the cord. The posterior nerve roots were also degenerated, and the nerve cells in the cord showed marked pigmentation; in some places the whole cell appeared to be transferred into a mass of pigment. The blood vessels all showed marked thickening of their walls. In the upper dorsal region at one spot there was a small hæmorrhage in the grey matter of the anterior cornu. The lungs presented the appearances of pneumonia of a low type, but otherwise the organs were fairly healthy.

Dr. Hale White¹ reported a case of tabes with unusual symptoms, and among them a degree of abductor paralysis of the vocal cords which necessitated the performance of tracheotomy. In my case the extent of the involvement of the pharyngeal muscles rendering nasal feeding a necessity I believe to be extremely rare. Bloch,² in reporting a case of tabes with bulbar symptoms, stated that this condition has been referred to by two other observers only, Howard and Charcot. In his case there was only partial paralysis of the larynx, and no dyspnoea. Hemiatrophy of the tongue in tabes dorsalis was first noted by Charcot, and since then several French physicians have referred to it. Marie and P. D. Koch² called attention later on to the association of hemiatrophy of the tongue, with paralysis of the soft palate and vocal cord on the same side, and inferred from their pathological examinations that the muscles of the larynx and soft palate are innervated from the hypoglossal nucleus, as well as from those of the vagus and spinal accessory nerves. In this case there was, besides hemiatrophy of the tongue, bilateral abductor paralysis with paralysis of the pharyngeal muscles, rendering swallowing very difficult. I regret much that no examination of the medulla and nerves was made in this case to determine whether the paralysis of the pharyngeal and laryngeal muscles was due to degeneration of the nuclei in the bulb or to degenerations of the nerve roots or nerves.

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- ¹ *Lancet*, vol. ii, 1886, p. 1128. ² *Neurologisches Centralblatt*, 18, 1899, p. 344.
³ Contribution à l'Étude de l'Hémiatrophie de la Langue, *Revue de Médecine*, 8, 1888, p. 1.

EXPERIMENTS TO DETERMINE THE EFFICACY OF THE DIFFERENT CONSTITUENTS OF HAFFKINE'S PLAGUE PROPHYLACTIC.

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IN Haffkine's anticholera inoculations in India it was noticed that, whereas the case incidence among the inoculated was much reduced, the case mortality was not influenced; the inoculations produced a resistance against the invasion of the body by the cholera microbe, but no resistance against the toxins formed if they once caused infection.

Gamaleia showed that it was possible to immunise an animal against virulent microbes without it being immune to the toxins of the same microbe produced artificially in the laboratory. Behring and Kitasato showed that by inoculating an animal with increasing doses of toxin it could be rendered resistant to a lethal dose.

Haffkine acted on these observations in devising the plan of antiplague inoculations. He says: "When in 1896 I was confronted with the problem of working out a prophylactic treatment against the plague, I determined to put to test the ideas originated by the observation on our cholera patients, and to attempt, in the new preventive inoculation, to obtain at once a lowering of the susceptibility to the disease and a reduction of the case mortality. This I resolved to obtain by treating the system with a combination of bodies of microbes and of concentrated products of them. In giving the above considerations I beg that they should be considered as temporary, subject to modifications or to complete refutation."¹

The following experiments, of which a preliminary note appeared in the *BRITISH MEDICAL JOURNAL* for September 2nd, 1899, were done at the Plague Research Laboratory, Bombay, to try and supply experimental proof to this theory:

I had previously remarked that when several rabbits were inoculated with varying doses of a ten-day-old living broth culture of plague those that received the larger dose showed the lesser mortality. Arguing that when the larger dose was given a quantity of certain substances capable of conferring immunity or reducing the severity of the case were injected along with the living microbes, and that since a young culture

was used and the microbes presumably all living, this substance was probably contained in the broth acted upon by the growth of the microbes, I proceeded to inoculate a series of rabbits with increasing doses of living plague culture in broth.

In some previous experiments I had found that about 2 c.cm. of Haffkine's prophylactic per 1,400 grams of rabbit were sufficient to give immunity. In these experiments a smaller dose was taken because immunity was not wanted; what I wanted to find was whether there was any benefit in the larger dose of metabolised broth. Moreover, if the rabbits became ill it would be from plague, since the culture was not sterilised, and if more recovered after receiving the larger dose than was the case with those receiving the lesser it would show that the larger dose of metabolised broth tended to lower the case mortality.

Seventeen rabbits were inoculated with a broth culture of plague from the laboratory stock. Letter P. denotes that a post-mortem examination was made and the plague bacillus recovered from the heart blood.

Experiment I.

No.	Weight.	Result.
1 ...	2,020 grams inoculated with 0.175 c.cm. 8 days' old living culture.	Survived.
2 ...	1,480 grams inoculated with 0.25 c.cm. 8 days' old living culture.	Died in 64 hours. P.
3 ...	1,910 grams inoculated with 0.5 c.cm. 8 days' old living culture.	Survived.
4 ...	1,470 grams inoculated with 0.75 c.cm. 8 days' old living culture.	Died in 20 hours. P.
5 ...	1,540 grams inoculated with 1.0 c.cm. 8 days' old living culture.	Died in 64 hours. P.
6 ...	1,810 grams inoculated with 1.25 c.cm. 8 days' old living culture.	Survived.
7 ...	1,750 grams inoculated with 1.5 c.cm. 8 days' old living culture.	Survived.

Experiment II.

No.	Weight.	Result.
8 ...	1,000 grams inoculated with 0.5 c.cm. 8 days' old living culture.	Died in 75 hours. P.
9 ...	1,050 grams inoculated with 0.75 c.cm. 8 days' old living culture.	Died 6th day. No P.M.
10 ...	1,300 grams inoculated with 1.0 c.cm. 8 days' old living culture.	Died in 60 hours. P.
11 ...	1,450 grams inoculated with 1.25 c.cm. 8 days' old living culture.	Died in 60 hours. P.
12 ...	1,280 grams inoculated with 1.5 c.cm. 8 days' old living culture.	Survived.
13 ...	1,430 grams inoculated with 1.5 c.cm. 8 days' old living culture.	Survived.

Experiment III.

No.	Weight.	Result.
14 ...	1,750 grams inoculated with 0.5 c.cm. 11 days' old living culture.	Died 6th day. No P.M.
15 ...	950 grams inoculated with 0.5 c.cm. 11 days' old living culture.	Died 6th day. No P.M.
16 ...	1,880 grams inoculated with 1.5 c.cm. 11 days' old living culture.	Survived.
17 ...	940 grams inoculated with 1.5 c.cm. 11 days' old living culture.	Died 3rd day. 10 hours. P.

As a control to these, some of the culture that was used for the last four rabbits was filtered through a porcelain filter, and the microbes were washed off the candle into a quantity of sterilised water equal in amount to the broth culture taken. Four rabbits were inoculated.

No.	Weight.	Result.
18 ...	1,420 Grams. inoculated with 0.5 suspension	Died 4 days 20 hours. P.
19 ...	900 " " 0.5 "	Died 5 days 20 hours. P.
20 ...	1,290 " " 1.5 "	Died 3 days 23 hours. P.
21 ...	840 " " 1.5 "	Died 3 days 22 hours. P.

Thus, out of 10 rabbits inoculated with doses of 1 c.cm. and under of living plague broth culture, 8 died, and of 7 rabbits inoculated with doses over 1 c.cm. and up to 1.5 c.cm., only 2 died. It is evident that the larger dose contained sufficient active substance to reduce the mortality, and as the cultures were young it is more likely the substance was contained in the broth than in the deposit, which would consist almost entirely of living microbes.

Another experiment was made in which the supernatant fluid in the broth acted upon by the microbe was separated from the sediment of microbes and the two constituents tested separately and together with respect to their prophylactic properties.

Experiment IV.

A 21-day old broth culture obtained recently from a patient was filtered through a porcelain filter, and the microbes remaining on the candle of

the filter were washed off into a quantity of sterilised water, equal in amount to the broth of the culture taken. The suspension was heated at 60° C. for thirty minutes. Rabbits were inoculated as follows:

No.	Weight.
1 ...	1,750 grams inoculated with 3 c.cm. filtrate.
2 ...	1,150 " " " 3 " " suspension.
3 ...	1,150 " " " 3 " " " "
4 ...	1,610 " " " 3 " " " "
5 ...	1,150 " " " 0.75 " filtrate, 0.75 c.cm. suspension.
6 ...	1,150 " " " 0.75 " " 0.75 " " "

Immediately after they were inoculated in the other flank with $\frac{1}{2}$ of a suspension of a 3-days-old agar culture of plague obtained from the same broth culture. Two controls were also inoculated with the same quantity of the living culture alone. The controls both died, one in forty-eight hours, the other in three to four days; a large number of bacilli were found in the heart blood.

Nos. 1 and 2 both survived, but No. 1 was ill for six days.

No. 3 died in three days, but very few bacilli were found in the heart blood, either by the microscope or by cultivation.

No. 4 survived.

No. 5 died in forty-nine hours, but no plague microbes were found in the heart blood, so it cannot be said to have died of plague.

No. 6 survived.

It appears from this experiment that the filtrate alone conferred power to prevent or to modify an attack of plague; rabbit No. 1 probably had plague, but survived.

The suspension of sterilised microbes seems to have conferred bactericidal properties, for the blood of the rabbit No. 3 contained few bacilli compared to that of the controls.

The mixture of filtrate and suspension of sterilised microbes protected rabbits Nos. 5 and 6 from plague infection, for no plague bacilli were found in the blood of rabbit No. 5. The dose of the mixture was equivalent to 0.75 c.cm. of culture; this dose was taken, and not 1.5 c.cm., as appeared from the first experiments to be required, because in this last experiment older, and therefore stronger, culture was used.

Lustig and Galeotti² state that the immunising property is a nucleo-proteid contained in the bodies of the microbes, and that if Haffkine's prophylactic has any immunising property, it is due to the nucleo-proteid dissolved or still contained in the bodies of the microbe. But this would not obtain in the above experiments, for the cultures were made in slightly acid broth—that is, ordinary beef broth without the addition of an alkali, so the nucleo-proteid would not be dissolved. Moreover, the cultures used were young and the microbes probably all living and not in a state to give up their nucleo-proteid.

These observers advocate a prophylactic made of a solution of the nucleo-proteid obtained from microbes grown on solid media, and they say that Haffkine concurred with their view when he tried to test the strength of his liquid by the quantity of deposit produced in the cultures. This no doubt is so, for inasmuch as the bactericidal property is conferred by substances contained in the dead bodies of the microbes, he naturally tests the strength of the prophylactic by the amount of deposit. The primary object is to produce a prophylactic substance, but Haffkine, on theoretical grounds, thought the supernatant fluid, by virtue of the toxins, conferred power to withstand the toxins formed if the persons did contract plague after being inoculated—that is to say, it reduced the case mortality; for these reasons he preferred to keep the supernatant fluid in his prophylactic.

The foregoing results show experimental confirmation of the theory. I recognise that many more observations should be made. I used up all the rabbits procurable in Bombay at the time, and was unable to obtain any more, but I hear that these experiments have subsequently been repeated and confirmed by Captain Milne, I.M.S., at the same laboratory.

REFERENCES.

¹ A Discourse on Preventive Inoculation. Delivered at the Royal Society, Sweden, on June 8th, 1899, by W. M. Haffkine, C.I.E. ² BRITISH MEDICAL JOURNAL, February 10th, 1900.

SOCIETY OF AMERICAN BACTERIOLOGISTS.—A society of American bacteriologists has recently been formed, and held its first annual meeting at New Haven in December last in connection with the meeting of the American Society of Naturalists and Affiliated Societies. Over thirty bacteriologists from various parts of the United States were present, and twenty-six papers were read. Professor W. T. Sedgwick, of the Massachusetts Institute of Technology, was elected President, and Professor Conn, of Wesleyan University, Secretary and Treasurer for the ensuing year.

A CONTRIBUTION TO THE STUDY OF THE PITUITARY BODY.

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(PRELIMINARY COMMUNICATION.)

OLIVER and SCHÄFER¹ found that a saline decoction of the pituitary body of the sheep produces a marked rise of blood pressure when intravenously injected. Howell² observed that this effect is due solely to the infundibular portion of the body. He noted also that the result of one dose is to diminish, or even annul, the action of a second, unless a considerable time be allowed to elapse. He concluded that the active substance of the infundibular part of the pituitary body was not derived from the grey matter of the organ.

Schäfer and Vincent³ describe both a pressor and a depressor substance. The pressor substance is soluble in salt solution, insoluble in alcohol and ether. The depressor substance is soluble in salt solution, in absolute alcohol, and in ether. An alcoholic extract, therefore, would contain only the depressor substance. The active substances are not destroyed by boiling, and can diffuse through parchment paper. The results of injection as observed by Schäfer and Vincent are that the first dose gives a marked elevation of the blood pressure, while subsequent doses produce a fall. This fall (due to the depressor substance) is evanescent, and can be repeated at frequent intervals, the pressor effect, on the contrary, being produced only by the first administration. The work of Schäfer and Vincent was performed with material taken from the ox, and the animals used for experiment were cats.⁴

Our own investigations upon the pituitary body have been performed, as were those of Schäfer and Vincent, with ox material, but we have employed dogs and rabbits for purposes of experiment. Our results have been in the main confirmatory of those obtained by the above-mentioned observers,⁵ and we are able to add some facts in regard to the histological, chemical, and comparative physiological aspects of the question.

1. Since a saline decoction contains both the pressor and the depressor substances, we have chosen it as the starting point for further research. If this saline decoction be treated with excess of alcohol, a precipitate forms which contains nitrogen, is evidently proteid in nature, and cannot be redissolved in saline. The alcoholic filtrate from this precipitate evaporated *in vacuo* to dryness yields a residue soluble in ether, and which in saline solution produces marked depressor effects only. If our saline decoction of infundibular pituitary be half saturated with ammonium sulphate, a flocculent precipitate falls. This precipitate may be freed from ammonium sulphate by dialysis, and presents the appearance of a proteid body which is insoluble in distilled water, but soluble to a moderate extent in normal saline 0.9 per cent. This latter solution, when injected intravenously, produces only marked pressor effects of a lasting character.

2. We find that saline decoction of the pituitary body of teleostean fishes (*Gadus morrhua* and other species) produce effects identical with those obtained with mammalian gland, namely, a marked rise on the first injection, and a distinct fall on subsequent injections. This renders it probable that the pituitary body is functionally the same throughout the vertebrate kingdom.

3. The infundibular part of the pituitary being presumably nervous in structure, it may naturally be asked if any of the above-described effects can be produced by similar extracts of nervous tissues generally. We have devoted considerable attention to this part of the subject. Briefly, our conclusions are that all parts of the nervous system, but especially grey matter of brain, produce depressor effects which are not abolished by section of both vagi. We believe that the depressor substance in these tissues is not choline. The results were obtained with decoctions from material absolutely fresh, in some cases practically living; no pressor effects were ever obtained from these nervous extracts. Is, however, the depressor effect of pituitary due to the presence of nervous