsophageal lining membrane. He is also confused on the subject of the œsophagus and stomach. Trossat had no idea of the three-rayed appearance of the former organ with its circular muscles.

"The pointed tail of the female results from the thickening of the fibres, which form the enveloping lamella of the intestine." This last sentence satisfactorily shows that the author has no idea of the structure of the nematodes. "The bursal ribs (digital-form prolongations) amount to seven," whilst the real members are either five or eleven.

Finally, it was concluded a double uterus existed from the presence of a double spicula. It is to be regretted that medical men, entirely ignorant of the subject of the anatomy of the parasites, should thus encroach upon the province of the zoologist. He who has not time to study the anatomy of the nematodes had better not employ himself with the subject at all, as his contributions are only calculated to confuse and to spread false views. With the imagination there is nothing to be done in this field.

In other treatises but few remarks are made concerning the anatomy. Leichtenstern gives straight off six chitinous teeth to the mouth-capsule, but there are in reality eight, viz., four bent, hook-shaped teeth, and four others (chitinous projections) which may be designated as teeth.

Further, it is an error when he speaks of eggs laid "in parallel rows in the genital tubes." The eggs are not laid in rows, but the tubes containing the eggs are laid in parallel rows. (See my work, pages 214 and 215.)

In an Italian work (14) there is a description of the mouth made up from other descriptions (Perroncito, Bugnion, &c.); also here there is mention made of teeth and of jaws, and besides the marginal teeth an extra one is mentioned as being inside, which in all my examinations I have never seen. The physiology of the parasite is but lightly touched upon, as is to be expected from the difficulty of the subject. Trossat alone is not here left in the lurch by his fertile imagination. How little worth is to be attached to his observations may be inferred from his utter ignorance of the anatomy of the worm. A description which appears in most of the works is that concerning the mode in which the animal fixes itself in the mucous membrane. From Lutz we learn that the worms are mostly or all found hanging on to the mucous membrane in all cases examined shortly after death. They are also, however, to be met with free in the intestine. They probably change their place for the sake of nourishment—*i.e.*, they wander. Concerning the mechanism by which they fix themselves, we must still refer to Leuckart's description, hitherto the best, and therefore always quoted.

Perroncito ascribes "to an elastic membrane met with in the mouth-capsule" a share in the sucking up of the mucous membrane of the bowel. Trossat considered it as self-evident that the hooked teeth at the margin of the mouth buried themselves in the intestinal mucous membrane, and that afterwards the muscles (which?) provide for the movements of the lower teeth. After I succeeded in making a little more progress than others in the anatomy of the parasite, especially of the mouth-capsule, I had yet to confess that the mechanism had gained very little in clearness for myself. In the first place, the question faces us, whether and which teeth of the mouth-capsule are movable, and which are not. Bugnion doubts whether any of them are movable. From my research I must believe that the four "famous" (because they are to be seen at the first glance) hook-shaped teeth of the ventral margin of the mouth-capsule are firm and immovable. I deduce that principally from the fact, that the maceration which destroys the whole of the mouth-capsule except the chitinous portions, leaves those teeth always in connection with the portion of the capsule to which they are applied. On destruction of the capsule they do not loosen themselves from it, but a portion breaks off with them. The chitinous ring discovered by me, and which surrounds the upper aperture of the capsule, in which also these teeth are inserted, helps to strengthen their position. The two teeth lying upon the dorsal margin of the capsule are likewise incapable of movement, as they merely correspond to a deposit upon the already-mentioned ring. It is otherwise with the pyramidal chitinous points lying at the bottom of the mouth-capsule, and always, and with justice, credited with the power of piercing the mucous membrane. These separate by long maceration, and it is probable that on suction of the intestinal mucous membrane into the mouth-capsule by some hitherto unknown mechanism, the teeth are not entirely passive. In favour of that view speaks the fact that they are here and there met with in connection with the chitinous apparatus of the œsophagus. Bugnion likewise seems to share this view.

Another question is, whether the mouth-capsule takes a share in the process of suction. It seems so to me, since I have succeeded in proving that the bell-shaped mouth of the *dochmius* (not only of *dochmius duodenalis*, but also of *dochmius trigonocephalus* and *tubæformis*) is

provided with a number of slits, of which one completely divides the dorsal portion, with the exception of a small bridge on the anterior margin. These slits are found, in the uninjured animal, constantly shut: they open themselves, however, when pressure is made on the chitinous lamellæ covering the slit. I cannot go further than leave the possibility of opening the capsule in this manner an open question. To say more, it seems to me that the knowledge of this complicated portion is as yet too little developed. As far as I know, there is no detailed description of it for any of the nematodes.

What Perroncito ascribes to his elastic membrane is likewise not clear to me. I do not even know what portion he looks upon as the elastic membrane.

That the muscles of the œsophagus can exercise powerful suction is clear from their anatomical relations. The three-rayed lumen with the strong chitinous walls will become almost triangular when the circular muscles are in action, and take up a larger space in the periphery than in their position of rest. As the opening of the mouth-capsule into the œsophagus is tolerably large and apparently capable of enlargement, the suction power of the œsophagus re-acts very well upon the cavity of the former, particularly because, as I believe, the capacity of dilatation of the anterior portion of the œsophagus is relatively greater than that of the posterior. I conclude that from the fact that the chitinous apparatus of the œsophagus in its anterior half is much stronger than in the posterior.

The following may also be taken into account in the suction process. The dorsal half of the capsule passes deeply into the muscles of the œsophagus, and makes it probable that at the moment of suction the head bends backwards upon the dorsum very powerfully. Through that the ventral border is pressed close to the intestinal wall, and suction rendered easier. The hook-shaped teeth of the ventral margin certainly serve, as almost all observers believe (see Leuckart, Bugnion, &c.), to hold the intestinal wall firmly, rendering the fixation certain without the help of suction.

The explanation of how the animal loses its hold again seems to me to be difficult, the more so as the hook-shaped teeth are not to be considered as movable. Whether the sucked-up portion of the intestine is destroyed by the teeth at the bottom of the capsule, is uncertain. The nutrition of the animal, which is *exclusively blood*, seems, as far as is yet known, to make large demands on the system.

Through some observations it is probable that the animal evacuates the blood again per anum without the blood corpuscles being completely destroyed. I have never succeeded myself in discovering uninjured blood corpuscles even in apparently well-filled worms.

According to Grassi (15) the blood mass would require to be much more highly taxed than it ordinarily is before such *small* daily losses would affect the system.

This deserves to be noted, as several authors, especially French authors, are of this view. Concerning the operation of copulation, Lutz has noted that for every hundred females he always found a pair in copula. Other observers have not found this number. Here we must accept the observations of those who have experience of the parasite in an endemic form. The copulation is *said* to last long, only I could not have inferred this from the male organ of generation. In this place I would like to mention that the curvature of the body, as it is met with in the male, is such that the bursa and buccal cavity approximate on the dorsal side.

It is accordingly possible that both animals are fixed to the intestines during copulation, as in the case of the female the generative opening is turned to the cavity, not to the wall of the intestine whilst sucking. It seems from this that fixation to the intestine is not only necessary for purposes of nutrition, but also for propagation. The duration of life of the anchylostoma is high. Should I speak in accordance with my present experience, I would give eight months as the maximum. With such statements, however, we cannot be too careful, especially in face of the history of its development, of which so very little is as yet known. In this connection the discovery of parasites in cavities under the mucous membrane is of importance (Bilharz, Grassi, &c.). The duration of their stay there is unknown, and the duration of life of the fully developed animal cannot be known accordingly.

On the other hand, in individual patients a self-infection is not impossible, at least when the patients remain a long time in the place where the worm prevails. In this connection it is further to be noted that the male has at all events a shorter period of life than the female. For diagnostic purposes it is easily understood that the form of the ova have received more attention from medical men than the anatomy of the animal itself. In the first place, statements concerning the size of the eggs are numerous (Bizzozero, Bugnion, Sahli, Schulthess, Perroncito, Menche, Leichtenstern, Hindenlang, Bäumlér, Roth). To avoid repetitions I may say that Bugnion, Bäumlér, Bizzozero, Sahli, Schulthess, and finally Leichtenstern also, with slight variations give the length as 0.06, the breadth as 0.04. Leuckart gives smaller measurements, because, apparently, fresh preparations were not at his disposal.

It were desirable that these measurements should be given in the text-books. This is the more necessary as these measurements distinguish the ova from those of the oxyuris.

The measurements of the latter are—length, 0.052; breadth, 0.024. They possess an absolutely and relatively smaller breadth than those of the anchylostoma. They do not show the beautifully ovoid flattening of both ends, but rather a cylindrical form, maintained towards the extremities with an asymmetrical bulged longer side, and contain almost always a living embryo. Compare the numerous sketches given by Bugnion, Bizzozero, Schulthess.

I may mention that the measurements made by me, a maximum length and minimum breadth, were always present. That the eggs have a double contour with from two to six elevations, is now well known. Eggs with undivided yolk, I cannot, like Leichtenstern, say are enormously rare. Further, I have observed a patient in whose fæces the eggs were in a high state of division, twenty to thirty elevations being present.

Concerning the further fate of the eggs I do not feel myself qualified to speak, as my own observations were confined to the primary stages of development some time ago. Now, Perroncito has described the development up to the formation of the larva and the incrustation of the outer covering. Leichtenstern has made the same observations, as well as Lutz, and we even read in Trossat the same. They have all, however, fallen into one mistake in supposing a state in which the animal is supplied with a second skin as a stage of encapsulating. This supposition has been constantly rejected by zoologists. Even Bugnion mentions that this occurrence has not its like among the nematodes. Lutz, in an appendix to his work, says that Leichtenstern, since his last publication, has pointed out the mistake. The stage of encapsulating is only a phase in the change of skin. The incrustation would then be only a process of degeneration. Finally, we learn from Lutz that the above-mentioned discovery by Griesinger and Bilharz of encysted specimens in the submucosa had been corroborated by Grassi. In connection with this a further stage has been found. Keeping this observation in view, Leichtenstern would not have been obliged to suppose a diseased condition of the female parasite by the vermifuge, and finally recovery of the same, as the reason that eggs disappeared from the stools for weeks together.

It is not my intention to give a clinical picture of the disease, as this subject has received full justice at the hands of Lutz. It is worthy of note that, in spite of most convincing facts, the irrelevance of the anchylostoma in the production of anæmia is still firmly held by French authors. I would most earnestly refer inquirers to the clinical picture of the disease given by Lutz. To connect the parasites with the disease by comparison of the number of worms present with the degree of the anæmia, is yet impossible. The cases published by Trossat, among others, of anæmia among miners do not give us the same picture of the disease as afforded by the Gotthardt workmen.

The Gotthardt anæmia is unconditionally to be looked on as acute (Lutz), whilst it can be easily imagined that in a mining locality, on a little overcrowding, the chronic form might be developed.

The cases recorded by Trossat might correspond with such chronic cases. The long convalescence on which Trossat lays so much stress originates from this. At the same time, no one will believe that the Gotthardt workman, freed once and for all from the anchylostoma, got over all his difficulties. The convalescence was often very slow, and the days following the exhibition of the drugs were severe days for him. It must have been rather a striking circumstance at the Clinic of Professor Wyss to observe that patients who harboured a great number of worms immediately felt relieved on the expulsion of the same. This must have been caused, as Moniglotti has remarked, by the satisfaction felt by the patient at their expulsion. The tables given by Lutz may be used as excellent examples. In the examination the following are to be observed. The intestines are not to be washed in water; they are to be cut in lengths; the fæces are to be gently washed off, and to be examined; and the following details are to be established:—

- (1) The number of the worms present.
- (2) Their position in general.
- (3) The number of those *free* in the intestines, giving sex.
- (4) The number of those adherent, giving sex.
- (5) The ratio between the sexes.
- (6) The position of the two sexes (whether free in the intestines or adherent, and where).
- (7) The number, or at least an estimation of the number, of *bites*.
- (8) The examination for submucous cysts or ulcers resulting from such an examination of any parasites found therein with reference to development.

A few post-mortem examinations carried out in this manner would contribute to the solution of a few of the questions referred to in the beginning of this paper.

When the above paper was finished, the latest treatise of Leichtenstern (Further Contributions on the Anchylostoma—Deut. Med. Wochenschr, Nos. 11, 12, and 13) came to hand. It necessitated this appendix. Leichtenstern's remarks on the mode of writing the anchylostoma are, I am convinced, justifiable, inasmuch as the word in France is not always written "anchylostoma."

Trossat and Favre write "ankylostoma," as well as Bugnion. That the Italians make use of "ch," and write "anchylostoma," cannot be placed on the same footing therewith. That the French and Germans have observed this mode of writing, very often depends on the fact that they have imitated the Italians without considering that this gives another result for our language, as well as for the French. Further, Lutz has spoken in favour of the orthography "ankylostoma" definitely.

The work of Leichtenstern announces the discovery of a rhabditic form, the segments of which have an independent life when separated, and are able to propagate the species. This is undoubtedly a great discovery, and one on which the author is at present engaged. Most instructive is the post-mortem appearance of a patient suffering from anchylostomiasis, who died of phthisis. It scarcely leaves anything to be desired; it would have been of interest to learn whether Leichtenstern was altogether justified in attributing the echymoses of the intestines to bites. In this case the seat of the parasites in the midst of a place beset with echymoses would speak in favour of the worm changing place for the sake of nourishment. The worms were removed from the canal, some of them still living. Leichtenstern could, like Grassi, observe on this occasion that pure blood was passed by the animal from the anus. In how far this process occurs in worms not actually fixed to the mucous membrane of their host, is not determined, but

certainly these and other observations point to the fact (accepted both by Grassi and Leichtenstern) that the worms are rather *choice* in their diet, and live chiefly on the blood plasma. Unfortunately the number of worms found in this case was small (twenty-three females and one male).

Leichtenstern further quotes two cases of a striking increase of the red blood corpuscles after the expulsion of the worms. These correspond to observations made by Sahli (Archiv. f. Klin. Med. XXXII.).

Leichtenstern also speaks of spontaneous cures which take place in the course of years. He was also of opinion that the phthisical case was on the way of recovery as far as the anchylostomiasis was concerned. As a reason he refers to the striking difference in the ratio of the sexes, twenty-three females and one male. The males in his experience get less in old cases. I must here remark that in 1882 I made the observation that the disappearance of the male indicated a spontaneous cure. Leichtenstern supposes that the disappearance of the males is due to their possible wandering in the canal and to their being gradually carried out of the system with the fæces. This explanation, only a hypothesis on the part of Leichtenstern, has been proved by Lutz to be an actual reality.

Leichtenstern finally asserts that endocarditis and pleuritis is a frequent complication of the anæmia of anchylostoma, and treats *in extenso* the interesting changes found in this respect in the phthisical cases.

TRICHOCEPHALUS DISPAR: CONTRIBUTIONS TO THE BERI-BERI QUESTION.*

(Translated from the German of DR. H. ERNI by DR. J. D. MACDONALD of the Ceylon Medical Department.)

IN the year 1882 there were found in Sumatra, during the examination of the intestines of patients who died of the beri-beri disease, three kinds of intestinal worms, all of which are capable of injuring the intestines, and live on the blood of the patient,—viz., the “*anchylostomum duodenale*,” the “*trichocephalus dispar*,” and the larva of a peculiar fly. The intestinal lesion caused by these parasites are easily distinguished from each other, even leaving the locality out of question. The *anchylostomum duodenale* makes oval wounds, as it bites with its bent mouth into the mucous membrane. These wounds stand usually close together, forming circular patches, are covered with mucus and blood, and in the middle of each may still be found the *anchylostomum* firmly attached to the membrane. Should these spots ulcerate, cicatricial strictures of the intestines may occur. A single parasite may destroy in the course of two or three days a spot of the intestine the size of a florin. The *trichocephalus dispar* penetrates with its hair-like head the mucous membrane, yet usually not deep. This penetration causes a round wound with a depressed margin and surrounded by a reddened border of mucous membrane. In rare cases the whole mucous membrane is undermined; further, small inflamed circular patches or circular holes, as if cleanly cut out by a gouge, are met with. The floor of these holes is formed by the muscularis. These little defects often increase in size, and form ulcers the size of a split-pea with ragged edges, and if these coalesce strips of mucous membrane are lost to a more or less extent. This destruction must be attributed to the larva of a fly. The *anchylostoma*, together with the lesions caused by them, are found in the stomach, in the duodenum, and most frequently in the small intestines. The *trichocephalus dispar* is found in the cœcum and in the colon, the mucous membrane of which it destroys in the same manner as the *anchylostomum* the upper portion of the intestines. On examination the colon shows itself alone affected—most frequently, however, the colon and cœcum together, less seldom the cœcum alone.

The larva of the fly, on the other hand, may be found everywhere in the intestinal tract, but its favourite place is the colon.

These three are to be regarded as genuine parasites, living at the expense of the blood of their host. The injuries caused to the intestines differ from other ulcers; for example, from tubercular ulcers by their form and by their fresh red appearance. After the affected portion of the intestine is exposed to the air for a few minutes, these become of a bright red colour. As a rule, they are covered with a thin layer of blood, but which can be easily washed off by a gentle stream of water. The parasites themselves are not always to be found; the larva of the fly almost never. The extent of the destruction caused by the *anchylostomum duodenale* is not always in proportion to the small number of parasites met with and often found firmly adhering to the intestine. The *trichocephalus dispar*, on the other hand, is very often found in numbers proportional to the extent of the lesion. It is very rare for one of these parasites to be found without one of the others. The three occur very often together; most frequently the *anchylostomum* and the *trichocephalus dispar* help each other in their work of destruction. If one only is present, the *trichocephalus dispar* is the one most frequently met with.

In more than fifty post-mortem examinations of beri-beri I have never missed these intestinal lesions, while they do not occur in patients dead from other diseases. The parasites are indeed to be met with also in such, but without *any lesion of the intestine*. This makes me assert that beri-beri is helminthiasis, the cause of which is the destructive process in the intestine caused by these parasites. Reflex symptoms arise from the lesions, whilst through the loss of blood and impaired digestion anæmia occurs. The chronic anæmia has in its turn a deleterious effect upon the different organs and degeneration of the heart, with atony and dilatation of the blood vessels, particularly of the aorta result. Finally, dropsy supervenes œdema of the ancles, feet, legs, face, &c., as well hydropericardium, less seldom ascites; and death results from œdema of the lungs

* Delivered by Dr. H. Erni at the meeting of German scientists and medical men at Berlin (September 18 to 24, 1886).

and paralysis of the heart. Should the patient survive the dropsical stage, general symptoms of atrophy, viz., the atrophic stage, set in. As the trichocephalus dispar occurred most frequently, and caused the most extensive destruction of the mucosa, this worm must be looked upon as the *peculiar beri-beri worm* more than the anchylostomum duodenale, whilst lesions through the larva of the fly occurred less seldom.

Scheffer, a military surgeon of Java, is opposed to this view, but admits that the anchylostomum duodenale and trichocephalus dispar occur frequently and cause anæmia; but that neither the one nor the other cause beri-beri. He asserts that both the parasites are met with in other bodies as well as in those who died of beri-beri; further, he asserts that anæmia is not a *conditio sine qua non* of beri-beri, but is often absent in that disease.

This question has, however, unexpectedly been solved by the appearance of Dr. Lutz's treatise upon anchylostomum and anchylostomiasis (Volkmann's "Vortrage," Nos. 255 and 256). Here are set down the symptoms of beri-beri so true to nature that this little work may be looked upon as the best authority on the disease.

The opponents of Dr. Lutz assert that the lesions attributed to the trichocephalus dispar are exaggerated, and that this comparatively harmless parasite is represented as a dangerous worm. This is specially asserted by the followers of Scheuber, who asserted that beri-beri was a polioneuritis epidemica, a theory depending upon the fact that peripheral nerves are found atrophied and undergoing fatty degeneration. But that this same degeneration was found in the muscles, in the blood vessels, and in almost all the organs of the body, has long been known. As also Ziemssen ("Handbook of Special Pathology and Therapeutics," vol. 7) is of the opinion that the trichocephalus dispar cannot penetrate the mucosa. I may be permitted to give the result of thirty post-mortem examinations:—

(1) Atjeh prisoner of war. Diagnosis: beri-beri (febris intermittens). Symptoms of trichocephalus dispar. About twenty-five trichocephali found in the cœcum and upper part of the colon. Mucus coloured with blood.

(2) Idem. Diagnosis: beri-beri (lithiasis). Symptoms: mucous membrane of the cœcum inflamed and eroded by numerous trichocephali, generally still small.

(3) Idem. Diagnosis: beri-beri. Symptoms: mucous membrane of cœcum and colon thickly beset with recent inflamed spots, and containing mucus coloured with blood. Numerous trichocephali found everywhere.

(4) Javanese convict. Diagnosis: beri-beri. Symptoms: mucous membrane of cœcum much inflamed and eroded in a few places. Not many trichocephali present.

(5) Idem. Diagnosis: beri-beri (chronic opium poisoning). Symptoms: eroded spots about the size of a florin found in cœcum. Several trichocephali found on these spots.

(6) Idem. Diagnosis: beri-beri. Symptoms: cœcum and first portion of colon found as a bleeding surface. Innumerable trichocephali present.

(7) A Java labourer. Diagnosis: beri-beri. Symptoms: cœcum red, inflamed; colon in several places also inflamed and eroded. Numerous trichocephali present, more in the colon than in the cœcum.

(8) A Java soldier.—Diagnosis: beri-beri. Symptoms: erosions red and inflamed in the cœcum and first part of the colon; *everywhere* trichocephali present.

(9) Chinese convict. Diagnosis: beri-beri (after enteritis acuta). Symptoms: cœcum and first part of colon showed a state of catarrh with erosions. Numerous trichocephali present, all of which had penetrated deeply into the tissues, and were firmly adherent.

(10) Java soldier. Diagnosis: beri-beri (chronic opium poisoning). Symptoms: about twenty trichocephali present. Cœcum is one large red superficial erosion, with numerous raised points coalescing, and numerous ulcers.

(11) A Java soldier. Diagnosis: beri-beri. Symptoms: about ten trichocephali present, firmly adhering to the mucous membrane of cœcum; several places eroded, and bleeding.

N.B.—In all these cases there were also erosions of more or less extent found in the stomach, duodenum, and small intestines, where numerous specimens of anchylostomum duodenale existed, so that the whole of the intestinal tract was affected. In case No. 4 there were also lesions due to the larvæ of a fly.

(12) Atjeh prisoner of war. Diagnosis: beri-beri (marasmus senilis). Symptoms: lower portion of cœcum much eroded and inflamed. About twenty trichocephali present.

(13) Idem. Diagnosis: beri-beri. Symptoms: the colon in its whole length beset with inflamed spots, forming erosions of recent date. Many trichocephali present.

(14) Java convict. Diagnosis: beri-beri (chronic opium poisoning). Symptoms: mucous membrane of cœcum inflamed and eroded. About twenty trichocephali present. Catarrh of colon.

In these three cases there were no other lesions of the intestines present. The anchylostomum duodenale was altogether absent.

(15) Java convict. Diagnosis: beri-beri (earlier febris intermittens). Symptoms: the cœcum was normal. About three trichocephali present.

(16) Idem. Diagnosis: beri-beri. Few trichocephali.

(17) Java sailor. Diagnosis: beri-beri (ulcus cruris). Symptoms: numerous trichocephali in cœcum and colon; mucous membrane intact.

(18) Chinese. Diagnosis: ulcus cruris. Symptoms: nihil.

(19) Java convict. Diagnosis: beri-beri. Symptoms: a few trichocephali in cœcum; mucous membrane intact.

Whilst the trichocephalus dispar was either absent or had left the mucous membrane intact, there were here considerable lesions of the intestines caused by the anchylostomum duodenale.

(20) Atjeh prisoner of war. Diagnosis: malaria cachexia. Symptoms: cœcum normal, only a few trichocephali present. No anchylostoma.

(21) Malay. Diagnosis: Dysentery. Symptoms: a few trichocephali and a few punctiform ecchymoses; a few anchylostoma in small intestines; mucous membrane intact.

(22) Chinese. Diagnosis: enteritis chronica. Symptoms: nihil. Also no anchylostoma.

(23) Chinese convict. Diagnosis: febris intermittens. Symptoms: no erosions in cœcum; only one trichocephalus; no anchylostoma.

(24) Java convict. Diagnosis: enteritis acuta. Symptoms: numerous trichocephali in cœcum and first part of colon; no erosions; numerous anchylostoma; mucosa intact.

(25) Java soldier. Diagnosis: carcinoma hepatis. Symptoms: few trichocephali in colon, a few eroded spots, cœcum normal; a few anchylostoma and a few eroded spots in small intestines.

(26) Soemdun woman. Diagnosis: febris, intermittens. Symptoms: nihil. Also no anchylostoma.

(27) European soldier. Diagnosis: cholera asiatica. Symptoms: nihil. One anchylostomum present; duodenum normal.

(29) Chinese. Diagnosis: dysenteria acuta (earlier), beri-beri. Symptoms: nihil. No anchylostoma. A few recent eroded spots in duodenum and small intestines.

(30) Malay. Diagnosis: malaria cachexia (abscessus perihepat). Symptoms: nihil. A few recent eroded spots in upper portion of intestines. No anchylostoma.

In the above eleven cases, in which there was no question of beri-beri, both the trichocephali dispar and the anchylostomum duodenale were either absent, or, if present, had caused so little injury to the intestine that their presence need not be taken into consideration at all. As far as the kind of lesions caused by the trichocephalus is concerned, these vary considerably in *intensity* and *extent*. Numerous trichocephali may be present, and yet the mucosa may remain intact. In the mildest cases there is found a limited inflammation of the cœcum and the first portion of the colon, the mucous membrane being swollen and red.

In other cases the trichocephalus had penetrated into the mucosa with its fine hair-like head, and caused a reddened punctiform spot, like the bite of an insect. This appears as a small *bleeding* wound, with depressed-edges and an inflamed halo. As a rule, numerous points of this kind stand close together, and appear to the *naked* eye as red spots, in the midst of which the trichocephali are still found, still not so firmly adherent as not to be drawn easily away.

It is only in exceptional cases that the trichocephalus passes with its whole body into the mucous membrane, undermining it extensively, and showing only a few small wounds upon the surface. The head and the tail project from the mucosa, whilst the rest of the body is buried under the membrane, resembling a surgeon's curved needle passed beneath the tissues, point and eye being only visible. It is with difficulty that these parasites can be withdrawn whole. Again, on the other hand, small ulcers may form from these little points, standing more or less close to each other, or the surface becomes soft, the epithelium is thrown off, and erosions are formed, which spread over the whole cœcum.

Trichocephali are often found upon such erosions. These erosions may increase and form superficial ulcers, which in their turn coalesce, destroying the whole of the mucous membrane. Numerous recent bleeding points are always found with these ulcers, so that the whole resembles the bleeding surface of a wound. There are cases in which ulcers have already healed, whilst others in the same locality are of recent origin. These eroded spots are covered with blood and mucus, but it is rare to find clots of blood in the canal. The following are the results of some of the worst cases:—

1.—Whilst the duodenum and upper portion of the intestine were normal, there were noticed in the lower portion, and especially in the cœcum, even externally, patches of hyperamia of the intestinal wall; internally, the mucous membrane was found swollen, and covered with tough mucus. In the mucous membrane itself there were found red punctiform wounds close to each other, the membrane appearing excoriated and hæmorrhagic. These little wounds stood generally in groups of more or less extent close to each other. The cœcum was affected worst of all, there being scarcely a sound spot on its whole surface, and little red ulcers occurring everywhere. The first portion of the colon stood next in order, but from there the lesions became less and less.

2.—(Cf. case 10.) The cœcum was a bleeding surface covered with mucus and blood.

The first portion of the colon, a foot in length, was covered with ecchymoses, whilst the rest of it was normal. In this instance about 100 trichocephali were present. The lesions caused by the trichocephalus are mostly met with in the cœcum alone (seven times in the cases quoted above), almost as often in the cœcum and colon together (six times), and rarely in the colon exclusively (once).

As far as the geographical distribution of the trichocephalus is concerned, it is common among the natives of the Malayan Archipelago. In the thirty cases already quoted the worm was completely absent only in six cases; in fourteen cases the worm caused considerable injury to the intestine, and these, whether accidentally or not, were all cases of beri-beri; in five cases of beri-beri, however, the worm was absent, and no lesions were found. The same statement may be made of the anchylostomum. In eleven cases, dead of other diseases, lesions caused by either the one or the other were absent.

The symptoms caused by the trichocephalus, as far as general results are concerned, must be the same as those caused by the anchylostomum, viz., loss of blood and dropsy, perhaps in a higher degree by the latter as the intestinal lesions are intense. The purely local symptoms, on the other hand, correspond rather to the symptoms of catarrh of the colon; fever, except at the commencement of a few cases, is rare. There may be blood in the stools. The hardened fæces are smeared with blood, and should a laxative be given then stools of liquid blood may be passed.

Then obstinate constipation follows almost without exception, during which three or four days pass before another stool occurs—sometimes it is even longer. The fæces are then dry and hard, and have the appearance of clay. It is exceptional for diarrhœa or acute enteritis to be present in the beginning, as happened in the following case (No. 9).

Tjang Atjang, a Chinese convict, came for treatment suffering from enteritis acuta. Symptoms: pain in the epigastrium and over the whole abdomen, the adductors of the thigh being very sensitive; evening, fever. Liquid stools with blood ten times a day. On this super-vened anæmia, strong cardiac action, and cardiac murmurs. In about twenty days the diarrhœa ceased, and the case developed into typical beri-beri, of which the patient died two months later

On section the following were found :—Well developed body, with a fair amount of panniculus adiposus ; œdema of the face and of the legs ; hydropericardium ; fatty degeneration of the heart, with dilatation of both ventricles ; atheroma of the aorta ; slight degree of œdema of the lungs ; spleen of normal size ; nutmeg liver ; hyperæmia of the kidneys ; catarrh of the stomach and small intestines, but without erosions. There was still found in the stomach dark granular remains of opium extract, which had been taken by the patient. Anchylostoma were not present, yet in the lower portion of the small intestines, close on the cœcum, numerous large patches were found, made up of small wounds and covered with mucus and blood. The cœcum and the colon were inflamed and full of trichocephali. The latter had penetrated deep into the mucous membrane, their heads and tails alone being visible ; it was with difficulty these could be drawn out. Everywhere in the cœcum and the neighbouring portion of the colon there were found numerous recent and bleeding erosions.

As no other cause can be assigned for these, we are forced to believe that the trichocephalus first caused inflammation of the intestines followed by diarrhœa ; as the latter ceased, beri-beri was developed. Without entering here further into the question of the origin of beri-beri from the cases cited above, it may be asserted that the trichocephalus dispar causes severe lesions of the cœcum and colon, even destroys the mucous membrane, and is inferior in no respect to the anchylostomum duodenale in the injuries which it causes.

A confirmation of this is found in a new publication of Dr. Haga, in which three such cases are given in detail. No. 12, beri-beri, in which an enormous number of trichocephali were found in the whole of the colon, and the most of which were firmly adherent to its walls ; No. 21, beri-beri, with numerous trichocephali, which caused in the cœcum and the ascending colon innumerable ecchymoses of the size of a pin-point with a pale centre, and some small erosions or loss of the mucosa of the size of a small pin-point. Further, there were found in a case of phthisis pulmonalis numerous trichocephali and many ulcerating spots in the cœcum, "which must be ascribed to the trichocephali" (likely tuberculous ulcers, as I myself saw, in one case). Conscientious as this work of Dr. Haga is, it is remarkable that among his thirty-three cases (post-mortem) not a single case of malarial cachexia is mentioned.

In a malarial country like Java this is scarcely possible, so that apparently no difference was made between malaria-cachexia and beri-beri, and *all* were classified as beri-beri. As no difference can be made out in the dead body, and as the cases were not seen during life, this is the more probable. *Therewith* falls to the ground his statement that internal parasites cannot be the cause of beri-beri ; but otherwise the work is worthy of consideration.

Batavia, *February*, 1886.