developing this method of technique we shall be able in the future to diagnose accurately the different species of tissues and of germs and even of the different strains, by pure biochemical analysis.

Even with the crude volumetric measurements which I have employed one can detect distinct differences in the biochemical composition of such closely allied organisms as *B. typhosus*, *paratyphosus A*, and *paratyphosus B*. I have already pointed out that

TABLE II.—Percentages of Content.

Germes or proteins.	Tubercle bacillus.	Gonococcus.	Staphylococcus.	B. typhosus.	B. coli.	Ox heart.	Ox testicle.
Alkali-soluble substance	28	75	48	60	25	76	36
Acid-soluble substance	25	7	26	27	26	10	22
Total proteose	7	17	3	11	44	8	7
Alcohol-soluble substance	32	1	23	2	5	5	34
Chloroform-soluble substance ...	8	0	0	0	0	1	1

some germes and tissues are very easily dissolved, even in weak alkali, whilst others are very difficult to dissolve and require strong solutions like antiformin. My analysis of many varieties of germes and tissues brought to light the interesting fact that this solubility depended upon the lipid content of the germ or tissue. The less the amount of alcohol-soluble substance (lipoid) present the greater is the solubility in alkali, and vice versa. The influenza bacillus contains only the merest trace of lipid, and is in consequence very soluble even in N/10 NaOH. The tubercle bacillus, on the other hand, contains some 32 per cent. of alcohol-soluble material, and on this account is very resistant to alkaline solution. It requires the action of antiformin for several hours. This fact is indeed so striking that one can prophesy a low lipid content in a protein which dissolves readily in weak alkali; and conversely, when a protein disintegrates with difficulty it assuredly contains a high percentage of this alcohol-soluble material. (See Figures.)

10. Antigenic and Comparatively Non-toxic Nature of Protein Split Products Described Above.

In the early part of my investigation I had ascertained that the alkali-soluble fraction of the gonococcus was antigenic, as estimated by the complement-fixation reaction and by the therapeutic results obtained when injected into gonorrhœal subjects. It was found, moreover, that this alkali-soluble fraction was very much less toxic than the actual germ itself. Further, the proteoses associated with the alkali-soluble fraction were also antigenic, and although they had a provocative power they were nevertheless comparatively non-toxic.

Similar experiments were now carried out with regard to the acid-soluble, alcohol-soluble, and chloroform-soluble fractions. It was found that the two former components gave good results when used as antigens in the complement-fixation test for gonorrhœa. Further inoculation experiments in human subjects showed that they were apparently no more toxic than the alkali-soluble component of the germ. These experiments were repeated with the component parts of the tubercle bacillus, with approximately the same results.

E. P. Pick⁷ and other observers have inclined to the belief that the alcohol-soluble "waxy" substances from the tubercle bacillus and other germes were toxic and non-antigenic, but it would appear that this belief is erroneous. It is now well known that lipid substances may be highly antigenic, one of the most notable examples being the alcoholic extract of heart employed in the Wassermann test. Lipoids, moreover, are not necessarily highly toxic, since the staphylococcus contains a large amount of alcohol-soluble substance, and yet is one of the least toxic of all germes. Pfeiffer's bacillus, on the other hand, is very highly toxic, yet it contains practically no lipid or alcohol-soluble material.

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Dr. Dan McKenzie has been elected Corresponding Fellow of the American Laryngological Association.

OBSERVATIONS UPON A CASE OF
FILARIA (LOA) LOA INFECTION.
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General Symptoms.

INFECTIONS with the nematode parasite *Filaria loa* (*Loa loa*), though often exhibiting few or no clinical symptoms of any definite importance, are nevertheless of great interest to the flariologist. Occasionally the adult parasites in their wanderings about the connective tissues pass under the conjunctiva on to the eye, and they have been removed from this position in many instances. Such an occurrence as a worm in the eye naturally makes a great impression on the layman, who does not forget it when he comes to detail his troubles to the doctor. Calabar swellings, swellings of a fugitive nature, about the size of a pigeon's egg or larger, are also met with; these come up suddenly, are painless, do not pit on pressure, and generally disappear in two or three days of their own accord. In rare cases¹ a generalised swelling of a part is met with or a pruritic condition may be seen, while in one case there was great pain in the eye with photophobia. We have recently seen a case where, instead of a small local swelling, there was a generalised swelling of the forearm of the nature of a solid œdema. This lasted for a considerable time and ultimately disappeared. When the adult worms are near the surface they often give rise to pricking sensations with itching, and the patients soon get to know those and can locate where the worm is quite accurately.

Pathogenesis of Calabar Swellings.

Students of the subject will remember that Sir Patrick Manson suggested² that the Calabar swelling might be produced by the adult female worm giving birth to a generation of embryos at that spot, and in one case he demonstrated embryos from such a swelling. The experiment was vitiated, however, by the fact that the patient had many embryos in the peripheral blood at the time; their presence in the films was no doubt due to the needle wounding blood-vessels on its way in. That such was so one of us (G. C. L.) was able to demonstrate recently in a case of *F. loa* infection where there were no embryos in the peripheral blood. In this instance, though the Calabar swelling—which was a perfectly typical one—was punctured in many directions, no embryos could be detected in the juice aspirated.

There is no doubt that those swellings are caused in some way or other by the worms; they are probably due to the excretion of a toxin into the tissues, a possibility rendered still more likely in such cases by the fact of the presence of a well-marked eosinophilia as well. This eosinophilia is a very constant feature, the numbers varying between 12 and 20 per cent. as an average. In the absence of other causes one has been able to diagnose loa infections correctly by this feature alone.

Diagnosis.

Four distinct points will help one, then, in diagnosing *F. loa* infection: (1) the actual presence of the adult worm or worms, have any been extracted from or definitely seen in the eye? (2) the presence of *F. loa* embryos in the peripheral blood—they are easily differentiated from *F. bancrofti* embryos by anyone who has studied the subject closely; (3) the presence or definite history of Calabar swellings; and (4) eosino-

¹ Low, G. C.: Jour. of Trop. Med. and Hyg., Jan. 2nd, 1911.
² Trans. Soc. of Trop. Med. and Hyg., vol. iii., No. 5.

philia in people from the endemic area, with nothing else to explain its presence.

One or more of those cardinal symptoms may be present in any individual case. Embryos are often absent from the peripheral blood; this absence, often of a prolonged nature, is difficult to explain. Those interested may consult the paper on this subject already mentioned.¹

History of the Case.

B., male, aged 28. Admitted to Hospital for Tropical Diseases Jan. 21st, 1921. Born in Scotland; went abroad to Southern Nigeria 1914; Cameroons 1916; came home to U.K. December, 1920, this being his fourth leave home.

Previous illnesses.—Suffered a good deal from malaria; gastritis in 1918; diarrhoea once; no definite clinical dysentery.

Present illness.—Went to doctor for fever in Nigeria November, 1920; an examination of the blood for malaria showed the presence of diurnal filarial embryos, as well as malarial parasites. On arrival in England as fever was still troubling the patient; he came into the Hospital for Tropical Diseases to have it treated.

Examination.—Temp. raised; spleen enlarged. These symptoms quickly disappeared on proper doses of quinine being administered, and, of course, had nothing to do with the filarial infection.

Filarial history.—No definite Calabar swellings; (?) perhaps one. Knocked his right forearm one day; on the same day his right hand became swollen, remaining so for two days, after which it went down of its own accord. No history of worm ever being seen in eye.

Blood examination.—Many *F. loa* embryos present in day blood; none in night blood. Also a few *F. perstans*. No malarial parasites found.

CHART 1.

In each of the Charts the shaded portions represent the time during which the patient slept. The figures at the side are the numbers of *F. loa* embryos in 20 c.mm. of blood.

CASE M.—Ordinary habits of life. Showing diurnal periodicity of *F. loa* embryos.

CHART 2.

CASE M.—Inverted habits of life—sleeping by day, sitting up and working at night. No change or inversion of periodicity.

CHART 3 (Case B).

(The actual time of the noon and midnight examinations in this case was 12.5.)

CASE B.—Inverted habits of life—sleeping by day, sitting up and keeping awake all night. No change or inversion of periodicity.

Count of corpuscles.—R., 4,108,000. W., 8800. Hb, 90 per cent. Differential: P.M.N., 45 percent; L.M., 6 per cent; L., 31 per cent; E., 18 per cent. = 100. Slight anaemia then, due, no doubt, to the malarial element in the case. Well-marked eosinophilia.

Stool examinations.—No ova of any helminths present. No protozoa.

Urinary examinations.—Nothing abnormal, no albumin, blood, or sugar.

Subsequent history.—The routine blood examinations will be seen on the charts.

In March a typical Calabar swelling developed on the right wrist, thus it will be seen that the patient had eventually three of the cardinal signs of the infection—viz., the Calabar swelling, the day embryos of *F. loa*, and the eosinophilia.

Experiments upon the Periodicity.

Filarial periodicity has never been satisfactorily explained, though many theories have been put forward from time to time. The term has been applied to the presence in the blood of the embryos of *F. bancrofti* by night and their absence by day, or conversely, in the case of *F. loa*, to their absence by night and their presence by day. Chart 1 shows the diurnal periodicity of *F. loa* very well. The maximum number of embryos are in the blood about midday or a little later and quite absent from the blood at night. This regular

habit goes on day by day without much variation. One of the suggested explanations of periodicity is that it is due to the habits of the intermediate host, this being nocturnal in the case of *F. bancrofti*, diurnal in the case of *F. loa*. This, however, will not explain the non-periodicity of most of the other filaria, such as *Dirofilaria immitis* of the dog, whose intermediate host is nocturnal, *F. perstans*, and *F. demarquayi*; nor does it completely explain the non-periodicity of the South Sea variety of *F. bancrofti*. The possibility of the latter being a different species, or at least a distinct sub-species, still remains. If not that, at any rate it is a very well marked variety, differing from the common *F. bancrofti* in other respects (pathologically) as well as in its irregular periodicity.

Inversion of Periodicity.

Stephen Mackenzie first showed that it is possible to change the periodicity of *F. bancrofti* by changing the habits of the patient—e.g., by making him sit up all night and sleep all day. If this is done the periodicity changes right round, the embryos now appearing in the peripheral blood by day and not by night.

Many years ago now (1904) one of us (G. C. L.) had the opportunity of trying a similar experiment on a case of *F. loa* infection, under the care of Sir Patrick Manson at the Albert Dock Hospital. Though the protocols and details of this work have never been published, mention of the bare fact that the experiment was unsuccessful has appeared from time to time in the different editions of Sir Patrick Manson's book on Tropical Diseases. I have had the opportunity of verifying those facts again, in the case at present under discussion, and have found that they harmonise completely with those obtained in 1904; it may therefore not be out of place to publish them together now. For convenience the results have been put in the forms of charts (Charts 2 and 3) and a perusal of those will show that though the habits of the patient were completely inverted no corresponding change in the periodicity of the embryos took place, this being in direct opposition to similar experiments on *F. bancrofti*, as just mentioned above. In both cases the patients went to bed at 9 A.M. and stayed there till 9 P.M. At the latter hour they got up and sat up all night, reading or doing some work about the wards. Both slept well during the day. Measured quantities of blood as first recommended and practised by one of us in 1903³ were always taken, the standard quantity of 20 c.mm. being adopted.

Attempts to Eradicate the Infection by Antimony.

A series of antimonium tartaratum injections were given intravenously to determine if they would have any effect on eradicating the infection. They failed entirely, just as they have done in a series of cases of *F. bancrofti*, treated in a similar manner by ourselves.⁴ A table of the examinations made and the amount of antimony injected has been constructed similar to those on our *bancrofti* cases, and a glance at it gives all the details necessary. There might be a slight diminution of the numbers of embryos towards the end of the course, but even this is not certain. A total of 25 gr. of antimonium tartaratum in all was given, the injections having no bad effects upon the patient.

In addition to the *F. loa* infection there was also a scanty infection of *F. perstans*, not sufficient, however, to do any accurate counts upon. These were not destroyed by the antimony either, an interesting observation, as this embryo is non-sheathed, and some have suggested that it is the sheath of the *bancrofti* and *loa* embryo that protects them. As regards eradication of the infection, of course, this is not the point; it is no use destroying the embryos, even if we could, so long as the adults are not destroyed, as the latter cause the symptoms, and if still alive will go on pouring embryos into the blood stream. The embryos are just an index or means of determining what effect, if any, the drug used is having on the adult worms. Whenever those are destroyed, as by an attack of lymphangitis in *F. bancrofti* infections, then the

embryos quickly disappear from the blood and do not return.

Table Showing Examinations made and Amount of Antimony Injected (Case B).

A = number of *F. loa* embryos in 20 c.mm. of blood.
B = number of grains of tartar emetic injected, these being given in the afternoons between 4 and 5 P.M.
The examinations were made at 12 noon on every occasion.

1921.	A	B	1921.	A	B	1921.	A	B	1921.	A	B
Jan.			Feb.			Feb.			Mar.		
24	32		7	30		23	15		9	14	
25	37		8	20		24	18		10	21	2½
26	40		9	23	½	25	14	2	11	10	
27	44		10	37		26	21		12	20	
28	35		11	25	½	27	14		13	15	
29	30		12	34		28	16	2	14	17	2½
30	27		13	30		Mar. 1	15		15	10	
31	25		14	27	1				16	11	2½
Feb.			15	15		2	12		17	10	
	24		16	25	1	3	17		18	10	2½
	2	35	17	24		4	11	2½	19	12	
	3	24	18	12	1½	5	18		20	22	
	4	21	19	20		6	12		21	15	
	5	15	21	22	1½	7	15	2½	22	20	
	6	12	22	10		8	19				25 gr.

J. B. Christopherson has recently again raised the question of the non-toxicity of large doses of antimony in different tropical affections in which this drug is used. We agree with him that, with ordinary care, there is little or no danger in giving such injections, and that if necessary large amounts may be given, as in our own series of cases of bilharzia.⁵ In cases of kala-azar and ulcerating granuloma quantities up to 53½ gr., 64½ gr., and even 114 gr. have been administered by us. In most of the tropical diseases now being treated with antimonium tartaratum such large amounts will not be found necessary, 30 to 40 gr. probably being the maxima required. The methods of giving the drug and the slight toxic symptoms which may follow its administration are now so well known that it is quite unnecessary to reiterate them here. These details may be studied in the paper referred to above and in the different publications of Christopherson and others.

SPINAL ANÆSTHESIA FOR SUPRAPUBIC PROSTATECTOMY.

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A FORMER report on this subject was published in THE LANCET of May 15th, 1915. Since then, owing to the kindness of Mr. John Pardoe and Mr. Sydney MacDonald, I have greatly increased my experience in the use of this method of anæsthetising for suprapubic prostatectomy, with the result that though I still use it for choice in almost every case I have modified my technique in some particulars.

I now use a 10 per cent. solution of stovaine (Billon's) without the addition of glucose. I have gradually cut down the dose of stovaine to a maximum of 0.03 of a gramme (three-tenths of a cubic centimetre of a 10 per cent. solution). In some cases, on account of great age, a much broken-down constitution, or comparatively low blood pressure, I have used a dose of 0.025 of a gramme of stovaine successfully. The patient is always operated on with the table slightly inclined, head downwards, and this position should be retained for carrying the patient back to bed, and when in bed until all effects of the spinal injection have passed off. The foot of the bed should be raised high enough to make a more decided slope than that of the operating-table. The Trendelenburg position can of course be used if desired. In every case I produce unconsciousness, never surgical anæsthesia, by administering some general anæsthetic in combination with oxygen.

³ Filaria Perstans, Brit. Med. Jour., March 28th, 1903.
⁴ THE LANCET, 1920, ii., 551, and 1921, i., 221.

⁵ Low, G. C., and Newham, H. B. G.: THE LANCET, 1919, ii., 633.