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.

By FRED. M. T. SKAE, M.B.,

Assistant Physician and Pathologist, Stirling District Asylum, Larbert.

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*.

think we have sufficient to account for the change. Disordered action, such as occurs in insanity, is—in the vast majority of cases, at all events—excessive action, and this means the necessity for increased oxidation and an increased blood supply, and if this is not forthcoming the necessary result is the formation of fat.⁷

Now, in all my cases, excluding general paralysis and epilepsy, there was, from diseased conditions of the heart, lungs, blood vessels, or the blood itself, some obstacle to the proper supply of blood to the brain. In epilepsy the sudden and excessive expenditure of nerve force is probably greater than can be compensated by any amount of dilatation of the blood vessels, even assuming, what is very doubtful, that extreme engorgement of the vessels encroaching on the perivascular lymph spaces favours an increased supply of oxygen to the cells. In general paralysis, though the blood supply to the cortex is evidently increased, the obvious interference with the lymphatic circulation must more than counterbalance any advantage gained by the mere passage of blood through the vessels. In concussion, the great disturbances of cerebral circulation, which, as Dr. Miles⁸ has shown, take place in that condition, appear quite sufficient for my theory. The influence of prolonged pyrexia, septicæmia, cancer, and exhaustion from acute mania in deteriorating the oxidising power of the blood are also necessary to account for some of my cases, and these, I think, will be admitted.

The exemption of the granular layer seems to me to favour the idea that defective oxidation is responsible for the change. These are comparatively small cells, situated at a depth in the cortex particularly rich in capillaries, and frequently escaping when all the other layers are extensively diseased. Their small size one would naturally suppose to render oxidation easier. The small cells of the first layer, on the other hand, are very liable to vacuolation, but these are in a region comparatively poorly supplied with blood.

My conclusions, then, are that the lesion is due to a disproportion between the blood supply and the activity of the vital processes going on in the cells, from increased action in the cells and interference with the circulation, or probably from either of these alone if extreme.

As to the frequency of the lesion, I can find no statement by any former writer on the subject. Of my 70 cases, it occurred to a greater or less extent in 56, or exactly 80 per cent., and this, I believe, shows it to be much more common than is generally supposed.

The early appearance of the lesion, and the large number of cells affected in acute cases, its occurrence in a case of typhoid reported by Dr. Campbell, and another in this asylum, in which no true insanity existed, and Dr. Miles's concussion cases, the subjects of which were not insane, all point to the possibility of a return to the normal condition from the early stages, as it seems hardly likely that a brain in which a large proportion of the nuclei are diseased can return to a normal performance of its functions without repair of the lesion. The discharge of oil from the nuclei, and its presence in spider cells if the theory of their depurative function be correct, are obviously an attempt at repair.

REFERENCES.

¹ *Textbook of Mental Diseases*, p. 481. ² Nuclear Vacuolation in Nerve Cells of Cortex Cerebri, James R. Whitwell, *Brain*, 1890. ³ BRITISH MEDICAL JOURNAL, December, 1891. ⁴ Vacuolation of Nerve Cell Nuclei in Two Cases of Cerebral Concussion, *Lancet*, May, 1891. ⁵ Vacuolation of the Nerve Cell of the Human Cortex Cerebri, *Journ. of Path. and Bact.*, February, 1894. ⁶ Microscopic Pathology of Cerebral Trauma, *Report from Laboratory of Royal Coll. of Phys., Edin.*, 1892. ⁷ Payne, *Manual of General Pathology*, p. 190. ⁸ On the Mechanism of Brain Injuries, *Report from Laboratory of Royal Coll. of Phys., Edin.*, 1892.

AN OUTBREAK OF SMALL-POX: VACCINATION AND REVACCINATION.

By SIDNEY H. SNELL, M.D. AND B.S. LOND.,
Medical Officer of Health for Grays, Essex.

DURING the year 1893 we had a series of some thirty cases of small-pox in Grays. As medical officer of health I saw all these cases, and as some twenty of them occurred in the private practice of myself and my partner, I gathered a few notes on the disease, and especially in its relation to vaccina-

tion. The outbreak was introduced by an unvaccinated child, the source of whose infection I could never discover. The disease in this child and also in a brother was strikingly mild, being, in fact, exactly like a case of small-pox modified by vaccination. The disease was not recognised, and the children were allowed about, when a neighbour, a woman aged 40, took the disease, and had a very severe attack. Of all the people in contact with the children this was the only unvaccinated person.

Of the six children who during the year suffered from the disease, four were unvaccinated. The other two children were aged 9 years and 13 years respectively. The one at 9 years showed very slight marks, and in her the disease was well marked. But the other, four years older, had four large marks, and the disease was limited to four vesicles on the face. There was no case of the disease occurring in any revaccinated person, although several such were closely and continuously exposed to the infection; but, on the other hand, of the twenty-four adult patients attacked, all except the one spoken of above were vaccinated in infancy, and many bore very good marks.

We had two deaths from the disease; one occurred in a woman aged 30, from confluent small-pox, and she had four distinct marks about the size of sixpences from infantile vaccination. The other death occurred in a woman aged 70. Two of the cases, men aged 35 and 29 respectively, had hæmorrhagic rashes preceding the proper eruption. In each case the rash occurred over both sides of the chest and abdomen, extending down to the thigh, but not over Scarpa's triangle, as usually taught. Both cases were extremely severe, with marked delirium, etc., though both eventually recovered. Infantile vaccination marks in each case were good. Three of the cases were second attacks, two in women above 60 who had their first attacks in childhood, and one in a girl aged 17 who had, or was supposed to have had, a former attack at the age of 7.

Practical acquaintance with this series of cases has altered somewhat my opinions on the relation of vaccination to the disease. In the first place, it seems a logical conclusion that infantile vaccination, efficiently performed, may not protect the individual after the age, say, of about 20 years, even from the severest type of the disease; but that vaccination and revaccination are a better protection than even an attack of small-pox itself.

I may mention two interesting points from the clinical side. The first is in the matter of diagnosis. Our first cases occurred towards the end of the influenza outbreak, which had been general. The pains in the back, the headache, and general *malaise*, especially the first of these symptoms, were strikingly similar, and I was surprised, on reading a very able little article last year in the BRITISH MEDICAL JOURNAL on the diagnosis of influenza, not to find this disease mentioned as one with which it might be confounded in the early stage. We found this at times a real difficulty.

The following case presents some interesting points. A woman, aged 24, about eight months pregnant, sent for me one night in the belief that her confinement was at hand, mistaking the very severe back pain for labour pain. She went well through a fairly bad attack, showed no symptom of abortion, and was confined in the ordinary way about five weeks afterwards. The baby showed no marks, but fifteen days after birth came out in a vesicular rash, the contents of the vesicles later becoming purulent. I presume this was an attack of small-pox, but the case certainly presents some deviations from what is usually taught.

I remember seeing some time ago, when resident obstetric assistant in University College Hospital, a case of small-pox in a woman pregnant about eight months and a-half. She did well, the child was born about the eighth day of the disease, and exactly six days after came out in a vesicular rash, obviously variola. In this case half the incubation period was *in utero* and half after birth. The former case would tend to show that the disease had occurred in the mother without rendering the child immune.

THE Medical Faculty of the University of Innsbrück has conferred the honorary degree of Doctor of General Medicine on the Austrian Minister of Education, Freiherr von Gautsch.