not disprove the existence of a body periodicity, they tend to show the importance of muscular activity in determining the maximum of the diurnal variation.

The temperatures in the case of H. P. after the race are interesting, and as follows:

TABLE III.

Subject.	Time.	Temperature.
H. P.	After race 5 p.m.	105° F.
	5.45 p.m.	102°
	6.45 p.m.	101°
	7.45 p.m.	101.2°
	8.45 p.m.	100.4°
	Next day 12.15 a.m.	100.1°
	3.45 a.m.	98.6°
	8.15 a.m.	98.8°
	4.30 p.m.	100.2°

Any doubt as to the health of H. P. is dissipated by the fact that he was afterwards thoroughly examined by both physician and bacteriologist, and no signs of disease of any kind were found; moreover the subject continues in perfect health at the present time.

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CALMETTE'S OPHTHALMO-REACTION.*

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It is well known to you that if Koch's tuberculin, a proteid glycerine extract of tubercle bacilli, be injected into a healthy animal no reaction follows, but that if the animal be tuberculous the temperature rises from 2° to 6° F. This tuberculin test is constantly used to detect tuberculosis in cattle. Exactly the same is true in man, and in the hands of an expert the reaction is perfectly safe. Osler¹ states that tuberculin is used extensively at the Johns Hopkins Hospital, both in the medical and surgical wards, with the most satisfactory results and without harmful effects.† In adults a milligram is injected, and if this has no reaction a larger dose of 2 or 3 mg. is given after an interval of some days. There is often slight local irritation following the injection, and within from ten to twelve hours the febrile reaction begins, the temperature rising to 102° or 104°.

This reaction, although valuable in large hospitals having a highly-trained staff, is of no real use to the general practitioner. After the injection, which should be made early in the day, the temperature must be taken every three hours. Special care is necessary in all cases of tubercle of the lungs or of the larynx.² In spite of all precautions the patient may become really ill, and very untoward accidents have been recorded. Living tubercle bacilli have been found in the New tuberculin,³ so that extreme caution is necessary in its use. Those of you who have received injections of the typhoid or plague prophylactics will be able to form an idea of the feelings a patient would nourish towards his medical attendant who administered an injection of tuberculin for merely diagnostic purposes.

C. von Pirquet⁴ has found that in tuberculous individuals vaccination of the skin with tuberculin produces a local reaction marked by redness and swelling coming on forty-eight hours after the operation. Lignières⁵ has shown that scarification of the skin is unnecessary. If tuberculin be rubbed into the skin of a tuberculous person the reaction can be obtained, especially if the skin has just been shaved. V. Pirquet obtained a reaction in all but 11 out of 80 tuberculous children.

* Read before the Coventry Division of the British Medical Association.

† See also Schumacher's paper, *Zeitschrift für Augenheilkunde*, March, 1906.

Even this cuti-reaction is not one likely to be tolerated by the average patient, and, as it involves a breach of skin surface, it cannot be entirely devoid of danger.

Last June, Calmette,⁶ the well-known discoverer of anti-snake-bite serum, announced that if tuberculin be placed in the eye of a tuberculous subject a conjunctivitis is produced, whereas in a healthy subject there is no change. This has proved to be approximately correct. Calmette's serum can be obtained from Martindale in two forms, the liquid and the dry. The liquid form is now supplied in 0.5 per cent. strength, as the original 1 per cent. solution acted too violently in some cases. It is sent out in a pipette ready for use. All that is necessary is to break off the ends of the pipette and squeeze out the contents, which are enough for four or five patients. The solid form is supplied in a small tube, and it is only necessary to add 20 drops of sterilized water to make a 0.5 per cent. solution. If 10 drops be added we get a 1 per cent. solution, which is useful for a second trial in cases which have not reacted to the weak solution.

The patient's eyes must be carefully examined, and the condition noted in a book. It is essential that there be no pre-existing conjunctivitis, for the reaction would then be masked. One or two drops of the solution must be instilled into the lower cul-de-sac and the eye held open for a few seconds. If the subject be tuberculous the eye will begin to redden in about three hours, and lachrymation will be complained of. At about the sixth hour the caruncle begins to swell, and there may be a slight fibrous exudation which gathers in filaments in the lower conjunctival sac. The reaction reaches its maximum in from six to thirteen hours; there is no rise of temperature and no general malaise.

The inflammation may vary in degree from slight lachrymation, and an almost imperceptible enlargement of the caruncle, to a severe conjunctivitis which may last for several days, or in some cases even for weeks. But there is little danger to the eye unless it be affected with tuberculous disease, a rare ocular condition. Two cases were mentioned by Kalt to the Paris Ophthalmological Society, in which an old tuberculous condition was lighted up by a drop of tuberculin placed in the conjunctival sac.† M. Morax regarded these effects as mere unfortunate coincidences, for the serum has been constantly used to diagnose tuberculous conditions of the eye with no such bad results. In many cases some experience is necessary to decide whether the reaction be positive or not; a careful comparison should be made between the carunculae on each side.

The intensity of the reaction bears no relationship whatever to the severity of the tuberculous process.

It is now necessary to inquire: Is Calmette's reaction such a simple practical test that it can be used as a routine diagnostic method by the general practitioner? It is a safe reaction and a simple one; it hardly inconveniences the patient at all; but is it perfectly reliable? The answer is that it is a very useful aid to diagnosis; but occasionally its answer is, to say the least, equivocal. Cases have been recorded in which a severe reaction has been obtained in apparently healthy men,⁸ and the reaction has failed in undoubtedly tuberculous individuals.

My personal experience has been very favourable. I have tried it in 5 or 6 cases of iritis and choroiditis which I did not believe to be tuberculous in nature but which might have been, and not one of them reacted positively. In another case of eczema of the brow a severe reaction was obtained, and as the child was apparently healthy I regarded the indication as false. But I had to take the child into the wards again, and this time she had a typically hectic temperature. We have not been able to find any tuberculous focus yet, but I think that a hectic temperature taken with a positive ophthalmic reaction make the presence of tubercle very probable. A second trial gave no reaction, but probably the tube, which had been opened some ten days previously, was not active, for it failed to elicit a reaction from three undoubted cases of surgical tuberculosis, which have since reacted to a second tube of serum.

Calmette's reaction is useful in cases of cerebral compression. Some months ago we had two cases of undoubted cerebral disease in the wards lying side by side.

† Other cases have now been recorded. See *Archives of Ophthalmology*, March, 1908. Knapp records a case where interstitial keratitis followed the test.

The first case was sent to me by the late Dr. Hird. She had severe optic neuritis, headache, vomiting, vertigo, and fits. She was almost blind, and had lost all sense of smell. She had been very deaf for some years. I concluded that she had a gumma somewhere in the anterior part of the brain. She did not improve under iodides in large doses, so she was readmitted, and ultimately very successfully decompressed by Mr. Bennett. This case gave a negative reaction, and the subsequent history showed that the tumour was not a tuberculous one.

The second case, under Dr. Hawley, had headache, optic neuritis, and vomiting, with severe retraction of the head. She was pale and tuberculous-looking. The reaction was in her case positive, and we considered that she had tuberculous meningitis. This patient unfortunately discharged herself, and we have lost sight of her.

A third cerebral case is of great interest. A man was sent to me by Dr. Hawley suffering from headache, vertigo, and vomiting. He had old-standing, quiescent tuberculous disease of the ankle. I found that he had slight optic neuritis, and he gave a positive ophthalmic reaction. Shortly afterwards he developed all the signs of typical tuberculous meningitis, and died.

All the cases of obvious tuberculosis in which I have myself performed the test have given a positive result, but in one the reaction was merely subjective, I could see no inflammation, but the patient, a medical man, assured me that his eye was glazed up when he awakened in the morning, the serum having been put in the last thing at night. The case was one of tuberculous kidney, which has since been excised. Tubercle bacilli were found in the urine.

I have so far seen only one very slight reaction in an apparently healthy individual, although I have tried several, including myself and my whole family. A negative result in cases of tubercle may be due to an inactive serum, or to its having been washed out by the tears. In all cases where tubercle is suspected and the eye does not react, the experiment should be repeated with a 1 per cent. or even stronger solution, before the reaction can be said to have definitely failed.

Since Calmette published his results the test has been widely applied and extensive statistics are now at our command. The average opinion appears to be that the test is a very valuable aid to diagnosis, but that it cannot be regarded as an infallible index of the presence or absence of tubercle.

During the past week the kindness of my colleagues and the help of Dr. Richards, our senior house-surgeon, have enabled me to apply the test to most of the suspected or proved cases of tuberculosis in the hospital. They were first tested with the 0.5 per cent. solution, and the reactions were slight and in some cases equivocal. After an interval of three days the tests were repeated, the opposite eye being used. The results were as follows:

No. 1. Old-standing, advanced *phthisis*. Tubercle bacilli in sputum; slight reaction to 0.5 per cent. solution. This case gave a similar reaction three months previously.

No. 2. *Tuberculous knee*. Slight result with 0.5 per cent., very marked with 1 per cent.*

No. 3. *Tuberculous ankle*. Doubtful with 0.5 per cent., good with 1 per cent.

No. 4. *Tuberculous ankle*. Slight with 0.5 per cent., very good with 1 per cent.†

No. 5. *Periostitis of tibia*. No result with either; the case is probably non-tuberculous.

No. 6. *Abscess of lung, with consecutive empyema*. No result with either strength of solution.

No. 7. *Case of Cystitis and Probable Nephritis*. Patient is suspected to be tuberculous, but no bacilli have so far been found in the urine. The reaction to 0.5 was very slight. Splendid reaction to 1 per cent., with filamentous exudate.

One or two of the cases reacted to the weak solution after twenty-four hours. The serum was placed in the eye last thing at night; next day there was a very slight and doubtful reaction, but on the second day it became marked.

These 7 cases are only the last series of some 30 I have examined, and so far, as I have already stated, my own results have been such as to confirm the usefulness of the test.

J. Eyre, B. Wedd, and A. Hertz³ have tested 138 cases—63, or about half, gave a positive reaction, and of these the majority were unquestionably tuberculous. Two cases almost certainly tuberculous gave no reaction. A case of meningitis, which died thirty hours after the test, did not

* This reaction became very violent in both eyes, there was a mucopurulent discharge for a month, and phlyctenules appeared in the eye which had received the 1 per cent. solution.

† Very violent reaction, both eyes inflamed for a month; phlyctenules developed.

react, although tubercles were found on the meninges, but this harmonizes with the view now held that no reaction is to be expected during the last week of life.

[Dr. Harrison Butler then referred to the papers recently published in the JOURNAL by J. S. Gibb,⁹ W. MacLennan,¹⁰ J. Webster and Kilpatrick,¹¹ and Parkes Weber.¹²]

P. Brons¹³ obtained an excessive reaction in 5 cases. He holds that the ophthalmic reaction has dangers of its own, and should not be used indiscriminately. Sydney Stephenson¹⁴ says that in his opinion the ophthalmic reaction is a valuable means of recognizing tubercle.

The final verdict must be that of the physician, for a sufficient number of tuberculous cases do not come under the notice of the ophthalmic surgeon. I personally now use the test as a routine procedure in all doubtful cases of choroiditis or iritis, but I regard it merely as a help in diagnosis, not as an infallible guide. It is not nearly so accurate as the injection of tuberculin, but is probably as useful an indicator as is Widal's reaction in typhoid.

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A NOTE ON THE SO-CALLED STIMULATING EFFECT OF ALCOHOL ON PROTOPLASM.

By W. HENRY KESTEVEN, M.R.C.S.

HAVING regard to the conflicting beliefs and statements as to the action of alcohol in the human body, it occurred to the writer that in one way—in one particular, at least—he was in a position to investigate and to see for himself the actual facts of the case, and thus to be independent of the evidence of others. This one point was the action of alcohol on simple living protoplasm as seen under the microscope. The following record of observations pursued steadily for several months seems to throw a considerable amount of light on the supposed stimulating action of alcohol.

The experiments were made upon amoebae, as they seemed to be the best examples of simple protoplasm, which were easily visible.

There are different varieties of amoebae, but the point which makes them most useful for our purpose is the fact that although some of them are very small, and of little or no use for observation, others are decidedly the reverse. The writer has measured one such when it was extended in active locomotion, and found it to be $\frac{1}{2}$ in. in length, and about a quarter of that in width, that is, about $\frac{1}{16}$ in., other specimens only measured $\frac{3}{16}$ in., and others even less than that. All, however, present, according to the textbooks (Butschli, Gilbert Bourne, Calkin), an identical structure. They are said to consist of an ectoderm more or less hyaline, and endoderm with granular appearance, in which is imbedded a nucleus or sometimes two or more nuclei. When in active condition they move from point to point by means of projections or processes of the hyaline ectoderm, into which stream the granules of the endoderm. These processes are called pseudopodia. By means thereof they attach themselves to the substances with which they come in contact, and then by contraction of the pseudopodia they move their whole body.

They find their food in the water in which they live. The ectoderm closes over nutritious particles, which then pass among the granules of the endoderm. After a time such particles are found to be enclosed in a vacuole, containing also a clear fluid, in which the particles float. These are gastric vacuoles, and it is possible to recognize among their contents a variety of different objects which have been thus enveloped by the creature, for these vacuoles grow in size by coalescence, the granular appearance of the endoderm being in truth largely due to very minute specimens of such vacuoles, several of which will attach themselves or gather round a foreign body which has been thus sequestered, and by coalescence form a vacuole large enough to contain the object and the solvent fluids secreted for its digestion. These, which may be called the secondary vacuoles, also coalesce, mingling their contents, so