dence of spinal disease. Albuminuria distinct, and physical signs of hypertrophy of left ventricle. No history of syphilis.

CASE XXX.—(By permission of Mr. N. M. MacLehose, M.B.) H. Y., aged 30. Homonymous diplopia observed over a period of six months without appreciable ocular paralysis; pupils of medium size, with definite Argyll-Robertson phenomenon; knee-jerks absent, and in later months decided ataxia and sensory defects in lower limb; visual acuity unaffected to ordinary tests, but gradual contraction of visual fields, especially on right side; chancre and secondary syphilis four years before.

There are in these series of cases many facts which might reasonably be made the subject of remark, and several of the cases are certainly of great individual interest. But they are here displayed in the above grouping for the purpose of illustrating the clinical order and sequence in which, as a matter of actual experience, the ocular disturbances of locomotor ataxia may manifest themselves in relation to the spinal evidences of that disease. Of course, in those cases in which there exists only a single ocular symptom unaccompanied by any sign of spinal disease, it may be objected that it has yet to be demonstrated that such cases are of the nature of locomotor ataxia. It is doubtless to be desired that such cases should be under exact observation as long as the opportunity for further developments exists—that is, for the entire life of the patient. But to insist upon such a condition is a mere counsel of perfection. One must make reasonable use of such evidence as the brevity of life and the exigencies of practice permit. And the evidence here set forth affords at least a very strong presumption, to say the least of it, of the truth of the doctrines stated in the earlier paragraphs of this paper. Probably the particular proposition which is most likely to be contested is the one which places the Argyll-Robertson pupil equally with optic nerve atrophy, and an ocular paralysis, as a possible first event in the eruption of the phenomena of locomotor ataxia. But on turning to the records it will be found that the facts support this suggestion almost as strongly as they support the corresponding suggestion in reference to optic nerve atrophy and ocular paralysis. Attention in this respect may be particularly given to Case XIII. The man complains of a quite recent diplopia, and he has undoubtedly had syphilis; the pupils show the Argyll-Robertson phenomenon. It is in the highest degree probable that had the patient been under observation a week or two earlier the condition of the pupils would have been the sole existing ocular abnormality. Yet in the light of the development of an ocular paralysis, it can scarcely be doubted that whether he develop spinal symptoms or not, his nervous system is the site of diseased processes of the locomotor ataxia order. When to these facts there are added, as in Cases XIV to XVII, illustrations of the various forms and degrees of evidence of spinal disease that may be associated with the Argyll-Robertson pupil, it seems impossible to resist the conclusions that the condition of the pupil so named may be the first evidence of locomotor ataxia; that it may precede by varying intervals other evidences of the disease; and that at least very probably, in a certain number of cases, the symptomatology of the disease may be permanently restricted to this one event. In some examples of its spinal form locomotor ataxia is undoubtedly an extremely chronic disease, with few and imperfectly developed symptoms; and it is thus not unnatural to expect that similar limitations may obtain in the ocular manifestations of the disease. That evidences of grave nervous disease may be limited to the pupil is well seen in Case XVIII, where a syphilitic patient was under observation for three years without the discovery of any abnormality other than paresis of each sphincter iridis. There is certainly no obvious reason why a similar restriction should not determine the Argyll-Robertson pupil as a purely isolated phenomenon with, it must be added, the same unfortunate possibilities that are undoubtedly attached to the patient whose case has just been quoted. The conclusions above adopted in reference to the Argyll-Robertson pupil are applicable *mutatis mutandis* to optic nerve atrophy and to ocular paralysis, as is abundantly demonstrated in the corresponding series of the cases recorded with this paper.

NOTES.

¹ In all the cases the ophthalmoscopic appearances were those of primary optic atrophy. ² This statement, both here and in other cases, must be taken as implying that there is a quite undoubted history of a primary sore followed by secondary symptoms; when the evidence is less conclusive the record carries a mere statement of the facts.

A SUM of 13,981 roubles has been collected in Russia for a monument to Pasteur.

CASE OF TABES DORSALIS WITH BULBAR SYMPTOMS.

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MANY observers have noted the affection of the larynx in tabes dorsalis, varying in degree from a slight alteration in the voice (depending, possibly, on ataxy of the intrinsic muscles of the larynx) to severe abductor paralysis, but I believe the following case to be exceptional from the severity of the laryngeal paralysis and the involvement of the other bulbar centres:

J. L., aged 50, married, and formerly a warder in a gaol, first came under my care as a out-patient at Prince Alfred Hospital some six years ago. He was subsequently admitted to the hospital as an in-patient on two or three occasions, and died while under my care in the early part of the year 1897. He gave the following history: About four years before he came to the hospital he suddenly lost power in the legs, and fell down as if he had been struck. He had no antecedent pains, and the weakness had been getting gradually worse. Up to a few months previously he had control over his bladder, but since then he had occasional incontinence of urine. His bowels have been very constipated. About two months before admission he noticed a difficulty in swallowing his food, and about a week later difficulty in breathing, especially at night; at the same time he began to make a great noise during inspiration, and to have some trouble in speaking. These symptoms have been getting gradually worse.

Previous History.

He had been a healthy man except for a slight touch of fever and ague about twenty years ago, and gonorrhoea seventeen years ago. This was not followed by any symptoms of secondary syphilis. He had been moderate in the use of alcohol. Family history showed nothing of importance.

Condition in February, 1895.

He is a tall thin man, but well built. Intelligence and memory good. No headache or pains anywhere; no convulsions, but has attacks of giddiness. Sleep is disturbed by his noisy respiration. His speech is thick and hesitating, and at times he appears to stammer.

Special Senses.—Smell is unaffected. Sight is fairly good, though he is presbyopic. Taste is impaired over the right side of the tongue. Hearing normal.

Cranial Nerves.—3, 4, 6. Pupils are unequal, left is slightly larger than the right. In the right eye the pupil does not react to light or on convergence, the left one reacts to light very feebly, and not at all on convergence. There is no ptosis or external ophthalmoplegia. 5. Tactile and painful sensation is impaired over right side of face; movements of jaws are normal. 7. No facial paralysis. 9, 10, 11. There is difficulty in swallowing, especially solid food. There is also complete paralysis of the abductors of the vocal cords, and during inspiration the cords do not separate, but tend to close together. The noise accompanying inspiration is so loud that he can be heard all over the ward. 12. Movements of the tongue are restricted; it is distinctly wasted on the right side, and it cannot be protruded very far. On protrusion the tip deviates to the right side.

Motion.—Muscular power is impaired in both legs, more so in the right than in the left. His arms are also weaker than normal, but there is no localised atrophy of muscle. He walks with difficulty, and cannot easily turn round.

Sensation.—Tactile and painful sensation is much impaired on both legs and arms. There is loss of muscular sense in the legs and arms, but more marked in the right than in the left arm. When standing on a hard floor he says he feels something soft under his feet.

Reflexes.—Abdominal and epigastric are feeble; cremasteric absent; plantar present on both sides. Left knee-jerk is very feeble, and right one is absent. No ankle clonus.

Sphincters.—Slight incontinence of urine, and bowels are constipated. There is complete loss of sexual desire and power. Romberg's symptom is well marked.

There are no vasomotor or trophic lesions. No gastric crises. He suffered somewhat from indigestion, but his other systems did not show any thing unnatural. His urine is normal.

Progress of Case.

The abductor paralysis seemed to progress, so that he became very cyanosed at times, and had great dyspnoea. This became so bad that tracheotomy had to be performed soon after his admission to hospital, and he was obliged to wear the tube up to the time of his death.

On his readmission to the hospital in February, 1897, the following notes were made: He is now very weak, and cannot walk in consequence of his inco-ordination. His eyesight has been failing much during the last few months; the pupils do not react to light, or on convergence. The tongue still deviates to the right on protrusion. He has lightning pains in the legs at times, but no girdle sensation. He has no control over his bladder, and the bowels are very constipated, so that he requires an enema always to secure relief. The knee-jerks are quite absent on both sides. His appetite is fair, but on attempting to swallow he almost chokes, so that feeding by the nasal tube is necessary. He subsequently developed signs of lobar pneumonia at the left base, and died after a few days' illness.

Necropsy.—There was some delay in getting permission to perform a necropsy, and the weather was very hot at the time. The whole brain and cord was removed and put into Müller's fluid, but as it was not in very good condition at the time, it did not harden properly, so that practically only the spinal cord could be examined microscopically. The cord showed sclerosis of the posterior columns, more marked in the upper dorsal and cervical regions than in the lumbar region, though some degeneration was found in those columns throughout the whole length of

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.

REFERENCES.

- 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