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. Brous¹³ 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.

REFERENCES.

- 1 W. Osler, *Principles and Practice of Medicine*, 6th ed., p. 350.
- 2 Libbertz, translated in Martindale's *Extra Pharmacopoeia*, 1898, p. 485.
- 3 BRITISH MEDICAL JOURNAL, vol. ii, p. 1235.
- 4 C. v. Pirquet, *Deutsche med. Wochenschrift*, May 21st, p. 885, and May 30th, p. 906; *Wien. med. Wochenschrift*, July 6th, 1907, p. 1370.
- 5 Lignières, *Académie des Sciences*, October 21st and 28th, 1907; see also S. Stephenson, *Ophthalmoscope*, December 1st, 1907, p. 689, for an account of these experiments in English.
- 6 *La Presse Médicale*, June 19th, 1907, p. 188.
- 7 Kalt, *Recueil d'Ophthalmologie*, October, 1907, p. 595.
- 8 Eyre, Wedd, and Hertz, *Lancet*, December 21st, 1907.
- 9 J. S. Gibb, BRITISH MEDICAL JOURNAL, February 22nd, 1908.
- 10 W. MacLennan, *ibid.* December 7th, 1907.
- 11 J. Webster and Kilpatrick, *ibid.*, December 7th, 1907.
- 12 P. Weber, *ibid.*, February 15th and 29th, 1908.
- 13 P. Brous, *Klin. Monat. für Augenheilk.*, January, 1908.
- 14 Stephenson, *Ophthalmoscope*, December 1st, 1907; BRITISH MEDICAL JOURNAL, October, 1907.

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

that in the larger specimens it is easy to recognize different varieties of diatom shells, desmids, crystals, vibriones, etc. When, however, by the action of the gastric secretion, the nutritious portions of the contained particles have been dissolved out and digested, the indigestible residue is expelled by the rupture of the vacuole at some point in the periphery of the body.

In the endoderm, and sometimes in the hyaline ectoderm, other vacuoles appear, from time to time, which contain only clear fluid. These, which in their earliest form, like the last described, are minute granule-looking bodies, increase in size in the same way as the others; that is to say, by coalescence until the repetition of the process causes distension beyond the retaining power of the surrounding body substance, when rupture takes place and the contents are expelled, sometimes with considerable impulsive force, as testified by the sharpness of the current formed in the water outside. These vacuoles are no doubt excretory in function.

For our purpose these three functions—locomotion, digestion, excretion—are sufficient, as they are the real measures of the vitality of the animals under examination. Solutions of alcohol in water from 1 per cent. upwards were used.

Having fixed upon the specimen on which the experiment was to be made, as soon as it was seen to be firmly attached either to the slide itself or to the cover-glass, by means of blotting paper as much as possible of the water was withdrawn from the slide, without actually leaving the specimen dry. Then the solution was allowed to take the place of the extracted water, thus drenching the animal. The process of withdrawal of the liquid was then repeated two or three times and fresh solution added until the drenching or immersion of the animal was complete.

ONE PER CENT. SOLUTION.

Several different specimens of amoebae were treated with this solution. The following is a description of the effect of the solution on a typical example of these.

The amoeba was a medium-sized one, actively moving about the field of the microscope. Immediately the solution reached it the locomotion ceased, and the granules of the endoderm stopped streaming. They massed together toward the centre, the ectoderm or hyaline portion surrounding them. The animal remained stationary for seven minutes; then movement commenced in the ectoderm, movement which is best described by the word "sprawling." Nodular pseudopodia were projected in all directions, without locomotion. A vacuole in the endoderm ruptured; this contained only clear fluid. The closure of the breach and the filling up of the cavity by the surrounding walls did not seem to be slower than usual, but there did not seem to be so much "snap" as in the natural animal. After twenty minutes the granules began moving about, but feebly, and did not stream into the hyaline portion, which continued "sprawling"; after thirty minutes locomotion recommenced, the granules streaming into the pseudopodia. At the end of an hour and a quarter vigorous locomotion was continuing, and the condition of the animal seemed to be identical with what it was before the solution was applied, although the supply thereof was kept up. In fact, the animal was now living, and evidently capable of continuing to do so in a 1 per cent. solution of alcohol.

TWO PER CENT. SOLUTION.

The animal, as before, a typical example of many under observation, was streaming in an elongated shape across the field, when the solution drenched it. Locomotion immediately ceased; an irregular spherical shape was assumed, the granules streaming hither and thither, but not into the processes of the ectoderm. These the hyaline ectoderm began to form in a sprawling manner, about twenty minutes after the solution reached it. In half an hour locomotion was resumed, but feeble and sprawling in character. This continued for an hour or so. Four and a half hours later the animal was found to be quite quiescent, in spherical form, and entirely detached from the glass. No further change was detected, although it was watched for some hours.

On the same slide, four and a half hours after the addition of the solution, a very large specimen was found, which was apparently quite unaffected by the solution. It seemed quite able to live therein, but all smaller animals were either torpid or dead.

On another slide the experiment was repeated with the 2 per cent. solution, but with no other result discoverable

upon two vigorous and fair-sized amoebae, than to produce temporary check to locomotion, followed by sprawling and irregular movements for about twenty minutes, after which living in the solution seemed to make no difference to either of them, though they were watched for eight hours.

THREE PER CENT. SOLUTION.

Movement of every kind suspended for seven minutes after drenching. Then the granules began to show movement, and the formation and rupture of vacuoles recommenced as before immersion in the solution. But there was no locomotion. In one specimen there were two or three vacuoles containing pigmented matter, reddish-brown in colour, and one that contained a clump of what looked like bacteria. This latter, about twenty minutes after drenching, ruptured, expelling its contents to a distance by the vigour of the closure of the space. After half an hour, all adhesion to the glass, either slide or cover, was lost, and the amoeba was floating loose, but occasionally projecting a nodular short pseudopodia, and the process of vacuolation still continued. No change took place for about twenty-two hours, except that when observed at that time the vacuolation had ceased, the animal was floating freely, no pseudopodia were being formed; it was, in fact, torpid or dead.

In some others observed the appearances were identical with that described. One only appeared to have greater resisting power, and recommenced locomotion about seven minutes after immersion; but it was jerky and irregular, compared with that of normal life. Vacuolation also seemed to have become slow; when the vacuoles ruptured the filling up was markedly deliberate. This retardation in the formation, rupture, and filling up of the vacuoles was observable in all the specimens.

FOUR PER CENT. SOLUTION.

Streaming locomotion, which was going on actively, was immediately suspended on drenching with the solution. After three minutes, sprawling projection of short pseudopodia commenced, with formation of vacuoles or clear fluid, then pauses lasting for periods varying from one to three or four minutes, during which no motion of any kind was detectable. About an hour later the torpidity became more marked; all attachment to the glass was lost, only a languid sprawling motion was occasionally visible. The animal assumed a mulberry shape and appearance, rolling about in every current excited in the fluid in which it was suspended. No change took place for seven hours, and though watched for twenty-four hours the condition remained the same, and was practically that of death.

FIVE PER CENT. SOLUTION.

A remarkably large specimen was found and drenched with the solution, but did not show any signs of being affected thereby for five minutes. Then locomotion quite stopped. Granular streaming became slow, sprawling set in, until about fifteen minutes after drenching, the body assumed a spherical shape, with the granules collected in a dense mass in the centre surrounded by a smooth hyaline margin. The appearance was very similar to that seen in the animal treated with 1 per cent. solution. It was quite detached from the glass, and in a state of complete rest. By close watching, however, about half an hour from immersion some slight movement was seen among the granules at one point. Also slight variations in the outer contour noted from time to time indicated that life was still present. Vacuoles then began to appear, first in the hyaline ectoderm, then, in about forty minutes later, in the granular endoderm.

About five and a half hours from immersion there was a formation of sprawling pseudopodia, the granular streaming being exceedingly slow. This condition without any locomotion continued for about sixteen hours, and then became more vigorous with sprawling locomotion, and in about two hours more—that is, in eighteen hours from immersion—the creature seemed quite recovered and as vigorous as in simple water.

This, however, was the only specimen that recovered; six other specimens, none of them so large, were examined, and all were undoubtedly dead in three or four hours, though watched for much longer.

SIX PER CENT. SOLUTION.

Immediate arrest of all motion. In about twenty minutes after drenching, it was a freely-floating, irregular,

spherically-shaped mass, all connexion with the glass having been lost, although it had been gliding along it with the regular streaming movement just before being drenched with the solution. In this condition, with absolutely no sign of life, it remained for six hours. At that point of time, the alcoholic solution in which it floated, was withdrawn entirely, and for it ordinary water from its native tank was substituted. But at the end of ten hours later there was no sign of change. The alcohol seems to have penetrated deeply into the bioplasm, for when the water took the place of the solution, the specific gravity of the body was less than that of the water, as shown by the fact that it floated against the under-surface of the cover-glass, rolling about with every current, in close contact therewith; whereas, when first discovered in the water, these creatures are always resting on the slide itself, though sometimes after they begin to project pseudopodia some of these in the larger specimens adhere to the under surface of the cover-glass. This specimen was a large and vigorous one, with vacuoles both digestive and excretory.

In another specimen treated with the same solution there was seen, following the arrest of voluntary movement, a peculiar shrinkage, the effect of which was to cause the hyaline portion of the body to appear almost to separate from the granular endoderm. In this latter there was observed for some hours a slow and irregular formation and rupture of vacuoles. But the result as to regaining activity and vitality was practically the same as that described above. This specimen was watched for about sixty hours, and with the exception of the formation of the vacuoles, mentioned above, and what was thought to be a slight attempt at sprawling motion in the hyaline part, about twenty-four hours after drenching with the solution, no signs of recovery were obtained. It might have been alive at the end of this period, as it was not tested with return to pure water. Admitting that it was still alive, it would appear that 6 per cent. of alcohol is really more than these creatures are capable of tolerating, and if it be not fatal to them yet renders them practically useless from deep torpor.

SEVEN PER CENT. SOLUTION.

This was a large-size specimen, streaming along firmly attached to the slide, occasionally changing its direction, by the projection of pseudopodia, at various angles to the original axis.

In it there was one conspicuously large vacuole among several other in the endoderm. This large vacuole contained a solid spherical granular mass, which slowly revolved by independent motion within the vacuole.

Directly the animal was drenched with the solution it stopped its locomotion, nor did it again exhibit that power. The mass enclosed in the large vacuole continued to revolve for some ten minutes after all other motion had apparently ceased. There were other vacuoles, smaller, and containing clear fluid—excretory—or fluid with a few granules which might be the remains of some absorbed material. About six hours later all these smaller vacuoles had discharged, and therefore disappeared. The large one was left, but the granular mass within it was disintegrated, and seemed to fill up the space. The hyaline ectoderm had become more distinct from the granular endoderm, but otherwise there was no change. It was watched for forty-eight hours, but was evidently dead, though preserved by the spirit from active decomposition.

Several other experiments were made with this solution, but the result was the same in all, death being practically caused immediately the animal was drenched.

CONCLUSIONS.

No stronger solutions were used. It was evident that although these animals could live in solutions of alcohol which did not exceed 5 per cent., yet that the effect upon them was in all cases the same, it being simply a question of the degree of paralysis induced. There was absolutely no sign of any stimulating effect. Torpor, followed in many cases to which the weaker solutions were applied by what is known as alcoholism, was the rule; and if life was maintained, it was rarely as vigorous as before the alcohol was added to the medium in which the creature was living.

MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL.

MUMPS REPRESENTED BY A PRIMARY ORCHITIS.

A boy, aged 7, was attacked by mumps. Three weeks later the disease appeared in the boy's mother. Finally, after another six days, the father began to suffer from left sided orchitis. He has now almost recovered. The parotid gland has not been affected. The many recorded instances of "metastasis" from the parotid to the testicle prove that, in not a few persons, the latter gland is almost as liable as the former to this strange affection. We ought not, therefore, to have much difficulty in believing that the testicle may sometimes be even less resistant than the parotid. Musser, indeed, writes concerning mumps: "The infection is recognized by the swelling of the parotid and submaxillary glands, or by the occurrence of orchitis" (*Medical Diagnosis*, p. 264). Most of the text-books, however, do not clearly indicate the alternative which Musser appears to recognize.

London, N.

O. E. HIGGENS.

HYPERSENSITIVENESS TO ANTIDIPHThERIAL SERUM.

THE interesting accounts given by Dr. Thorne Thorne¹ and Dr. Bligh² of the effect of antidiphtherial serum on them, encourage me to narrate certain experiences of the introduction of horse serums into my own person.

In the spring of 1901, as the result of infection of a scratch on my left thumb, the lymphatic glands in the corresponding armpit became red, swollen, and tender, and inflammation spread thence to the cellular tissue of that side of the chest. This was accompanied by vomiting, headache, sleeplessness, continuous high temperature for several days (104° F.), hæmorrhages from the nose and bowel, and great prostration. Antistreptococcal serum was injected subcutaneously, and decided amelioration occurred in the symptoms, whilst shortly afterwards suppuration took place at various points over the left side of the chest and axilla, necessitating numerous incisions. Another injection of serum was given about four days later. On neither occasion was any ill-effect produced beyond slight itching in the neighbourhood of the punctures.

Some eighteen months later a child suffering from diphtheria coughed some of its membrane into my eye. The same evening a small dose (1,000 units) of antidiphtherial serum was injected beneath the skin of my left forearm as a prophylactic. Two hours later, feeling far from well, I went to bed, but within a few minutes itching, quickly followed by swelling of the skin, began on the fronts of the thighs, and rapidly spread over the whole of the body, limbs, and head, until I felt like one huge urticarial wheal. The irritation was intolerable, and it was quite impossible to refrain from scratching—indeed, the only difficulty which seemed at the time to be of any consequence was to scratch a sufficient number of parts at once. This urticaria was accompanied by pain behind the sternum, palpitation, and a feeling of faintness, but no vomiting. These symptoms lasted about two hours, and then gradually passed off, and on the following day I was quite well.

Not unnaturally I was inclined to attribute this catastrophe—or, at least, its occurrence so soon after the injection—to the extensive destruction of my axillary glands eighteen months previously allowing the alien serum to escape the usual delicate attention by these structures, and to pass almost directly into the blood stream. The sequel seems to show that this hypothesis was not correct.

Last year I suffered from an attack of unilateral membranous tonsillitis, in all probability diphtherial. Within twenty-four hours of the onset antidiphtherial serum was administered, but this time I was very insistent that it should be into the *right* half of my body, and it was put into the right flank. Notwithstanding this precaution, within two hours the same phenomena occurred as on the former occasion—intense itching and swelling of the skin,

¹ BRITISH MEDICAL JOURNAL, January 18th, 1908.

² *Ibid.*, February 29th, 1908.