of confirmation than in seeking for exceptions whose existence would point to some fallacy in my proof. No such exceptions were found, but much valuable and interesting confirmation was forthcoming.

2. *Effect of these Winds on Phthisis Patients.*⁵—Cases of phthisis in Devonshire exposed to these winds have been shown to run a shorter course than cases sheltered from them. Unpublished clinical evidence also has accumulated pointing strongly in the same direction. I have also tried to compare the statistics from variously placed sanatoriums; this proved impossible, but it was significant that some exceptionally exposed sanatoriums kept no records of results! There seems to me no doubt that some at least of the disappointment generally expressed with the results of sanatorium treatment in this country is due to the ill-chosen sites of some of our sanatoriums.

Perhaps now that an able independent investigator has confirmed my conclusions, a little pains may be taken to place the new sanatoriums for our phthisical sailors and soldiers in situations where failure shall be less of a foregone conclusion!

3. *Effect of these Winds on Bovine Tuberculosis.*—Bovine tuberculosis is much commoner in areas exposed to strong rain-bearing winds than in areas sheltered from them.⁶ Professor Delépine's valuable paper⁷ on tuberculosis in the farms supplying Manchester with milk gave me a unique opportunity of investigating this important point. This fact surely calls for some attention.

4. *Altitude and Phthisis.*⁸—When the influence of rain-bearing winds had been taken into account and, as far as possible, eliminated by considering only localities sheltered from them, the contradictions, which had rendered a satisfactory conclusion on the relations of altitude and phthisis prevalence impossible, disappeared, and the important generalization was reached that altitude, *per se*, has no influence on phthisis prevalence. The fact is that, as altitude increases, exposed situations increase so much in bleakness that the population is more and more forced into shelter; consequently, as altitude increases the proportion of the population living in shelter increases and the prevalence of phthisis falls. This conclusion does not affect my belief in the beneficial effect of high altitudes in shelter on phthisis patients.

5. *Subsoil and Phthisis.*—Dr. Brownlee must have given my paper⁹ on this subject a very hasty glance, or he would have recognized that not only did it deal with a much more extensive field than Buchanan's—all England as against three counties—but that it was much more elaborate and safeguarded from error; also (most important of all) that instead of leaving the question one of mere surmise, mine left it practically proved that certain geological formations are definitely associated with higher phthisis death rates than others. I say "practically" proved because, until larger populations in pronounced shelter from rain-bearing winds have been dealt with, I shall not consider the investigation complete. Dr. Brownlee's results in Norfolk, Suffolk, and Essex are very suggestive, but, in view of the varying exposures of his districts, must be regarded as inconclusive.

6. *Occupation and Phthisis.*—I wrote in 1913¹⁰: "The evil eminence of the tin-miner may not be entirely occupational; he lives for the most part in a district swept by strong rainy winds. Also the Midland coal-miner, who suffers less from phthisis than coal-miners in other parts of England, may not owe his good fortune altogether to the conditions of his work, but partly also to the slighter exposure of his district to rain-bearing winds."

7. *Density of Population and Phthisis.*¹¹—I have shown that in certain rainy wind-swept regions the self-protection of a town from winds may more than compensate for its comparative crowding.

PHTHISIS IN WALES.

Dr. Brownlee's section on this subject is instructive and interesting. But I fear he will find the problem of subsoil in Wales as disappointing as he found his Welsh study of rainy winds. I have tried it myself, for I observed how heavy were the death rates on some of the Welsh formations. Rainy winds, race, modes of life and occupation, seem perversely arranged so as to confuse the problem and almost to defy elimination. It will be observed that Dr. Brownlee's map of the districts is almost as suggestive of

the effect of rain-bearing wind as of subsoil, when it is remembered that in the east and south-east of Wales the mountains afford much shelter, and that, in the south-east, occupation must modify the figures, the phthisis death rate of coal-miners generally tending to be low. My table of the phthisis death rates in the Welsh registration districts, 1881-90,¹¹ indicates at least some effect produced by rain-bearing winds.

A MISAPPREHENSION.

Before concluding, I should like to clear up a misapprehension. Dr. Brownlee has referred to me as a "follower in Haviland's footsteps." So far from being a follower of Haviland, I was fortunately quite unaware of his work until I had found the fact on which I lay such stress. Haviland's statements were quite different from mine, and, had I been familiar with them, it is not unlikely that I should have missed my point, as he did.

SUMMARY.

1. Dr. Brownlee has introduced a new method of investigating phthisis death rates at successive age periods which promises to be valuable.
2. He has not proved his first proposition regarding the existence of two or three types of human tubercle.
3. He has himself disproved his second proposition, dealing with the cause of the decline of phthisis.
4. His confirmation of my conclusions in Devonshire in respect of the influence of strong prevalent rain-bearing winds on the prevalence of phthisis, once more emphasizes the necessity for recognizing this influence.
5. Incidentally his papers illustrate the need for applying, in climatological research, what I have called "the principle of approximate isolation of influences."

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FURTHER WORK ON ANTIMONY INTRAVENOUSLY IN FILARIASIS.

BY

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LAST year I published a preliminary report on short trials of sodium antimonyl tartrate solutions injected intravenously in filariasis, and showed that the drug had some action in reducing the number of embryo filaria in the evening peripheral blood and in lessening their motility, but I had not been able to follow up the cases long enough to ascertain if the effect was permanent or not, although I had arranged to do so. Thanks to the kindness of Lieut. Colonel Thornley, I.M.S., Civil Surgeon of Cuttack, I have now been able to follow up a series of eight cases in the central jail of that filarial infected station, with the results recorded in this communication.

Method of Investigation.

Thick blood films of 100 prisoners under sentences of three months and over were sent to me for examination, while 50 more were taken during a visit to Cuttack; all were taken at 9 p.m., which is quite late enough for Indian patients. In 18 per cent. of these healthy men filaria embryos were found, and eight, who showed from 17 to 126 embryo filaria in 20 cubic millimetres of blood and a total of 732 in the eight slides, were selected for treatment. Five controls were also taken with from 22 to 117 filaria in a slide and a total of 168. The blood slides were taken every evening at 9 p.m. at first and later at longer intervals, but always at the same hour, and the injections of a 2 per cent. solution of sodium antimonyl tartrate were given in the mornings. I am greatly indebted to Subassistant Surgeon Kailas Chandra Rao, demonstrator

TABLE I.—Doses and Amount of the Drug given in Successful and Unsuccessful Cases respectively, and Embryos Before and After.

SUCCESSFUL CASES.						UNSUCCESSFUL CASES.					
No. of Case.	Doses.	Grams.	Embryo Filaria.			No. of Case.	Doses.	Grams.	Embryo Filaria.		
			Before.	After.*					Before.	After.*	
17	21	1.99	12	No. 0.25	Per Cent. 2.1	47	21	1.99	121	No. 83	Per Cent. 68.6
71	11	0.79	98	6.25	6.4	62	11	0.79	83	99	112.5
72	19	1.79	126	16.75	13.3	65	19	1.55	77	54	70.0
106	21	1.97	99	1.5	1.5	125	21	1.99	111	35	31.5

* Average of last four weekly counts.

of pathology in the Orissa Medical School, for his careful work in taking the slides and giving the injections. All the counts were made by me.

Doses, Duration of Treatment, and the Effects Produced.

During the first six days the doses were respectively 3, 4, 4.5, 5, 5, and 5 c.cm. of the 2 per cent. solution, after which, as toxic symptoms appeared, the latter dose was given every other day as far as possible up to six weeks from the commencement of the treatment. On one occasion all the injections were stopped for three days on account of toxic symptoms in the form of nausea or sickness, while the same trouble or difficulties due to inflammation of the injected veins reduced the doses in several of the cases, so that the number of doses and the total amount of the drug in grams were as shown in Table I, in which the cases are classed as those who eventually showed very great reduction in the number of the filaria embryos, indicating success of the treatment, and those in which a rapid return to about the original numbers took place as soon as the injections were stopped, showing failure to kill the adult worms.

It so happens that the number of doses given was the same in each group and the total amounts of the drug also almost identical, although the amounts varied considerably in individual cases, showing that it is not yet possible to lay down the amount of treatment required in any given case.

Results of the Treatment.

The results are best brought out by the accompanying chart, showing the percentages of embryos as compared with the original numbers before the treatment was commenced, found at each count, which were made daily for eighteen days, then every third day up to twelve days after the injections were stopped, and finally weekly for the succeeding four months up to the date of discharge from the jail of some of the patients. Separate curves are given of the combined figures of the four successful (broken lines) and of the four unsuccessful cases (continued line) so as to bring out important points of difference between the two, which became apparent on studying the figures obtained during some weeks after the injections were stopped. The two curves closely coincide throughout the course of the injections, although that of the eventually unsuccessful cases showed greater fluctuations and tendency to occasional rises in the number of the embryos than that of the successful ones. Both showed an extremely rapid and great fall in the numbers during the first six days of daily injections to reach a minimum of 13

and 6 per cent. of the original numbers on the fifth day; both showed a considerable rise when the injections were given only on alternate days, while both showed a steady low rate of 30 to 40 per cent. of the original numbers during the last twelve days of the injections. On cessation of the treatment a striking contrast between the two curves for the first time showed itself, for, whereas in the four unsuccessful cases the number of embryos showed an immediate rapid rise, carrying them up to the original count within nine days, in the successful ones there was no rise during the first six days after the drug was stopped, and subsequently only small fluctuations—such as also occurred to an even greater extent in the control cases—accompanied by a steady general decline in the curve to from 13 to 3 per cent. of the original numbers during the last four weeks. In these four cases I think there can be little doubt that the adult female worms

had been killed by the antimony salt—a conclusion which I believe is confirmed by an interesting observation I made in the unsuccessful cases—namely, that the rapid increase in the embryos immediately after the injections were stopped was accompanied by the appearance in the slides of very numerous long, thin, and presumably young forms, indicating that the adult females were

once more producing a numerous progeny; no such change was noticed in the successful cases. The immediate great rise in the number of embryos in the failures on stopping the injections is also of practical importance, as regular counts on the plan I adopted will enable a judgement to be formed in any individual case as to the duration of treatment required, any rapid increase in the embryos of too sustained a nature to be attributed to periodic variations being an indication for further treatment; the appearance of a number of long, thin forms would point in the same direction.

Variations in the Counts in Control Cases.

During the first seven weeks, and occasionally later, counts were also made by me in the five control cases, and a curve has been worked out showing the variations from the average count. It will suffice to say that, owing to great fluctuations in the one case with a large number of embryo filaria, the percentages varied between 45 and 160 per cent., and showed rapid variations without any very regular periodicity, thus indicating that prolonged and repeated counts are necessary to establish the effect of any given treatment. The control curve showed no such immediate rapid fall as occurred at first in all the treated cases, or any such continued low counts as in the successful cases after cessation of the injections, indicating that the latter were due to the antimony injections.

Periodicity in the Daily Numbers of Filarial Embryos at the same Hour of the Evening.

The periodical variations in the number of embryo filaria in the peripheral blood at different hours of the day and night is well known, but as far as I am aware less attention has been paid to the variations at the same hour from day to day, such as are well illustrated in the latter part of the upper curve of the four cases in which the antimony treatment failed permanently to reduce their numbers. During the four months from October to January there was a regular rise in the numbers at about new moon, and a fall at full moon, which is very suggestive in view of the popular opinion that filarial fever is influenced by the phases of the moon. To examine this hypothesis further I have plotted out the curves of each of the four cases separately, and found that in two months three of the four curves followed this rule, but in the other two months only two of them did so, which indicates that the coincidence in the combined curve is probably accidental. Moreover, the daily counts in the control cases showed great fluctuations occurring at shorter intervals and less regularly. These daily variations are deserving of more detailed study, as they may well furnish a clue to the periodicity of filarial fever, which has always puzzled me, but which may possibly be explained, if the fluctuations referred to are produced by a periodical discharge into the circulation of a large number of newly-born embryo filaria, as, indeed, has been suggested by Bahr. As long as the lymphatic channels are free this need not cause any material inconvenience to the host, but when the lymphatics become blocked by inflammatory changes, then such a brood of young embryos may well cause some further blocking of the lymphatic channels with the excitation of inflammatory changes in the already damaged tissues, without invoking the aid of Manson's hypothesis of the abortion of immature ova. Secondary infections, with staphylococci and streptococci, doubtless also often play an important part in the febrile process, as I (unpublished records), as well as others, have cultivated these organisms from the inflamed superficial tissues of the legs in cases of elephantiasis and obtained considerable amelioration of the febrile attacks by auto-vaccines. On the other hand, cultures during these attacks have often failed, while the frequently very regular periodicity in filarial fever attacks could be more easily explained by the above hypothesis, which may serve a useful purpose if it stimulates further research into the variations of the filarial embryos in the blood from day to day on similar lines to those adopted in my present research, which circumstances will not allow of my continuing at present.

Further Investigations at Puri by Dr. P. N. Das.

In my first paper I mentioned that Dr. P. N. Das was continuing the investigation I commenced at Puri with his help, and he has kindly sent me reports of his progress. As he recently read a paper on the subject at the Indian Science Congress at Nagpur, which will eventually appear in the *Indian Journal of Medical Research*, it will suffice here to say that in five out of eight cases the embryo filaria had completely disappeared from the peripheral blood after from twelve to thirty-seven intravenous injections of sodium antimonyl tartrate, and had remained absent for from a few days up to one month and a half, while in the remaining three cases the parasites had become greatly reduced. Moreover, in two additional patients, who were suffering from weekly attacks of filarial fever, the attacks had ceased under the treatment, and in one case had remained absent up to three and a half months. These are most promising results.

Recent Cases Treated by the Writer.

The following brief notes of cases recently treated by me may also be of interest, although I cannot follow them up very long, as I am about to proceed on leave.

CASE I.—Early Elephantiasis.

A European lady consulted me for recently developed swelling of the forearms just above the wrists and of the feet highly suggestive of commencing elephantiasis. The evening blood showed 50 embryo filaria in 20 c.mm., so I gave thirteen injections of sodium antimonyl tartrate, mostly in 4 c.cm. doses, into a small wrist vein, which was the only one available. At the end of this course the swelling had gone down by nearly an inch, only two filaria could be found in 20 c.mm. of blood, and she had lost the slight periodical febrile attacks she formerly suffered from.

CASE II.—Filarial Orchitis.

A European patient was admitted to the General Hospital for orchitis; numerous filaria were found in his night blood. Major Green Armitage, I.M.S., very kindly treated him with sodium antimonyl tartrate, and sent me blood films of measured quantities taken at 10 p.m. Counts on five consecutive evenings prior to treatment varied between 44 and 96, and averaged 64. They were also made on alternate evenings while the injections were being given daily, working up to 4 c.cm. of the 2 per cent. solution. During the first ten days of the treatment the filaria varied between 21 (the first day) and 5, and averaged 9, while the next three counts gave 4 on one day and none on the other two days. Another count after only one injection had been given in four days also showed only one embryo in two slides, so as the decrease of the drug has not been followed by any definite increase in the filarial embryos the result is promising.

CASE III.—Chyluria.

I am indebted to my colleague, Lieut.-Colonel D. McCay, I.M.S., for an opportunity of treating this Indian patient in the Medical College Hospital. The average of four counts before treatment showed 86 embryo filaria in 20 c.mm. evening blood. The man then received nine injections of a 1 in 500 solution of colloid antimony sulphide, varying from 2 to 6 c.cm., such as I have previously found to be more effective in kala-azar than sodium antimonyl tartrate, while it is very much less toxic for man. This solution, however, failed to reduce the filarial embryos, which averaged 93 on the evenings of the injections. As the solution employed contains only approximately one-fifth the amount of antimony in the sodium tartrate this is not altogether surprising, as such a worm as the adult *Wuchereria bancrofti* is likely to be more resistant than a minute protozoal parasite to the prolonged action of a colloid preparation, which is retained in the blood longer than a soluble salt.

Dr. P. N. Das has just reported to me four cases in which 5 to 6 injections up to 5 c.cm. doses of the colloid preparation also failed to reduce the filarial embryos, so it is evidently not very active against them, although longer trials might possibly yield better results.

CONCLUSION.

The results above recorded appear to indicate that intravenous injections of soluble antimony salts have a definite effect in greatly reducing or causing the disappearance of the filarial embryos from the peripheral blood, presumably as a result of the destruction of the adult filaria, as the effect may last in some cases in an increasing degree for several months after cessation of the treatment. Moreover, clinically favourable results have been obtained in a few cases of filarial fever and elephantiasis. A rather long course of intravenous injections of a highly toxic drug is, however, required to produce this effect, so the new method of treatment requires care in its use, and much further experience will be necessary before its precise value can be decided.

CYCLOPLEGIA IN ROUTINE REFRACTION WORK.*

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ONE of your number recently put a question to me which may very well form the subject of our consideration to-day. He asked: "What is the best means of obtaining cycloplegia for routine refraction work in children?" That is a very pertinent question. There is a vast amount of refraction work being done for children. A cycloplegic is necessary for satisfactory work. We must be satisfied of the efficiency and safety of the drug used, and that the manner of its usage gives the least inconvenience to the child, its parents, the school teachers, and to your own department where the eye work is done. It is scarcely necessary to defend the statement that cycloplegia is necessary for satisfactory work in children. It is true that, given unlimited time, much skill in handling children and in the use of the mirror, it is often possible to make a good retinoscopy without a cycloplegic; but the most experienced will agree that, even under the best conditions, the results so obtained are open to doubt. When, however, we have to deal with a dozen or more children at the out-patient department of a hospital or a school clinic, it is manifest that without a cycloplegic the work could not be done at all.

* A lecture delivered at the West London Post-Graduate College.