ON THE LIFE HISTORY OF ASCARIS LUMBRICOIDES L. (A. SUILLA DUJ.) AND A. MYSTAX ZEDER. (A. MARGINATA R.)

by

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In this thesis I propose in the first place to describe certain experiments conducted by myself and to outline the results obtained from them, and thereafter to summarise the literature of the subject - both that preceding my work and that subsequent to it. In this order it will be possible to interpret the earlier experiments in the light of later knowledge.

I. Note on the Species of Ascaris under consideration.

Ascaris lumbricoides L., the round worm of man, is probably specifically identical with A. Suilla Duj. the round worm of the pig. No satisfactory morphological distinction has been found between them although the latter is on the average smaller than the former. This difference is probably due to the fact that the pig is not quite so favourable a host as man. In the same way A. mystax of the cat is probably identical with A. marginata of the dog.

In experimental work it is of course impossible or at least not desirable to use man as a subject. It may however be assumed that any facts discovered by experiments with A. Suilla on the pig would be equally true regarding the relations of A. lumbricoides to man.

II. Conditions required for the development of the eggs of A. lumbricoides.

Three conditions are required for the complete development of the eggs, - warmth, moisture, and the absence of putrefaction in the surrounding medium.

Warmth. A temperature between 80° and 90° F. is very suitable. I have not been able through lack of time to determine the upper and lower limits of temperature under which development will proceed.

Moisture. Eggs allowed to dry in an open vessel perish. The egg shell buckles inward and the ovum disintegrates. This is true even in a very moist climate such as that of South China where the humidity is often as high as 90%. The most favourable nidus is the surface of damp soil. Complete immersion in water is not so favourable even when the water is not deeper than ¼".

Experiment 1. Eggs of A. lumbricoides removed directly from the uterus and placed on the surface of moist clay soil - covered with a tin cover. Atmospheric temperature 80 - 90° F. Humidity about 90%. On the 10th day curved embryos had formed in practically all the eggs. On the 12th day fully formed active vermiform embryos.

Experiment 2. Eggs as above - placed in Petri dish covered with ¼" water. Temperature 80 - 90° F. On the 10th day a few eggs contained curved embryos, a considerable number had undergone no development - the remainder exhibited all stages between these two extremes.

Experiment 3. Eggs washed out of human faeces - placed in a closed vessel containing water, but above the water level. On 11th day eggs contain active vermiform embryos. Temperature 80 - 90° F. Atmosphere in closed vessel never evil-smelling.

Experiment 4. Portions of pigs' faeces (about ⅓" in diameter) containing Ascaris eggs placed on squares of cardboard on the ground and covered with perforated tins. Temperature 80 - 90° F. Humidity of atmosphere about 90%. On 7th day eggs in advanced segmentation (gastrula). On 9th day they contained curved vermicules. On 15th day - one specimen has become very wet from heavy rain, almost all the eggs are degenerated. Another specimen has remained only moderately damp, eggs contain vermiform embryos.

Absence/

Absence of marked putrefaction.

Experiment (3) above illustrates the process of development of the eggs when removed from a putrefying nidus and Exp. 4., this development in a nidus only slightly evil-smelling and freely exposed to the air: In a putrid nidus or a foul-smelling atmosphere development does not take place at all, or only to a slight degree.

Experiment 5. Eggs washed out of a 3 day old human stool - placed in a closed vessel containing water, but above the water level (as in Exp. 3). The atmosphere became foul. On the 11th day 1 - 2 - 4 cell stages and more advanced morulae. On the 12th day transferred to a non-foul atmosphere. On the 23rd day eggs contain vermiform embryos.

III. Hatching of the ripe eggs in the alimentary canal of the Rat, and the passage of some larvae directly in the faeces.

When eggs of Ascaris suilla or lumbricoides containing active embryos are given to the rat (Mus decumanus) they hatch in the alimentary canal and larvae are/

are to be found in the faeces from 6 - 22 hours after the feeding. The exact site of hatching in the alimentary canal has not yet been determined.

Experiment 6. At 2 p.m. on April 6th 1916, ripe eggs of A. lumbricoides were administered to four white rats. The faeces passed between 8 p.m. on the 6th and midday on 7th contained free Ascaris larvae which moved in a languid manner when placed in normal salt solution. Ripe eggs of A. Suilla were administered to the four rats on April 7th and 9th, and to rats A, B, and D on April 10th. Eggs of A. lumbricoides were given to rat C on April 10th. The faeces of all four continued to contain Ascaris larvae. Specimens of the faeces were preserved in an incubator between the temperatures of 25° and 30° C. Live larvae were found in these specimens after the lapse of three days.

(This is the experiment of Davaine - vide infra.)

IV. Entry of the larvae into the body of the Rat, Mouse, Pig and Man, and their migration as far as the trachea.

After hatching in the alimentary canal a large proportion of the larvae do not pass out in the faeces but enter the tissues of the host, penetrating the mucosa of the alimentary canal, probably work their way into the terminal venules of the mesenteric vein and then to pass by the mesenteric and portal veins to the interlobular veins of the liver. Larvae have been found in large numbers in the interlobar veins of the liver in Rats and Mice between the 2nd and 5th days after infection. The exact situation at which this penetration of the wall of the alimentary canal takes place and the exact course taken thereafter up to the interlobular veins remain to be worked out.

The larvae are arrested at these points where the interlobular veins divide into the hepatic capillaries since their diameter is greater than that of the capillaries. The hepatic cells in the immediate neighbourhood and along the blocked capillaries undergo fatty degeneration and the larvae are enabled to work their way through the dilated capillaries to the hepatic veins.

I/

I have with me at present notes of only three experiments - 2 rats and 1 mouse - in which the experimental animal was killed between the 2nd and 5th day after infection with A. lumbricoides. In all three, larvae were found in the interlobular veins and hepatic capillaries. Out of five mice, however, which were killed or died in the first three days after infection with Ascaris marginata, larvae were found in the liver in three. In one of the two unsuccessful experiments the eggs used were too young, in the other the dose was probably too small to ensure the recovery of larvae.

The following typical experiment may be detailed. It is of special interest as being the first case in which the migration was demonstrated.

Experiment 7. Rat C - had received ripe eggs of A. lumbricoides on April 6th 1916, eggs of A. suilla on 7th and 9th, and again of A. lumbricoides on 10th, and as noted above in Exp. 5, larvae were found in its faeces. On April 12th a further development of the experiment took place - Rat C died. I was prevented from examining this rat until April 15th and during the interval the body was fortunately preserved in an ice/

ice chest. On April 15th then it was examined. A small quantity of blood had escaped from its nostrols. No nematodes - larval or adult - were found in the stomach or intestines. The lungs were found to be congested. Portions were removed and teased out in normal salt solution. Numerous nematode larvae in active movement escaped from the tissue. The liver was also examined and a small number of larvae found. No larvae were found in the spleen or kidneys.
(For indication of this stage in man see Lutz's experiment

After leaving the liver in the hepatic vein the larvae are carried by the blood stream through the inferior vena cava, the right side of the heart and the pulmonary artery, and are lodged in the pulmonary capillaries. This point may be reached as early as the 4th day and larvae have been found in the lung of the mouse as late as the 15th day.

The larvae have been demonstrated by me in the lungs of the rat, the mouse and pig. I have at present with me notes of three positive experiments on rats, twelve on mice and three on pigs. Evidence as regards man is contributed by the experiments of Mosler and Lutz (vide infra) in which the subjects of experiment (2 or 3) developed fever and bronchitis several days after/

after the administration of the eggs.

I will quote a double experiment on the pig:-

Experiment 8. Sucking pigs Nos. 6 and 7 , on 20th Feb. 1917 at age of nine days were given very large doses of the eggs of A. suilla 43 days old. On 26th Feb., being the 6th day, both pigs were suffering from severe dyspnoea and cyanosis. On the night of 28th (8th day) both died. Ascaris larvae were present in enormous numbers in the lungs and trachea; 200 specimens were counted in a watch glass in which a fragment of trachea 1" long had been dipped.

In sections through infected lung A. larvae are found in the alveoli, bronchioles and bronchi. The alveoli are filled with red blood corpuscles, a fact which suggests that the larvae being impacted at the commencement of the pulmonary capillaries are liberated into the alveoli by the forcible rupture of the walls of the minute blood vessels. When the number of larvae is great - (over 20 - 30,000 in a young pig) the lungs become solidified from the haemorrhage and death results.

The/

The larvae reach the trachea about the 8th day and have been found in this situation as late as the 13th (in mice). They pass up the trachea and (in the great majority doubtless) into the oesophagus - it is occasionally possible to demonstrate a few larvae in the mouth of the mouse.

V. Migration through the alimentary canal in Mice.

Up to the point which we have now reached the fate of the larvae is identical in the rat, mouse, and pig, and there is reason to believe in man as well. Hereafter we will find a different fate in different hosts.

In rats I have not succeeded in tracing the larvae further than the trachea. In one which I examined on the 16th day no larvae were found in the stomach or intestines, in three others the faeces were examined carefully on the 9th, 10th, 11th, 12th and 13th days and no larvae were found.

In mice however the larvae begin to travel down the alimentary canal on the 9th day and may be found in small numbers in the stomach, small intestine and caecum. On the 10th day this stage is fully established, the larvae travel with some rapidity through the stomach and small intestine and accumulate in the caecum and upper colon where as many as 60 - 70 may occur./

occur. On this day they also commence to pass out in the faeces. The passage from the lungs to the caecum continues up to the 15th day and larvae occur in the faeces on the 16th day.

Experiment 9. Mouse L. received a moderate dose of eggs of A. suilla. Killed on 10th day. No Ascaris larvae in stomach, two in small intestine, 40 - 50 in the caecum, 20 in colon. These larvae are associated with a species of Oxyuris from which they can however be readily distinguished even under the dissecting microscope. Faeces passed on the previous day contained A. larvae. In eight consecutive faecal pellets the numbers of larvae counted were - 0, 3, 2, 1, 12, 0, 1, 6. The pellets were dry. The larvae did not exhibit movement, one half of them were slightly shrunken, the remaining half not shrunken.

VI. Anatomy and development of the larva of Ascaris lumbricoides during the migration described.

At this point it is necessary to consider the anatomy and development of the larvae in order to appreciate the difference in fate between those which have penetrated into rodents such as the mouse, and those/

those which have attacked the definitive hosts - man or the pig.

The embryo or the larva immediately after hatching measures .28 mm. in length, the oesophagus .087 mm. the proportion length of oesophagus to total length being $\frac{1}{3.3}$. The head is conical without distinct lips, the tail pointed and slightly curved towards the dorsum. The most conspicuous organs are the club-shaped oesophagus, the nerve ring and the ventral longitudinal line.

A larva from the liver of a mouse on the 6th day measures .735 mm. in length, .034 in maximum breadth, length of oesophagus .14 mm., relation of length of oesophagus to total length $\frac{1}{5.2}$. The ventral line is no longer so prominent, the lateral lines have increased in size, and the intestine has become obvious and pigmented. In sections the ventral gland can be distinguished as early as the second day lying between the left lateral line and the posterior quarter of the oesophagus.

Larva from lung of pig on 6th day. Total length 1 mm., maximum breadth .038 mm., oesophagus length .176 mm., oesophagus length /total length $\frac{1}{5.6}$. Lateral membranes extend from head to tail, only slightly chitinised. The muscular system more developed.

Larva/

Larva from the trachea of the mouse on 13th day - total length 2.10.

Larva from the caecum of the mouse on the 12th day - 2.02 mm., length of oesophagus .3 mm. length of oesophagus / total length = $\frac{1}{6.7}$. The head still without definite lips. The lateral membranes are more chitinised.

Larva from the faeces of the mouse. 13th day, - length 1.47 mm., oesophagus .2 mm., length of oesophagus / total length $\frac{1}{7.3}$. Body slightly shrivelled, as a rule are immobile or execute only very feeble and slow movements.

It will be seen that in the course of its wanderings from the intestine, through the liver and lung back to the intestine, the larva increases in length nearly tenfold. It develops the organs necessary for an active swimming existence - the muscular fields and the lateral membranes. On passing from the trachea to the alimentary tract a firm membranous cuticle is formed. Permanent lips are not found in any of these young forms although in the living animal three small retractile protrusions can be distinguished, corresponding with the three lips of the adult.

VII./

VII. Migration into and through the alimentary canal of the pig.

In Section IV the larvae have been followed in their course through the body of the pig as far as the trachea, which they reach about the 8th day. Our knowledge of the further development in this host rests on only two satisfactory positive experiments by myself, which prove that the larvae enter the alimentary tract from the trachea, may be voided on the 11th day and may continue to inhabit the intestine (undergoing an ecdysis and further development) up to the 14th day, if not later.

Experiment 10. Pig No.11, on 28th February 1917, at the age of 2½ months, was given a large dose of Ascaris eggs 3 months old. On the 9 - 10th March it was suffering from marked dyspnoea and cyanosis; its temperature rose to 105°F. (normal 102.5°F). On 11th March it had recovered. On this day two dead and partially macerated larvae were found in a small portion of its faeces.

Experiment 11. To a sucking pig, aged 4 days, about 22,000 ripe eggs of A. suilla were given. The eggs were

31 days old and contained active embryos. On the 8th day after treatment the pig showed signs of pneumonia, it was breathing at the rate of 140 per minute. It was killed on the 14th day. No Ascaris larvae were found in the trachea or in a fragment of the lung which was examined. Numerous larvae were however found in the small intestine, caecum and rectum. Measurement of specimens fresh in salt solution as follows:-

From Small intestine	2.5, 2.72, 3.04, 3.20, 3.80 mm.
" caecum	2.96, 3.04 mm.
" rectum	2.4, 2.48, 2.9 mm.

Anatomy of these larvae:-

General outline cylindrical, tapering slightly to the head, more markedly to the sharp tail which is slightly curved to the dorsum at the tip. The head bears three lips as in the adult. The dorsal lip is furnished with two papillae, the sub-ventral with one each. The inner surface of each lip is lined by thickened cuticle which is grooved longitudinally. The cuticle of the body surface is marked by a series of rings .004 mm. in breadth. In sections stained with iron haematoxylin it is not very deeply stained and is consequently not markedly cuticularised. Each lateral line bears a lateral membrane extending nearly from the head to the tail and supported by a firm/

firm triradiate cuticular skeleton, the basal plates of which are embedded somewhat deeply in the lateral lines. The muscular system shows a marked advance as compared with the larvae from the trachea of the mouse. The rudiment of the gonads is situated just behind the middle of the body length; it consists of two rudimentary tubes leading backward to a rudimentary external opening in the ventral line.

VIII. Negative and doubtful experiments on the infection of the intestine of pigs from the eggs of A. suilla.

The experiments detailed in Sect. VI taken in conjunction with the number of successful experiments on the infection of the lungs of pigs, would appear almost as satisfactory proof that the normal life history of the worm is completed in one host, the larvae migrating from the intestine through the blood stream, liver, lungs and trachea again into the intestine where they become adult. There are however certain negative experiments directed to find more advanced (over 14 days) or adult worms in the intestines of the pig after administration of eggs which have proved negative and are opposed to this view. It is highly probable that the negative results are due merely to accident or to defective technique. It is however necessary to examine/

examine them carefully.

Eight such negative or doubtful experiments on pigs have been carried out by myself. In three of these (a. b. c.) the pigs undoubtedly suffered from Ascaris pneumonia - proving that the larvae had reached the lungs. In one there was also some evidence of this condition (d). The culture used on three of the remaining four was proved active on mice (e. f. and g.), while in the last case four different cultures were employed, the eggs in each containing active embryos (h.)

Results.- In six (a.c.e.f.g.h.) of these eight animals no worms were found in the intestine on section (with the exception of (c) in which one small Ascaris was found which was certainly not connected with the experiment performed several months previously). In one (b) although a large number of worms were found it is probable that they did not originate in the experiment. In one (d) a number of worms were found which may have originated in the experiment but which may also have originated in accidental infection. Comparing the measurements of the worms in (b) and (d) and the period which elapsed between the administration of the eggs and the finding of the worms, it is not possible that the worms in both (b) and (d) originated in the eggs given. (Exps. 12 & 13 infra.)

Out/

Out of the eight experiments therefore seven are negative and one only possibly positive. Of the pigs used 25% were constantly found to be suffering from natural Ascaris infection.

Experiment 12. A sucking pig (a) aged 4 days, in the same farrow as Exp. 10 received 22.000 ripe eggs of A. suilla from the same culture as Exp. 10. On the 8th day it was also suffering from pneumonia - proving the presence of Ascaris larvae in the lungs. It was killed on the 19th day. Stomach and intestines were carefully examined but no worms were found. The pig had not suffered from diarrhoea.

Experiment 13. Pig (b) age 2½ months, which proved to already contain adult Ascaris (same as in Exp. 9) given large dose of 3 months culture. On the 9th day was suffering from pneumonia and passed two dead Ascaris larvae on the 11th day. Was killed on the 20th day . 38 ♀ and 19 ♂ Ascaris were found in the intestine. The females measured from 105 to 250 mm., the males from 65 to 160 mm.

Experiment 14. Pig (d) 2½ months old, given dose of ripe eggs. On the 7th day it was slightly dyspnoeic and its/

its temperature was half a degree above normal. Killed on the 30th day. 22 Ascaris found in the intestine measuring 20 - 70 mm.

IX. On the possibility that an intermediate host is necessary.

Influenced by two failures to find adult worms in the pig after the administration of active eggs and by the recorded negative experiments of Leuckart (vide infra), I in 1916 suggested the possibility that rats and mice acted as intermediate hosts - infection being carried by the larvae in the saliva or faeces of the rodents. At this time I had not worked out the pulmonary infection in pigs and two experiments on guinea pigs and one on a dog had not produced pulmonary infection in these animals. It seemed at the time, therefore, that pulmonary infection was confined to rats and mice.

It is true that the shrivelled appearance and lack of obvious life of the larvae passed in the faeces of mice do not suggest that they would be capable of coming to life again if swallowed by the definitive host. On the other hand the example of Tylenchus tritici should be recalled, in which the larvae after being so dried that they are blown about as/

as dust, are still capable of further life when placed under suitable conditions.

I performed two experiments on the infection of pigs from the larvae in the intestine of mice.

Experiment 15. Sucking pig 4 weeks old. - faeces examined - no Ascaris eggs found. The caeca of four mice on the 10th day after infection were given to the pig. On the 14th day it was killed. 12 Ascaris were found in the intestine - 2 large - 124 and 183 mm., and 10 smaller worms - 47 - 73 mm.

Experiment 16. A similar experiment with negative result.

X. Development and life history of Ascaris mystax, Zeder (A. marginata, R.)

Cultures of the eggs of the round-worm of the cat (A. mystax) or dog (A. marginata) in a closed vessel containing water at a temperature, 25 - 30° C., the development was markedly more rapid than in A. lumbricoides.

1st day	three cell stages.
2nd day	Gastrula.
4th and 5th days	Curved vermicules.

7th/

7th day. Plump vermiform embryos.

8th day. Active embryos.

When ripe eggs are administered to mice the larvae have been traced as far as the liver. Owing to difficulties in obtaining large numbers of worms my experiments numbered five only.- 3 positive, 2 negative.

Experiment 17. Mouse P. given eggs of A. marginata 11 days old, died 20 hours after infection. Eight larvae found in a portion of the liver, none in the lungs.

In one of the two negative experiments the eggs used were too young - only six days old, in the other the dose of eggs given was too small.

The life history of this species also remains therefore to be completed.

XI. Recent experiments by Messrs Ransom and Foster, United States Dept. of Agriculture.

Following the publication of my work in 1916 and 17 ("Parasitology" IX. p.155. Feb. 1917. Brit. Med. Journ. July 1st, Oct. 7th, Dec. 2nd 1916, and Ind. Med. Gaz. Aug. 1917) Messrs Ransom and Foster took/

took up the investigation on similar lines. Their results have been published so far as a "Preliminary Note" in the Journal of Agricultural Research. (U.S.A.) Nov. 19th, 1917, and in the "Journal of Parasitology" March 1919.

They repeated my experiments on the feeding of rats and mice with ripe Ascaris eggs and obtained results agreeing very closely with mine: They made further attempts with negative results to infect pigs, but suggest that the failure may have been due to the use of pigs several months old which may have passed the age of susceptibility. They also obtained the pulmonary infection in a pig of two weeks old. They state that they have found the same phenomena in guinea pigs and rabbits as in rats and mice, i.e. migration and elimination of the larvae. A lamb aged two days was given ripe eggs of A. suilla and was killed 103 days thereafter, - 50 Ascaris were found, 60 - 130 mm. in length. A goat received doses on its fourth day of life and on its 21st day. Seven days after the second dose it showed signs of pneumonia and died three days later. In the intestine were thousands of young Ascaris measuring about 10 mm. in length "traceable to the first feeding 27 days previous". The lungs and trachea contained numerous larvae /

larvae 1 - 2 mm., traceable to the second feeding 10 days previous.

It is somewhat remarkable that with all the resources at their disposal two such distinguished helminthologists have as yet failed definitely to prove direct infection in the pig.

They believe however that direct infection does occur and that hosts can be grouped in three classes according to their susceptibility to Ascaris lumbricoides. Lowest - Rats, mice, rabbits, guinea pigs. Intermediate - Sheep and goats. Highest - Pigs and man.

XII. Literature previous to 1916.

Davaine - Summary in Leuckart. Parasiten des Menschen . Journ. de Phys. 1859. p. 295. Mem. de la Soc. Biol. T.4. 1863. p.261., found that if ripe eggs of A. lumbricoides are administered to rats, free larvae are to be found after 12 hours in the lower part of the intestine. Also that if ripe and unripe eggs are introduced in glass capsules closed with linen, into the intestine of a dog, the ripe eggs disappeared, the unripe remained. He concluded that hatching and development occurred in the gut of the definitive host.

Grassi - /

Grassi - Centralb. f. Bakt. 1888. p. 612 - reared puppies in a box containing ripe eggs of Ascaris marginata. The puppies became heavily infected. He regarded this as indicating direct infection since the only other animals present - free living nematodes and fly larvae - were excluded as intermediate hosts. It is certainly unlikely that rodents would frequent such a box.

Calandruccio - Centralb. f. Bakt. Vol.I. p.133 - recorded by Grassi. Calandruccio experimented on himself with Ascaris eggs without result. To a boy of 7 years who had been cured of a previous infection 150 Ascaris eggs given in a pill. He remained under observation for 20 days without result. After two months many Ascaris eggs were found in his stool and he evacuated 143 worms. In criticising this experiment it should be noted that accidental infection was not excluded.

Lutz - Centralb. Bakt. 1888. p.425 - in Brazil administered to a woman aged 32, who is stated not to have been exposed to infection, repeated doses of about 12 eggs at a time, of which about one half were ripe. These doses were given on 4th, 5th, 6th,7th, 19th, 23rd, 25th and 27th January. In the first few days the patient suffered from dyspepsia acida, followed by unusually severe bronchitis with slight remittent/

remittent fever. Thereafter symptoms of catarrh of the bowel became more and more prominent. On 1st Feb. after an anthelmintic she passed 35 worms - 5.5 - 13 mm. in length.

This experiment is of course as definite and positive as a single experiment can be, and is also of very great value as showing that the course of migration of the larvae is the same in man as in the pig.

It must be noted however that in tropical South America the proportion of infection in the population is very high - reaching in places 80%. Accidental infection cannot therefore be completely excluded.

Epstein - (Summary by Wharton. Indian Med. Gaz. Feb. 1918. p. 74). Three children who were known to be free from infection were given eggs containing living embryos on January 28th. Two children remained under continuous observation. No eggs were demonstrated up to 12th April inclusive. On 24th April, however, great numbers of eggs were found in the faeces of both children. After Santonin one child expelled 22 worms and the other 72.

The length of time elapsing between the administration of the eggs and the appearance of eggs in the faeces - more than 2½ months - is somewhat remarkable.

The above experiments have given results claimed to be positive for the theory of direct infection. The following are negative.-

Mosler - (Summary Leuckart. Menschl. Parasit. II. pt.1. p.222 - fr. original paper Arch. Path. Anat. XVIII. 249). After a preliminary and negative experiment on himself, administered ripe eggs of A. lumbricoides to a number of children. No worms were at any time evacuated after anthelminthic treatment, but in one (or two) children fever with dyspnoea occurred a few days after the administration of the eggs.

Leuckart adds that it is of course doubtful whether the fever was due to the experiment. The observation is of great interest as confirming pulmonary infection in man (Compare Lutz. supr.).

Davaine made a negative experiment on the ox.

Leuckart (Mensch. Parasit. p.207. 1867) experimented on the rabbit, dog and pig with A. lumbricoides - results negative.. On the horse with A. megalocephala, on the dog with A. marginata, on the cat with A. mystax - results again negative. It is possible that he did not allow a sufficient length of time to elapse after the administration of the eggs as he was/

was of course ignorant of the migration of the larvae. He believed that development would be found to include an intermediate host and supported this view by observations on the encysted Ascarids of fishes and of the mole.

Von Linstow suggested that Julus Guttulatus might prove to be the intermediate host. (Zool. Anz. 1886. p. 525).

SUMMARY.

The following new facts have emerged from the investigation described.

The larvae of Ascaris lumbricoides after the hatching of the eggs in the intestine of man, the pig, rat and mouse, bore their way into the portal circulation and passing through the liver, right side of the heart and lungs, reach the trachea. In mice and pigs and probably also in man they then again descend the alimentary canal. In the pig they have been followed only up to the 14th day at which date they are still to be found in the intestine, have undergone at least one ecdysis and have reached a stage of development after which probably only one further ecdysis is required before the assumption of the adult form. In mice, on the other hand, they pass out as 2 mm. larvae in the faeces.

That the development to the adult in the intestine of the pig has not yet been completely worked out is possibly due to errors in technique. It is however also possible that some further stage of migration intervenes between the 14th day larva in the intestine of the pig and the adult in the same situation and also that the larvae passed in the faeces of mice may be capable of carrying on the infection.

A D D E N D U M.

A. Toxins produced by Ascaris.

Torai Shimamura and Hajime Fujii have isolated a highly toxic albumose peptone from the perivisceral fluid and the dried powder of Ascaris lumbricoides and A. megalocephala. (Askaron). It produces symptoms like those associated with Ascaris infection. (Journ. College Agric. Univ. Tokyo. 1917. 3. p. 189. Summary Journ. Micro. Soc. 1918. p. 383).

Benjamin Schwartz finds that the body fluid of A. lumbricoides is not haemolytic to the erythrocytes of mammals when taken from worms shortly after removal from the host. At this time the body fluid contains oxyhaemoglobin. After the worms have been kept in vitro for some days the perivisceral fluid is haemolytic - it has also lost its oxyhaemoglobin. Extracts in salt solution of fresh or dried bodies of the worms are haemolytic. The addition of blood serum inhibits this haemolysis. Salt solution in which worms have been kept is not haemolytic. Schwartz considers this latter fact to be opposed to the hypothesis that the anaemia of Ascariasis is due to the absorption of a toxin. He quotes Schimmelpfennig and Friedberger and Fröhner who assert that Ascaris sucks/

sucks blood, - the presence of oxyhaemoglobin in the perivisceral fluid is in favour of this opinion. (Journ. Agricult. Research. XVI. p. 253.)

B. Epidemiological and Clinical facts concerning Ascariasis in man.

I. Distribution and frequency.

Ascaris is cosmopolitan.

Europe. It is common among children of the country districts of continental Europe. Leuckart (Parasit. des Menschen. 1867) states that it is present in 56% of children in rural Germany. Epstein (Jahrbb. f. Kinderheilk. 1892. p.3) gives a similar figure for Bohemia. In towns however only about 5% of children are affected (Zürich and Prague).

Asia. It is extraordinarily common in the Near East. A leading Armenian physician of Aintab, Cilicia, told me that in normal times 50 - 60% of the population was affected, and that at present owing to the hardships the people have undergone - deportations, destruction of their dwellings, etc., etc., the degree of infection at least in the young is over 80%.

In/

In Mesopotamia it is also frequent.

In India it is extremely common - though no definite figures are available. Of 2,000 Indian troops examined recently in Cairo, 138 - 6.9% were infected with Ascaris.

China. Hong-kong - in a mixed series of Europeans, Chinese and Japanese examined, 40% were infected with Ascaris (Bell, Hcng-kong. Med. Congress 1913). Shanghai - out of 180 Europeans 6.7% affected (Fischer. Arch. Schiff. and Tropenhyg. 1914. p. 615). Setchuan - West China - of 500 adult Chinese 86.6% had Ascaris, 14.2% Ankylostomum.

Annam. - Of 449 persons (300 sick, 149 healthy) 271 carried Ascaris, 170 Ankylostomum. (Bernard and Koun. Bull. Soc. Path. Exot. 6. 1913. p. 343).

Phillipines - Out of 7843 adult prisoners examined on admission to Bilibid prison, Manilla, Ascaris present in 41%. (Willets. Philip. Journ. Sci. B. IX. 1915. p. 231.) Among 100 Philipino soldiers 52 were infected (Tenney, Boston Med. and Surg. Journ.) In 500 autopsies in Manilla, 41.2% subjects contained Ascaris.

Africa.

Oran - Arab tribe - 90% infected with various worms - Ascaris the most common. (Foley, Bull. Soc. Path. Exot. IV. 1911. p.421). Ivory Coast - only 1.5% (Sorel. Bull. Soc. Path. Ex. 1911. p.117).

Togoland/

Togoland - about 79% Ascaris (Rodenwaldt. Arch. Schiff. and Tropenhyg. 1910).

In Egypt it is very prevalent - figures not available.

Gr. Comora Islands - 92% Ascaris (Lamoureau, Bull. Soc. Path. Exot. 1913. p.455). Madagascar 10%. (ibid). South Africa - among natives 19.8% harboured Ascaris. (Turner, Journ. Trop. Med. and Hyg. XIII, 1910.)

America.

In the West Indies over 80% of the native population are affected (Macdonald - B.M.J. 1916). Panama - in 195 Negroes - Ascaris present in 10%. (Whipple, Americ. Journ. Med. Sci. 1909.).

It appears to be frequent among School children in the United States (Stiles, Public Health Reports 1915. p. 2990.)

II. Clinical Effects on the Individual.

During the years 1914-1916 I was in charge of the Indian Garrison of Hong-Kong, of whom about 40% were commonly infected with Ascaris. After some experience I found it not difficult to pick out those affected, by their sickly, slightly anaemic and slightly icteric appearance. The usual complaint was salivation, dyspepsia, weakness in the legs.

Occasionally/

Occasionally the symptoms are more marked. The following are a few illustrative cases.-

(1) V. V., an Englishwoman, age 19, Nursemaid in Hong-Kong. Complaint - giddiness, breathlessness on exertion, palpitation, severe pain during menstruation. Very markedly anaemic. Examination of stool - numerous Ascaris ova, no Ankylostome ova. Treated with Santonin, expelled 6 Ascaris. No return of dysmenorrhoea. Other symptoms disappeared in a month. About a year later the same symptoms returned - found to be again infected with Ascaris - no Ankylostomes. Again cured by Santonin.

(2) M. P., an Indian Transport Driver. Admitted to hospital in Cairo. Temperature swinging to 104°. Severe persistent vomiting. Blood examined - no Malaria parasites. After two days vomited an Ascaris. Treated with Santonin - passed a considerable number of worms, with complete relief of symptoms.

(3) J. S., a Jemadar of Imperial Service troope. Admitted to hospital in Cairo, complaining of slight fever and extreme prostration - during three weeks. On admission patient was in a typhoid condition, lips covered with sordes. Some Vincent's Angina in mouth, marked emaciation, no malaria parasites found in the blood on repeated examination, spleen slightly enlarged./

larged. Faeces contained eggs of Ascaris. After Santonin - evacuated 4 - 5 worms. Four days later slightly better but eggs still present. Santonin repeated, several more worms evacuated - patient was walking about a week afterwards and returned to duty.

(4) N. B., trooper in an Indian Cavalry regiment; admitted to hospital complaining of general weakness and of pains in his legs. Somewhat anaemic. Muscles of legs and arms small and flabby. Tenderness all over the legs - not confined to the calves. Knee jerks absent. Gave a doubtful history of specific disease. Ascaris ova in stool. Treated with Santonin. A number of worms expelled. On the same day his temperature rose to 102°. Patient improved slowly; discharged to duty in 14 days; his knee jerks were beginning to return and he stated that he was quite well.

The above four examples have of course not been completely worked out, and a large number of carefully checked observations would obviously be required to establish the importance of the disease or to refute such an hypothesis. I quote them merely as examples to show the impression left in my mind from the large mass of clinical material with which I have had to deal in the last five years.

Schwartz/

Schwartz in the paper quoted above writes - "That Ascaris may cause anaemia is the opinion of various observers. According to Schimmelpfennig (Über A. megalocephala. Inaugural Dissert. Berlin 1902) and Weinberg and Julien (Hyg. Viaud. et Lait 1913. p. 225) the post-mortem appearance of horses infected with Ascaris suggests a condition of anaemia. As far as man is concerned, a number of clinicians have emphasized the importance of A. lumbricoides in relation to anaemia. Thus Demme (Med. Ber. Thatigk. Jennersche Knidersp. Bern. 1891) reports two cases of grave anaemia in children, resembling pernicious anaemia which he attributed entirely to the presence of A. lumbricoides in the intestine. In one case death occurred, the cause of the disease not having been recognised; whereas in the second case complete recovery followed anthalminthic treatment. Francois (Anaemie des Mineurs. Paris 1906) cites a number of cases of grave anaemia resembling that of ankylostomiasis, in which A. lumbricoides was evidently the causal factor. Guiart (in Bouchard & Roger, Nouv. Traite. de Path. Gen. Paris 1914. p.839) considers Ascaris to be a causal agent in anaemia ranking close to Dibothriocephalus and Ankylostoma in importance". (Journ. Agricult. Research. XVI. March 3. 1919, p.253.)

A/

A very thorough investigation of the results of Ascaris infection appears called for from the following reasons.-

(1) The very extensive prevalence of the infection.

(2) That even if it does not occasion dramatic or acute illness, it produces at least a lowering of vitality and of working capacity in a very large proportion of the entire human race.

(3) That the prevalence of such parasites in native populations who live habitually on the border line of starvation (and especially of vitamine starvation) may turn the scale between comparative health and nutritional disease such as beri-beri and pellagra.

It is probable that Ascaris infection will prove to be the third great problem of Medical Zoology comparable only with Malaria and Ankylostomiasis.

B I B L I O G R A P H Y.

1. Calandruccio. Centralbl. Bakt. vol.I. p.131. 1886, reported by Grassi.

2. Davaine. Rech. sur le dev. et le propag. du Trichoceph. et de l'Ascaride. Journ. de phys. 1859. p.295. (Summary - Leuckart - 4).

3. " Nouv. Rech. C. R. Soc. Biol. Paris. 4. p.261. 1863. (Summary Leuckart - 4).

4. Epstein. Jahrbb. f. Kinderheilk. 1892. p.3.

5. Grassi. Centrbl. Bakt. 1887. p. 131.

6. " " " 1888. p. 748.

7. Jammes et Martin. C.R. Ac. Sci. 1896. p. 67.

8. " " " " " " " " 189.

9. " " " C.R. Soc. Biol. 1906. p.719.

10. " " " " " " 1907. p.15.

11. " " " " " " " p.137.

12. " " " " " " 1908. p.208.

13. Leuckart. Menschliche Parasiten. Vol. II. Part. 1. 1867.

14. V. Linstow. Zool. Anz. 1886. p. 525.

15. Lutz. Centrbl. Bakt. 1887. p. 713.

16. " " " 1888. p. 425.

17. Martin. Ann. Sci. Nat. (Zool.) 1913. p.1.

18. Mosler. Arch. Path. Anat. 1860. p. 249. (Summary in Leuckart - 4).

19. Ransom & Foster. Journ. Agric. Research. 1917. 11. p. 395.

20. " " Journ. of Parasitology. March, 1919. p. 93.

21. Schwartz. Journ. Agric. Research. March 1919, p. 253.

22. Shimamura & Fujii. Journ. Cell. Agric. Univ. Tokyo. 1917. p.189. (Summary. Journ. Micr. Soc. 1918. p. 383.)

23. Stewart. Brit. Med. Journ. 1916. Vol.2. p.5.

24. " " " " " " p.474.

25. " " " " " " p.486.

26. " " " " " " p.753.

27. " Indian Med. Gazette. Aug.1917. p.272.

28. " Parasitology. (Cambridge) 1917, Vol. IX. p. 213.

29. Stewart. Parasitology. (Cambridge) 1918. X. p. 189.

30. " " " 1918. X. p. 197.

Critical and Controversial.

1. Lane, Clayton. Indian Med. Gaz. Aug. 1917. p.269.

2. " " " " " " " p.301.

3. " " " " " Oct. " p.380.

4. Low. Brit. Med. Journ. 9th March, 1918. p. 286.

5. Pantin. " " " 14th Sept. 1918. p. 287.

6. Stewart. Ind. Med. Gaz. Oct.1917. p.379.

7. Brit. Med. Journ. Editorial. 1st July, 1917.

8. " " " " 2nd March, 1918.