eye vision $\frac{1}{2}$ to $\frac{3}{4}$. No error of refraction. No muscular derangement. Fields and colour perception normal. Things seen by the left eye appeared smaller than by right (micropsia). In both eyes optic neuritis presenting the typical "choked disc." The difference in refraction measured by the ophthalmoscope between retina and top of swollen disc equal to 4 D. Haemorrhage near disc in left eye. Macula lutea normal.

On December 7th, 1891, she was admitted to St. Mary's Hospital under the care of Mr. Critchett; and on December 10th she was also examined by Dr. (now Sir William) Broadbent. She left the hospital on December 22nd. There was a constant improvement in her sight and general health until the beginning of February, 1892. During the whole time the treatment consisted of iron, strychnine, and simple aperients, as she had been suffering continually with constipation. Neither mercury nor iodide of potassium had been given. She came to see me because some of the old symptoms, especially the headaches, had reappeared, when she presented the typical appearance of a patient suffering from chlorosis. She was put by me on iron and arsenic, from which time she made an uninterrupted and complete recovery, which has lasted now without any relapse for more than twelve months. Menstruation became normal at the beginning of 1893, and has remained so since; she has now the appearance of a perfectly healthy girl, in good spirits and able to fulfil all her duties with energy and pleasure. Her vision in both eyes is normal, both discs have cleared completely without showing any trace of former mischief.

It is apparent that the combination of symptoms which the case presented from November, 1891, was one pointing to brain disease, and although the treatment which was suggested by the accompanying evidence of extreme chlorosis proved successful, I still feel inclined to take this view of the cause of the double optic neuritis; looking upon it as brought on by some basilar meningeal disease of probably inflammatory character. Leber¹ was the first to regard this class of cases as "latent meningitis," and this view has been taken up and strengthened by Haab.² Although in this way the appearance of the optic neuritis becomes explainable as caused by central mischief, the connection between the latter, chlorosis, and irregular menstruation still remains obscure. It seems to me an unwarranted scepticism to look upon the combination of symptoms as a mere coincidence as some do. From a clinical point of view, a disease which appears during well pronounced chlorosis, uncomplicated with any other mischief, and which disappears together with the chlorosis after treatment directed against the latter, may rightly be looked upon as either due to the anæmia or to the irregularity of menstruation; but as for the explanation of this connection, we may still say what Foerster³ said in 1876, that as far as the connection between optic neuritis and disorder of menstruation is concerned, we only know that it exists. In my case the differential diagnosis⁴ between brain tumour and transitory brain mischief was difficult for three reasons: (1) The general brain symptoms were most in evidence; (2) the optic nerve presented the typical "choked disc," which at one time was considered pathognomonic of brain tumour; and (3) the diplopia. Cases of the same kind with the diplopia have been published by Oursel⁵ and Ray,⁶ while the appearance of neuritis with more or less severe brain symptoms without diplopia in disorders of the menstruation are of more frequent occurrence.

CARDIAC FAILURE IN INFLUENZA.

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THE extreme nervous prostration and vascular congestion of tissues which obtain in severe cases of influenza conduce to the gravest feature of the disease—failure of the action of the heart. The congestion, however, is really the result of the nerve affection, for, the sympathetic system being as much involved in the prostration wave as the cerebro-spinal, there is

to a greater or less extent paralysis of the vaso-constrictor fibres which maintain the tonicity of the arterioles; and undue dilatation of vessels, as a matter of course, means vascular congestion of tissues. For this reason, hæmorrhage from various mucous membranes, effusions into serous cavities, sudden and profuse diarrhoea, apoplexy or meningitis, congestion passing into inflammation of organs, may occur during the course of the disease; while the ordinary symptoms of uncomplicated attacks, sweating, pink eye, headache, etc., may also be traced to the same cause. That cardiac failure and sometimes fatal syncope, sudden or gradual, should tend to occur under such conditions is not to be wondered at. Manifestly this failure may arise from two causes, which may operate separately or in combination. The heart itself may be the prime factor at fault. Its own muscle, its ganglia, or its vagal centres may so suffer from the wave of nerve prostration as to cause impairment of its function. Or, secondly, the unusual fall in the blood pressure which is the necessary result of the general vascular dilatation, the great loss of weight of the column of blood against which the systole of the heart is directed, may be such that the heart, accustomed as it is to feel a given resistance to its energy, relieved of this sense, runs riot, beats against insufficient resistance, exhausts itself, and tends to stop in diastole. The following are cases illustrative of the heart failure to which I refer.

CASE I.—J. S., shepherd, aged 35, strong, healthy man, while engaged watching his sheep in the winter time, suddenly became unconscious; he remembered nothing till he found himself lying on the snow and his dog licking his face; he had been insensible for at least twenty minutes. When I saw him an hour later he was suffering from all the symptoms of the onset of influenza. After a severe illness, complicated by pneumonia, he eventually recovered.

CASE II.—R. B., gasfitter, aged 26, married, a healthy young man and a good athlete, with no constitutional weakness, early one winter's morning rose to go to his work. A short time afterwards he was found insensible, lying over a low stone "dyke" at the side of the road. An uncomplicated attack of influenza followed, characterised by excessive prostration.

CASE III.—M. R., healthy young woman, aged 18, after returning from a horseback ride, influenza being epidemic in the district, was suddenly seized with faintness and prostration. The heart and pulse gradually failed, coma ensued as if from cerebral effusion, and death took place ten hours after the onset of the seizure. The failure of the heart was only explicable on the hypothesis that it was the result of a wave of intense prostration, such as sometimes ushers in an attack of influenza.

CASE IV.—Mrs. W., healthy married woman, aged 39, the mother of a healthy family, in the course of asthenic influenzal inflammation of right lung, was attacked by palpitation and heart weakness. Failure of the heart set in, and death ensued three weeks after the onset of the illness.

CASE V.—W. G., gentleman's servant, aged 54, on reaching home after a long drive on an excessively cold night, fell heavily on the floor, was helped to bed, and for the next few days was the subject of extreme prostration. Heart failure then set in, accompanied by drowsiness, which developed into coma, such as might arise from serous effusion into the ventricles, and death took place four days after the onset of symptoms.

CASE VI.—Mrs. R., aged 52, mother of healthy family and a woman of strong constitution, was seized at bedtime with intense pain in the lumbar region. For the two following days she was unable to draw up her legs in bed. Gradually the pain left the back, and the symptoms of a severe attack of influenza followed. Pulmonary congestion developed into pneumonic consolidation at the bases of both lungs. The heart became weak and irregular; at one time she was pulseless and collapsed; under treatment, however, she rallied, and in a month's time was able to seek a change of air. This last case is interesting in reference to treatment. When pneumonia set in, one or two small poultices with mustard were applied, but soon discontinued for a wet cold pad between the lower angles of the scapulae posteriorly. As there was evident danger of heart failure, although the tincture of digitalis had been given regularly, two granules of Nativelle's digitalin, $\frac{1}{16}$ grain in each, dissolved in water, were administered by the stomach. Twenty minutes afterwards, the patient appeared to be sinking rapidly; the pulse at the wrist could hardly be felt; it was small, weak, and fluttering; the features, hitherto suffused, were blanched and drawn; the temperature in the axilla, taken with two different thermometers, registered only 95° ; the intellect was dull; the breathing short and superficial; only one sign was wanting to make one believe the patient moribund; there was no cyanosis. Under appropriate restorative treatment the signs of collapse abated; half an hour later, the heart and pulse were firmer than before the administration of digitalin. The blanching of the face, the loss of the pulse, and the fall in the surface heat (95°) were certainly the result of the digitalin by causing vasomotor constriction. The dose, $\frac{1}{16}$ grain, was not large, only moderate; given as it was, its action was certainly in this case much too sudden on the vaso-constrictor mechanism. The action of the drug on the heart, which was apparently manifested after the symptoms of collapse had passed, could not be said to counterbalance the serious primary symptoms which followed its administration.

Digitalis and its active principles must be used with caution. The sudden increase of blood pressure caused by vaso-constriction would in many cases of inherent heart weakness be certainly fraught with danger to the individual.

But the important question arises as to whether the action of digitalis upon the heart is not the mere consequence of

¹ *Die Krankheiten der Netzhaut und des Sehnerven*, 1877.

² Heinrich Wunderli, *Klinische Beiträge zur Ätiologie und Heilung der Sehnervenzündung*. Thesis, Zürich, 1890.

³ *Beziehungen der Allgemein-Leiden und Organ-Erkrankungen zu Veränderungen und Krankheiten des Schorgans*, 1876.

⁴ I may here mention a case exactly like the above with the exception that up to three weeks before death, when the last examination was made, no trace of optic neuritis could be found, although frequently looked for. She was seen by some of the most eminent neurologists, who considered the disease functional. She died suddenly during sleep. The post-mortem examination revealed a large tumour of the cerebellum.

⁵ Contribution à l'étude des affections oculaires dans les troubles de la menstruation. Thèse de Paris, 1885.

⁶ Eye Diseases from Suppression of Menses, *American Journal of Medical Science*, 1882, p. 383.

the increased blood pressure against which its work is directed. It is a well-known physiological fact that in cases of syncope due to loss of blood, the injection of a neutral fluid into the main arterial system will cause the flaccid heart to recommence its pulsations, simply mechanically, by giving the heart a heavier column to beat against.

The experiments of Brunton and of Schmiedeberg show that digitalin tends to paralyse voluntary muscle. Be that as it may, its primary action on the unstriated muscular fibres concerned in vaso-constriction is certainly of anything but a paralyzing nature. Its action on the heart muscle, which can neither be considered voluntary nor involuntary, is another matter. Further, my contention is borne out by the very precautions given as to the use of digitalis: "its administration is to be stopped on the appearance of a tendency to faint, and the patient must not be permitted to rise, especially not to rise to make water, lest fatal syncope occur." Such advice would be unnecessary if the heart muscle were really strengthened; if, however, the increased blood pressure caused by the action of digitalis on the arterioles be the true cause of the heart's efforts, any increase of this, such as would occur on the individual suddenly assuming the upright posture, would be liable to throw too great a strain upon the heart, and result in syncope, in cases where there was some inherent weakness of that organ.

Certainly digitalis is a most valuable remedy in the conditions which obtain in influenza; given in the stage where there is much vascular congestion of tissues, it must of necessity help to ward off further complications by its action on the vaso-constrictor mechanism; but, at the same time, it must be remembered that, in so doing, there is increased strain thrown upon the heart, and the patient must be kept as quiet as possible and in the recumbent posture, the more so if there be reason to suspect that there be inherent heart weakness.

Where there are signs of heart failure, it must be given with caution; it is good, inasmuch as it causes vaso-constriction and by the rise in the blood pressure steadies the action of the heart; it is bad, inasmuch as it tends to throw too much strain upon it and renders the patient liable to the occurrence of syncope.

VACUOLATION OF THE NUCLEI OF NERVE CELLS IN THE CORTEX.

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SINCE this morbid change was described by Bevan Lewis in connection with epileptic insanity, there has been considerable difference of opinion among various writers as to its cause and significance and the forms of insanity in which it occurs, and it is with the object of throwing some light on these points that this paper is written. My conclusions are based on the examination of seventy brains, taken indiscriminately. Fresh aniline blue-black sections were examined in every case under powers of $\times 450$ and $\times 950$.

The process, which has been frequently described, consists evidently first in a fatty degeneration of the nucleus, probably beginning in the nucleolus. The fatty matter is discharged into the cell protoplasm, and the nucleus retains its contour, but shrinks from within, leaving a vacuole.

Different opinions have been expressed as to what cells are most liable to the change. Bevan Lewis¹ found it "peculiarly common to the smaller cells of the upper layers, in fact, often limited to the second layer"; while Dr. Whitwell² states that it is most common in the deeper cells, and in this he is corroborated by Drs. Middlemass³ and Macpherson in cases reported by them. I find it most common in the second and third layers, while the granule cells of the fourth layer in the sensory cortex are much less liable to it than any others, and frequently escape entirely when vacuolation is common and advanced elsewhere. Drs. Whitwell and Macpherson⁴ found the fronto-parietal region specially subject to the change, the latter stating that in one of his cases it was only faintly apparent in the occipital lobe. The whole frontal

lobe, however, usually suffers severely, especially its orbital surface.

In the earlier stages the nuclear change may be the only morbid appearance, and, but for this, many of my cases might have passed for typically healthy brain. Later, however, other degenerations usually make their appearance. Vacuolation of the cell protoplasm has usually been described as part of the same process, but it appears to me to be, in the majority of cases at any rate, secondary to the change in the nuclei. It is rarely, if ever, present in brains which do not show vacuolation of the nuclei, while in many cases where large numbers of nuclei are in the early stages, the cell protoplasm is invariably healthy looking. Where the two coexist, it is usually the cells whose nuclei are most degenerated that show vacuolation. It is invariably accompanied by granular degeneration, with disintegration of the processes. I am inclined to regard it as part of a general break down of the cell due to disease of the nucleus and consequent impairment of the nutritive influence which Bevan Lewis suggests is normally exercised by the latter over the cell. In many of my cases, excluding those of general paralysis, the spider cells were increased in number and size, and stained fairly well with aniline blue black. Many of these contained oil globules. Dr. Campbell⁵ mentions fatty degeneration of the muscular coat of the smaller arteries as a constant accompaniment.

Bevan Lewis attributes nuclear vacuolation in epilepsy to "an intrinsic morbid factor in the cell itself." Dr. Middlemass has reported a case of phosphorus poisoning in which it was found with fatty degeneration of other organs. Drs. Miles⁶ and Macpherson have found it in several cases as a result of blows on the head. Recently Dr. Campbell has attempted to show that it is due in all cases to toxæmic conditions. The forms of insanity in which it occurs are so various, and in all except epilepsy it is so inconstant, that it is impossible to believe that the mental symptoms have any direct connection with it. I have found it in mania (acute, recurrent, and chronic), melancholia, dementia, paralytic, alcoholic, and senile insanities, and general paralysis. Dr. Campbell expresses some doubt as to its occurrence in dementia uncomplicated by toxic conditions, but I have found it advanced in three cases of dementia, dying of cerebral atrophy, in which the only other morbid appearance was marked atheroma of the arteries. With regard to Dr. Campbell's view, it must be admitted that the presence of toxins in the blood in his cases, and in many of my own was highly probable, but this does not prove them to be the cause of the lesion, and it seems hardly probable that so many different poisons should produce exactly the same appearance. Among my cases are three in which death resulted from syncope, due in two to valvular disease of the heart, and in one to fatty heart without any valvular lesion. In the latter, especially in those dying from cerebral atrophy and senile decay, and in those reported by Drs. Miles and Macpherson, in persons dying from the effects of blows on the head, it is difficult to see how a toxic element could exist. Again, in several cases in which vacuolation was well marked in the cortex I could find no trace of it in the cord, which would be equally exposed to toxic influences.

My opportunities of examining normal brains have been small, but I think it may be assumed that if vacuolation occurred without disordered functions, it would have been described before now. Taking for granted that it is necessarily associated with disordered action of the nerve cells, we have to consider whether it is a cause or effect of this disordered action, or whether the two together are produced by a third factor.

That it is the cause is rendered improbable by the fact that it is not constant in cases presenting as nearly as possible exactly the same mental symptoms; by the various and almost antagonistic character of the symptoms in different cases—exaltation, depression, convulsions, and unconsciousness; and by its occurrence as a result of blows on the head, where the interference with the functions, as shown by unconsciousness, was instantaneous.

That it is the effect of disordered action alone is contradicted by its occasional absence even in cases of great severity and long duration. Given, however, an additional factor in the shape of interference with the blood supply, I

¹ Dr. Lauder Brunton's *Pharmacology and Therapeutics*.