.616962 M.D. 1909.

There are few diseases the parasite of which is known by so many names as is the case in Dracontiasis but the following four names may I think be taken as the commonest & best known viz: -

- (i) Filaria Dracunculus
- (ii) Guinea Worm
- (iii) Medina Worm
- (iv) Farentit

The name Frentit, although rarely seen mentioned in text books, is the only name by which this disease is known all over the Anglo-Egyptian Sudan, & it is primarily in connection with this country that this Thesis is written.

On looking into the history of this disease, there is no doubt that a knowledge of the Filaria dracunculus extends back to quite remote times.

Plutarch in connection with a communication made by Agatharchides of Knidos, a tutor of Ptelemaeus Alexander (about 150 B.C.), relates that the people by the Red Sea suffered from a severe dissease, in which small snakes ( Seakov Tia MIKEX ) came out of the skin and gnawed arms & legs & when touched (on their appearance out of the skin) drew back again and caused the patients insufferable pain.

The Greeks called the worm & PKKOVTIOV, & it was from this that the Roman Doctors originated the word Dracunculus.

A knowledge of this worm is stated to date back to 1550 B.C. for Yoachim is of the opinion that the "Sepworm" mentioned in the Papyrus Ebers refers to the Filaria dracuculus, (Die Heilkunde der alten Aegypter nach dem Papyrus Ebers. Verch. des Xi intern. Med. Konge Berlin 1890 vol. V.,16 abt p. 40.) while Barthelin & Küchemmenster believe that the "fiery serpents" with which the Lord afficted the children of Israel during their stay near the Red Sea in the fortieth year of their Exodus were the Filaria dracumculus.

Book of Numbers ch XXI V. 6, " and the Lord sent fiery serpents among the people & they bit the people; & much people of Israel died".

Etiology of Dracontiasis, namely that the disease was due not to an actual worm but to a disease of the veins similar to varices, & it is worthy of note that this opinion prevailed amongst medical men until the commencement of the nineteenth century in spite of the fact that many doctors and naturalists of the seventeenth & sixteenth centuries such as Welsch, Kämpfer, Lind, Gallandat etc, had confirmed the parasitical nature of the diasease.

As regards the distribution of this disease, it is almost entirely limited to the tropics.

Although Dracontiasis is sometimes seen in Europe this is only in natives of, or recent visitors from the endemic area.

The disease is very markedly endemic in the mest coast of Africa. On the slave coast according to Sicil-

iano almost half the population are said to be inflicted with the parasite.

Dracontiasis is also found in certain parts of India, in Persia, Turkestan, Arabia & in a very limited part of Brazil (Feira de Santa anna) (Manson).

In the Indian Archipelago according to Scheube, it is only found in African soldiers & in Eurpeans who had resided for a time on the west coast of Africa.

The Filaria Dracuculus has been reported as occasionally occuring in the lower animals such as ox, horse, dog, leopard, jackal, canis lupaster etc but as I have never been able to confirm this even in districts markedly infected with disease, an inclined to agreed with Manson who says that "Possibly some of the parasites in the lower animals described as Guinea worm may belong to quite a different species."

Sporadic cases of Dracontiasis have been reported from Uni the United States, one in particular worthy of note being reported by Von Harlingen, a man aged forty seven who had never been out of Philadelphia & in view of this Osler holds that the Filaria dracunculus must be included among the parasites of that country.

It seems probable that this disease has been carried to the United States by negroes from the west coast of Africa, for since the importation of negroes has ceased the number of cases of Dracontias-is in the United States has become considerably less.

A point of some interest in the distribution of Dracontiasis is its tendency to be confined in narrowly

circumscribed districts.

The disease is endemic in the Sudan in Darfur, Kor-defan Bahr El Ghazal, Nubia & in some of the Arab villages on the borders of Abyssinia.

In the Bahr El Ghazal Province where I saw the great majority of my cases the disease seemes to be limited to a very large extent to the town of Wau.

A very large number of cases occur among the native population in Omdurman.

In lower Egypt the cases observed are imported from the Sudan.

It is worthy of note that while no case of Dracontiasis originating in Europe has been reported, Cholodk -awski has brought to notice (Wratsch, 1896, N°3:Ref. Chl. F. Chir., 1896, N° 21), that there exists a still unclassified Filaria in the Russian district of Twer which causes ulcerations on the hands & fingures with occasio -nally extensive inflammations & gangrene of single pha--langes.

It is stated that this worm is several inches long & is found on incising the ulcer.

It would be a point of some interest if the nature of this worm & its relation to the Filaria Dracunculus could be determined but up to the present date so far as I know no further work has as yet been done towards set -tling this question.

Etiology. While at Wau in the Bahr El Ghazal Province Southern Sudan during the summer of 1907 I had the opportunity of making a few observations on the much debated question of the Etiology of Dracontiasis, & in many my opinion there can be no doubt whatever in the view that this disease is acquired by drinking polluted water, i.e. water which contains the Cyclops quadricoruis & which acts as an intermediate host of the parasite.

The other view is that the worms in the form of :-

- (a) The Embryoas discharged from the parent worm; or
- (b) The mature larva evolved from the Embryo in water marshy soil; or
- (c) The young adult, the product of the continual growth of the larva in water enter the human body by penerating through the sweat glands into the subcutaneous cellular tissue while the person is standing or bathing in the infected water, has been founded on the fact that the disease in by far the majority of cases attacks the lower extremities. It is curious to note that in districts which are largely infected with this disease & in which the natives are themselves well acquainted with its treatment & effects that this theory is very firmly adhered to.

N.B. That the Nubas of Kordofan believe that infection takes place by way of skin is shown by the fact that they wear wooden pattens when crossing wet or marshy places, whence as experience has taught them infection may be derived.

In opposition to the opinion that infection takes place by direct invasion of the worms through the skin of the lower extremities, Scheube mentions in his work how that Ewart contends with justice that many other parasites, concerning which there is not the slightest doubt but, the channel of the introductioninto the human body is by means of the digestive tract), undertake extensive journeys in the human organism & that each parasite has its seat by predilection in certain organs and tissues far removed from the place of incorporation, such as the Echinococcus in the liver, the Cysticercus in the connective tissue, the Trichina spiralis in the muscles etc.

Manson has pointed out that from his studies of the Life History of the Filaria Dracunculus, & especially from his observations regarding the expulsion of the Embryos through the mouth of the female by means of the prolapsed uterns on douching the neighbourhood of the ulcer with a stream of cold water, (an observation which although I have tried many times I have not altogether been able to confirm), that the reason why the female parasite on attaining maturity in the great majority of cases makes for the legs & feets, is that these are the parts of the human body most likely in tropical countries to come in contact with water which not only aids the expulsion of the Embryos but also contains the Cyclops quadricornis their intermediate host.

In connection with Manson's theory for the cause of the seat predilection of the Filaria Dracunculus

being in the majority of instances in the lower extremities, it is interesting to note that Harrington has in India observed the disease on the backs & loins of water carriers where the water-skin has come in contact with the body & which have consequently been continually wet.

With a view to satisfying myself during the summer of 1907 when I was working at Wau in the Bahr El Ghazal as to the occuracy or otherwise of this viewI carried out a carefully conducted experiment on a monkey by placing a few drops of water containing large numbers of fresh Embryos on a shaved portion of the back of the monkey which had been previously anaesthetised. After half an hour by which time the water had evaporated,

I removed a small portion of the skin with which the infected water had been in contact& after preparing it according to the method as given in the Appendix of this thesis, I stained the sections cut from it for 12 hours in a watery solution of Delafields Haemotoxylin, counter-staining in a watery solution of Eosin, but was quite unable to find any trace of a single Embryofrom which I am quite convinced as to the impossibility of the Embryos entering the body by penetrating through the sweat glands into the subsutaneous cellular tissue.

## The Parasite.

Until quite lately the male worm had only been observed once, viz: by Charles who while dissecting a body in Lahore, discovered two female Filaria Dracunculia in the subperitoneal tissue to each of which a smaller worm about 4 c.m. in length was attacked with its posterior

end at a spot about 14 c.m. distant from the head end of the female, & Braun states that it may therefore be concluded that the male as in Syngamus Trachéalis was seated on the vulva of the female & that it dies off after coition, while the vulva becomes atrophied.

Leiper however, who has done much valuable work on this subject, in describing the results of a post mosten examination he made on a monkey which had 6 months previously been fed on bananas containing Cyclops which had in them mature larvae of the Filaria Dracunculus, (Leiper Jan. 19th. 1907 British Med. Journal p 129 Vol. I), states that he found two remarkably small males (22 m.m.) which were obtained one from the Psoas muscle, and the other from from the connective tissue bhind the oesophagus, at is remarkable that in spite of the fact that the knowledge of this disease extends back to the distant ages that theseare the only two occasions in which the male worm is known to have been seen.

The female is the important worm as it is this which causes the disease, and I am very strongly of the opinion that the great amount of physical infirmity due to this Filaria is not fully appreciated.

A description of the female worm is unnecessary as I have always found it to agree exactly with the accounts as may be found in any of the modern Text books on Tropical Medicine.

In length it averages from 60 to 80 c.m. but far larger mask specimens have been described more than 6 feet in length but I would point out however that owing

to the elasticity of the cuticle of the fresh worm it impossible to obtain any exact measurement & I have frequently found that it is possible to stretch the worm to at least half as much again of its ariginal length.

Although as has already been mentioned the commonest place for the Filaria Dracunculus to appear is on the lower extremities, there is no part of the body on which it may not be seen.

I have seen several cases of Dracontiasis occurring on the hands and arms & not an uncommon site especially among the Sudanese is the external genitals, the worm appearing on either the Penis or Scrotum.

I know of one British Medical Officer who suffered from this disease & in whose case an adult female Fularia Dracunculus was removed from under the fore-skin.

An Egyptian doctor told me that once while making a post martem examinations at Wau he discovered a female worm of some considerable length embedded in the muscle of the heart.

It is unusual in cases of Dracontiasis to find the patient affected with more than two worms .

In one case however, an Arab who came under my care in Kassala Civil Hospital during the summer of 1908 I found no fewer than eleven adult female worms all of which were successfully removed.

Two from the back of the left hand and nine from the lower extremities, two appearing just above the left knee, one on the external aspect of the leg just be low the left knee joint the remainder around both ankles.

and on the dorsum of the feet.

The Embryo. It has been computed that the uterus of the female Filaria is capable of containing some eight to ten million Embryos and on examination I found their length to vary from 580 -  $656 \,\mu$ .

As these Emryos are immediately killed if dried it is essential that they should be discharged into water very soon after the parent worm appears on the surface of the skin.

I found that I could very rarely obtain living Embryos from the parent worm 24 hours after it had succeeded in creating a break in the ower-lying skin espectially if the wound had become septic.

The Embryos of the Filaria Draeunculus are distinctly flat in shape & have long awl-shaped tails which are not quite sharp pointed.

While working in the Wellcombe Research floating
Laboratory of the Gordon College Khartoum, Dr. Wenyon of
of London School of Tropical Medicine kindly showed me
his method of staining the Embryos with a watery solution Delafields Haemotoxylin the exact process of which
is given in the appendix of this Thesis, & by means of
which the internal structure of the Embryo can be made
very clear.

I attach a sketch I made from one of these Embryos which had been stained according to this method, which clearly demonstrates the alimentary canal, and and the two peculiar gland like organs placed opposite to each other on either side of the and which were alluded to

by Manson & the function of which is unknown.

The Embryos of the Filaria Dracunculus on being discharged from the uterus of the adult female worm possess a distinct transversely striated cuticle which as will be seen is lost during the second period of its Life-History.

While working at this subject during the summer of 1907 I was able to confirm Leipers observations on the influence of Acid on Guinea-Worm Larvae encysted in Cyclops Quadricornis, (British Medical Journal Jan. 6th 1906 p. 19 Vol. I).

By placing some Cyclops in a few drops of water containing the Embryos of the Filaria Dracunculus I was able to obtain some infected Cyclops, the time taken for the Embryos to effect their entry into the body cavity of the Cyclops varying from two hours to three days, although I found that in the majority of cases each Cyclops contained but one Embryo, I was on one occassion able in this way to obtain a single Cyclops containing as many as four Embryos.

It is curious to note that although the Embryos of the Filaria Dracuculus immediately prior to their entry into the body cavity of the Cyclops Quadricornis are extremely active, swimming about by a sort of side to side lashing of the tail, & tad-pole like motion of the body, once they have gained admission there is an entire cessation of this activity and either lie in a completely dormant condition, or else the only movement observable is an occasional rythmical coiling motion of

their bodies.

I observed that the smaller Cyclops Quadricornis were more easily infected by the larvae, probably due to the fact that the cuticle of the smaller Cyclops is more easily penetrated as compared with that of the larger specimens, and even when this small Crustacean contains as many as three or four larvae in its interior it does not appear to suffer from any immediate effects.

At the end of eleven days I placed one of my infected Cyclops in a 0.2 per cent solution of Hydrochloric Acid representing the Gas-tric juine in man and the result was remarkable, for the Cyclops was gradually killed while the larvae immediately become more active, wriggling about in the interior of the now almost motionless Cyclops and trying first at one place and them at another to foce its way through the cuticle of their host.

Eventually after half an hour one Embryo escaped, followed half an hour sates by the second Embryo, and both could be seen swimming about in the Acid solution by wriggling movements, a leaving their previous host Cyclops quadricornis dead, its body cavity having become completely disintegrated.

On examination the average length of the Embryo at this stage was shown to be  $532\,\mu$ , and the most noticeable fact was that the long awl shaped tail had disappeared and in its place was a bifurcated extremity the upper lobe of the bifurcation being the larger of the two.

The transversely striated cuticle observed on the

Embryo on its discharge from the uterus of the parent worm had disappeared, was instead replaced by a delicate enveloping pellicle.

A curious paint was that while the body cavity of the Embryo at this stage appeared to be full of gut contents, I was not able to find any trace of either the anus or peculiar gland-like structures described as being so distinctly shown by Wenyon's method of staining with a watery solution of Delafields Haemotoxylin.

Having confirmed the observations of Leiper concerning the effect of Acid or larvae encysted in the Cyclops Quadricornins I proceeded to investigate the effect of this 0.2 per cent solution of Hydrochloric acid on the Embryo as discharged from the female and the result was that in three hours time all the Embryos were dead.

This is I think a very important result, as it forms another proof as to the inability to infection by the direct invasion of the Embryos as discharged from the parent worm without first having entered an intermediate host, and as was lately found by Leiper in his experiments in Nigeria, Cyclops Quadricornis alone is capable, infection.

On reviewing the disease of Dracontiasis it is at once apparent that there are several very necessary factors which must be present in order to enable the Life-History of the Filaria Dracunculus to be completed.

and of these it is obvious that the most essential is the presence of the Cyclops Quadricoranis.

From the results of my work which has been described in detail, I have shown that it is impossible for the Embryos to enter the body by penetrating through sweat glands into the subcutaneans cellular tissue, and also that even if they are taken into the body by means of infected drinking water without having first entered their intermediate host that they are innoccuous, and are killed in a very short time by the action of the Gastric juice.

It is necessary for the parent worm to reach and penetrate the surface of the skin, and having done so to to discharge its larvae into fresh water containing the Cyclops Quadricornis within twenty four hours of its appearance and before any septic complications can arise.

The Embryo having once gained admission into the body Cavity of the Cyclops must stay there for at least ten days in order to complete its metamorphosis before being in a position to infect man by means of the drinking water.

The infected Cyclops having once entered the stomach is acted on by the Gastric juice which causes the imprisoned larvae to be set free, these then penetrate the Gut wall and enter the muscles and connective tissue of the body where they breed.

The males having performed their function die, & it is necessary for the female worm having become mature

tomake its way to the Surface of the body & so the Life-History of the next generation is begun overagain, the whole cycle taking about one year.

The amount of time which must necessarily be spent in making microscopical observations regarding the Life-History of such minute living organisms as the larvae of the Filaria Dracunculus & their host the Cyclops Quadricornis is enormous, & at times almost disheartening but it is a subject of the utmost importance to the Medical man working in districts where this disease is endemic & where one sees such a large amount of physical infirmity as its result.

There are skimm still many points for future investigation chiefly as regards the conditions under which the intermediate host lives & multiplies in tropical countries which remain to be cleared up for it is obvious that once a thorough knowledge of this Crustacean is obtained it will be possible to take prophylactic measures on the lines of either preventing its its entry into drinking water or means for its destruction in suspected waters without rendering these useless or dangerous to man.

M.B. Ch. B. (Univ. Edin.)

My sill.

Lieut. R.A.M.C.

attached Egyptian Army.

Kassala 8 - 2 - 09

## Appendix I.

Process used in preparation of skin of monkey for cutting sections.

- (i) The skin was placed in a saturated solution of Hydrarg. Perchlor. acidified with Acetic acid for 24 hours.
- (ii) Washed in water and placed in 70% Alcohol to which a few drops of Grams Iodine had been added, (Iodine to act an any remaining Hydrarg. Perchlor & convert it into the soluble Iodide).

This was changed several times for five days until the Iodine ceased to be decolourised.

- (iii)Placed in Methylated spirit for 12 hours.
- (iv) Placed in absolute Alcohol for 4 hours with several changes.
- (v) Cedar Oil until cleared.
- (vi) Xylol Paraffin.

## Appendix II.

Method for staining the Embryos of the Filaria
Dracunculus

- (1) Fix in saturated solution of Hydrarg. Perchlor for 5 minutes.
- (2) Centrifugalise & wash in distilled water several times centrifugalising between each washing.
- (3) Fill up small test tube containing Embryos with distilled water and add twelve drops of watery solution of Delafields Haemotoxylin and put aside to stain for 48 hours.
- (4) Wash in several changes of distilled water as in (2).
- (5) Add one drop of Ammonia to test tube containing Embryos in distilled water .
- (6) Add two drops of Glycerine and put aside for twelve hours.
- (7) Mount on slide with cover-glass and ring with Beeswax.

- alientary canal - Striated entier anus - Gland-like Structure Larva of Litaria Draementes Bahn al Chazal Sudan