only sugar, since other reducing substances may be included). Further, in most of the cases which have been under observation for any length of time a definite excretion of sugar in the urine (as tested by Nylander's fluid) has appeared from time to time. So consistent have been the results that we have recently felt able to rely on this test to differentiate between simple and malignant cases. For example:

1. A fluctuating swelling in the neck, possibly inflammatory, showed reducing substance 0.34 per cent., and proved to be sarcoma.

2. A case with long-continued gastric symptoms, possibly malignant, gave a normal sugar content, and on laparotomy showed only simple ulceration.

3. Two cases diagnosed as tubercle of the lung gave reducing substances 0.24 per cent. and 0.32 per cent. respectively. Both proved to be malignant, whereas other cases of phthisis gave a normal result.

4. A case of acute pain in the pelvis, without obvious cause, gave reducing substance 0.29 per cent., and *post mortem* an annular carcinoma of the rectum was found.

We do not wish at this stage to enter into any discussion as to the relations of the high percentage of reducing substance as cause, effect, or concomitant, but merely to relate that through finding it we were led to try the experiment of feeding rats on sugar after they had been injected with a bacillus with filtrable spores isolated from a case of human sarcoma. This sarcoma was of the melanotic type, but the pigment was scanty.

Injections were made into the tails of eight rats. Three of the animals were large enough for the emulsion to be injected into the tail vein, but in the five smaller rats the injection was subcutaneous. All external evidence of the injection had disappeared in a week, but after five weeks a nodule the size of a split pea was found at the point of injection in one of the small rats. This proved to be mainly a spindle-celled growth with a few giant cells, but some of the cells contained pigment.

One of the larger rats died after six weeks and showed extensive growths in both lungs. Microscopically large areas of necrosis were seen with a margin of cells some of which contained pigment. The original sporing bacillus was regained from this growth.

Two large rats remaining alive at the end of two months were killed and found to have nodules of growth in the lungs; one also had a primary nodule in the tail.

Six rats inoculated with the same culture, but not fed on sugar, showed no evidence of growth locally or in the lungs after three months. Six other rats fed on sugar, but not inoculated with bacteria, likewise remained healthy.

In view of the interest of the subject and the fact that rats are so difficult for us to obtain, we shall be pleased to supply a subculture of this bacillus to any cancer research institute that may care to repeat our experiments on a larger scale, and we should like to suggest to those working with simple inoculable overgrowths that they try the effect of feeding the inoculated animals on sugar.

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THE PATH OF TOXINS TO THE CENTRAL NERVOUS SYSTEM.

BY

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THE statement that the infection of the central nervous system probably takes place from the mucosa of the nasopharynx is frequently made, and an examination of the possible routes of such an agent, toxin or whatever it may be, would appear to be of interest as affording a possible explanation of the sequence of phenomena commonly observed.

Two possible routes present themselves: (a) By the blood stream, either directly or after lymphatic absorption; (b) along the nerves. A consideration of the facts would seem to indicate that both routes are made use of.

In the condition encephalitis lethargica we might suppose the toxin to work its way up the motor fibrillae of the facial nerve.

The path through the cribriform plate—in spite of the fact that the nasal lymphatics have been injected from the subdural space, and the short route offered by the nasal nerves as far as the meninges and olfactory nerves through

the meninges—is negatived by the fact that a toxin arriving in the anterior cerebral fossa could hardly manifest itself first by a lesion of nuclei in the tegmental region of the pons.

The facial nerve, supplying the buccinator and labial muscles in relation to the oral cavity, and probably the levator palati and musculus uvulae (lesser palatine branch of sphenopalatine ganglion, via vidian, and great superficial petrosal), in relation to the nasopharynx, could afford a mode of entrance. In the substance of the pons the ascending portion is in the closest relationship with the medial longitudinal bundle, and in all probability contributes fibres to that bundle. In addition it embraces the nucleus of the sixth nerve, in much the same manner that the loop end of a hairpin, bent on the flat, might hold a pea in its concavity.

The nucleus most intimately related to the medial longitudinal bundle is the oculo-motor, the cells of which are indeed divided by that bundle into several collections, which have been supposed to preside over separate orbital muscles. Whether the fibres for the orbicularis palpebrarum arise from the oculo-motor and descend to the facial in this bundle, as was supposed by Mendel, or whether they arise in a superior part of the facial nucleus, it is not difficult to believe that the most intimate connexion between the latter nucleus and the third is with that part of the third which presides over the levator palpebrae superioris. The trochlear and abducent nuclei are also, of course, closely placed to the same bundle.

What, then, are the symptoms we might expect from a toxin ascending by way of the facial fibrillae and medial longitudinal bundle? They are facial paralysis, ptosis, abducent or other ocular paralysis. In fact, the localizing signs commonly found in encephalitis lethargica.

MacNalty has suggested¹ that the stupor in this condition is occasioned by the cutting off of the afferent sensory stimuli, by involvement of the medial lemniscus, owing to its proximity to these medial somatic nuclei in the tegmental region.

I would submit that, in the region of the third nucleus, the medial lemniscus is pushed some distance laterally by the nucleus ruber; also that the lateral lemniscus, conveying auditory impressions, would not be involved; and that the lesions, though bilateral, are usually asymmetrical, so that one half of the sensory tract would probably be but slightly damaged. Therefore, one could hardly suppose that the afferent stimuli could be so entirely cut off as to produce the degree of lethargy observed. In fact, the type seen more approximates to that produced by drugs.

It would seem easier to explain it on the assumption that it was the general effect on the cerebrum of the toxin absorbed by the blood stream. There could hardly be doubt that toxin so absorbed would reach the cerebrum far more rapidly than it could travel up the nerves; but that it would be diluted by the total amount of blood in the circulation, come in contact with a greater amount of antibody, and would be supplied in equal amount to all the body cells. To suppose that, distributed in this way, it could pick out individual cranial nuclei would necessitate the assumption of a special affinity of certain motor cells for a particular toxin, and that such affinity was not possessed by other motor cells serially homologous and structurally identical—a hypothesis which does not commend itself.

Group 1, therefore, in which we have lethargy and asthenia but no localizing signs, might be supposed to be caused by absorption from the blood stream, in which death or recovery takes place before sufficient toxin has ascended by the nerve paths to cause such signs. The succeeding groups are those in which we have the effects of both in varying degrees.

The twelfth nucleus may be affected either by spread along its own fibrillae or from its connexion with the medial longitudinal bundle. Professor Marinesco, in the report quoted, expresses the opinion that the toxin travels by the way of the nerves. I have merely endeavoured to find an anatomical explanation for the sequence of events.

If we apply this hypothesis to the conditions met with in diphtheria, we have the causative organism living, and pouring out its toxin, on the walls of the pharynx and larynx, separated by a devitalized mucosa from muscles innervated by the cerebral part of the accessory (by way of branches of the vagus to the pharyngeal plexus). Toxins ascending along the fibrillae of these nerves would

be conducted to the nucleus ambiguus, which also contributes to the vagus motor fibres for the heart. This would explain the association of dysphagia, and regurgitation of food through the nose (paralysis of the palatopharyngeal), with cardiac disturbance—an association commonly met with in post-diphtherial paralysis.

I saw an interesting example of the association of these nerve paths in a case of paroxysmal tachycardia. The patient, in the early stages, was sometimes able to cut short the attack by the act of swallowing—a reflex action in which the nucleus ambiguus would be predominantly concerned.

Turning to the problem presented by tetanus, we find two points in which there is a contrast with the conditions previously discussed. In the first place, the effect of this toxin upon the motor cells, if indeed its effect be upon those cells, is the reverse of paralysis; it produces increased excitability with increased output. This phenomenon is more readily interpreted as due to interference with the inhibition normally imposed upon external stimuli reaching the motor cells from the sensory side; so that the paralysis probably occurs somewhere in the reflex arc, between the synaptic endings of the afferent nerves round the cells of their terminal nuclei and the dendrites of the motor cells.

Secondly, it would seem that the toxin does not ascend along the fibrillae; for if that were the case the muscles of the reflex arc, along which it travelled, would, it might be expected, be the first affected. Presumably, then, it makes its way beneath the sheath, and on reaching the spinal medulla may be supposed to ascend beneath the membranes. When it is remembered that the motor nucleus of the trigeminal nerve derives most of its sensory stimuli from the terminal nucleus of the trigeminal afferent fibres, alongside which it lies; and that the tractus spinalis comes to the surface in the postero-lateral area of the inferior part of the medulla oblongata, in the region known as the tuberculum cinereum of Rolando; and that a toxin ascending beneath the meninges might be conducted up that tract, reason can be seen for what is otherwise difficult to understand—namely, why trismus should be the earliest, and in mild cases the only, manifestation of a toxæmia which, when sufficiently prolonged, affects the whole motor mechanism.

REFERENCE.

¹ Report on Encephalitis Lethargica, Local Government Board, New Series No. 121.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

A CASE OF SUDDEN MONOCULAR DILATATION OF THE PUPIL.

THE notes on the following case afford a striking example of how a purview of all the facts in connexion with a case, both relevant and apparently irrelevant, may help towards establishing a diagnosis, and how a quite justifiable absence of knowledge of an apparently irrelevant factor may cause failure to make a diagnosis.

A medical practitioner recently sent me a lady who had suddenly developed complete dilatation of the left pupil, accompanied by supraorbital neuralgia, some apparent slight paresis of the upper lid, and some nasal catarrh.

The condition came on after a cold motor drive. It had caused the practitioner some alarm, and he, in my opinion quite rightly, regarded it as a case for investigation. The possibilities were many and various, and the condition might well have been the precursor of serious nerve lesion.

When I saw her every trace of abnormality had disappeared; the eye was normal in appearance and function, the musculature of the eye, extrinsic as well as intrinsic, acted normally; the nasal mucous membrane was healthy and normal. I was convinced that some mydriatic had got into the eye, but there was no history of any "drops" of any kind having been used. I was not satisfied, and after an examination I elicited the fact that she had a sprained knee, that she had consulted another medical practitioner about this in another town, and that she had been given a liniment to rub the knee. She did

not know what the liniment was, but said that it contained "ammonia." The practitioner who sent her to me was not aware of this condition of the knee.

She told me that she had the prescription at home, and I asked her to go home and to telephone to me if it contained the word "belladonna." She rang me up in half an hour. The prescription contained belladonna, and the case was now clear. Unquestionably she had conveyed some of the liniment into her eye.

The case was not one in which I consider that I am entitled to credit, nor the practitioner who sent her to me to discredit; but I learnt a lesson and I pass it on as possibly being of value to others.

The accompanying supraorbital neuralgia, which had evidently not been severe, may have been due to the action of light (it was bright weather) on the relatively unprotected retina, and I have no doubt that the drooping of the eyelid was due to the unconscious lowering of the lid to shut off excessive light. I met the lady a few days later; there had been no further trouble.

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THE FORMOL-GEL REACTION IN SYPHILIS.

It has been said that "the performance of the Wassermann test involves one of the most complicated methods that have been applied to diagnosis in medicine,"¹ and many laboratory workers must have hoped that some day a simpler and more direct method of diagnosing syphilis would be found.

The *formol-gel reaction* recently discovered by Gaté and Papacostas² gives promise of reducing the diagnosis of syphilis to a degree of simplicity altogether unexpected. The method is as follows:

One cubic centimetre of the serum to be tested is placed in a test tube, two drops of formalin (40 per cent. formaldehyde) are added and the tube is shaken to mix the contents. After standing at room temperature for twenty-four to thirty hours the tubes are examined and the results read. A positive serum is found to have coagulated into a firm jelly, while a negative serum remains fluid. Gaté and Papacostas found that, in a series of over 400 serums examined, the results corresponded with Wassermann results in 85 per cent. of cases.

I have had opportunity so far of testing only a small number of serums by this method, and the results are given in the following table.

	Formol-gel.		Wassermann.	Condition of Serum.
	Fresh Serum.	Heated Serum.		
1		+	++	Jellied.
2		±	±	Semi-liquid.
3	++		++	Firm jelly; tube can be inverted.
4	—		—	Liquid.
5	—		—	Liquid.
6	—		—	Liquid.
7	±		±	Liquid.
8		—	—	Semi-liquid.
9		—	—	Liquid.
10		—	—	Liquid.
11	++	++	++	Liquid.
12	—	—	—	Firm jelly; tube can be inverted.
13	—	—	—	Liquid.
14	—	—	—	Liquid.
15	—	—	—	Liquid.
16	—	—	—	Liquid.
17	++	++	++	Firm jelly; tube can be inverted.
18	—	++	++	Firm jelly; tube can be inverted.
19	—	—	—	Liquid.
20	—	—	—	Liquid.
21	—	—	—	Liquid.
22	—	—	—	Liquid.
23	—	—	—	Liquid.

The following notes have been made during the tests:

1. The test tubes employed should be of the same internal diameter, so that the results may be strictly comparable.
2. A diameter of half an inch has been found the most suitable for use with 1 c.cm. of serum.
3. The amount of serum for a tube of this diameter should not be less than 1 c.cm. If less than this amount is used the result is obscured by capillary attraction.
4. In the case of a strongly positive serum there is definite coagulation into a firm jelly, which remains unbroken when the tube is completely inverted or even roughly handled—for example, thrown upon a table.

¹ Med. Res. Com. Spec. Report, Series No. 21.

² C. R. Soc. Biologie, November 20th, 1920.