traced by a pen—if there be another—like the one which has wielded the most stately periods on traits of normal and abnormal human nature in the English or any other tongue —that of Henry Maudsley.

CLINICAL NOTES AND CASES.

*A Case of Chorea Gravis,** reported by J. W. Geddes, M.B., C.M., Assist. Med. Officer, and T. Aldous Clinch, M.D., Pathologist, Durham County Asylum.

The interest of the following case centres in the severity of the lesions, both macroscopic and microscopic, which were found post mortem.

The patient, aged 26, six or seven months pregnant with her first child, was admitted to the Durham County Asylum shortly after midnight, 17th May, 1898, in a state of continuous bodily movement and confined in a strait-jacket.

Family history.—An aunt is an inmate of this asylum. A father's half-sister died of phthisis. Several sisters died before the patient was born; one of these was very young, and succumbed to "brain fever."

Life history.—Previously healthy; has never suffered from chorea, fits, or insanity.

Present illness.—About two months before the illness began she moved with her vicious husband from one home to another, which, with systematic maltreatment and starvation, caused considerable depression. A month later choreic movements commenced, but she was not seen by any medical man till three days before her admission. Dr. Gordon Russell found her sane, but unable to walk owing to chorea, which increased in severity, while her mental state deteriorated *pari passu*. He recommended her removal to the workhouse infirmary, where she was certified insane and removed at once to the asylum.

On admission the choreic movements were wild and uncontrolled to an extreme degree, not limited to the limbs, but affecting the head and trunk also. Her face was flushed; she was bathed in perspiration; her limbs were considerably bruised. She paid no attention to questions, and only made inarticulate sounds.

* Read at the Annual Meeting of the Medico-Psychological Association, Edinburgh, 1898.

About 12.30 a.m. two drachms of paraldehyde were administered by the nasal tube. She slept till 3 a.m. In the forenoon of the same day she tossed wildly about, held in bed, for five or ten minutes, then she lay in an apparently comatose condition for about five minutes alternately. Paraldehyde again procured sleep till the afternoon. The lungs were then found to be congested, and the heart showed a mitral systolic murmur. On waking she fell into the same state as before. At six p.m. abortion commenced, and at 6.15 the membranes containing a dead fœtus were expelled unbroken. The uterus contracted well. Her strength rapidly failed, and she died at 8 p.m.

Post-mortem report.—Sectio cadaveris 18½ hours after death.

Body well nourished. *Rigor-mortis* passing off; lividity very marked, blotches on face and anterior aspect of trunk and limbs.

Head.—Scalp thick, tough and congested. Skull-cap thin, hard and very congested. *Dura mater* congested, otherwise normal. The great longitudinal sinus contains clot; the other sinuses contain fluid blood.

Beneath the dura on the right side, and practically corresponding in extent with the temporal bone, is a large blood-clot—soft and friable, evenly coloured throughout, and perfectly free in the subdural space. Its thickness at the centre is about 1·6 cm., and its volume, taken by the displacement method, is 28·4 c.c. Inferiorly it extends over the right side of the middle fossa and over the floor of the whole posterior fossa, descending into the spinal canal as far as the first cervical nerve-roots anteriorly. The source of this hæmorrhage was probably the posterior branch of the middle meningeal artery, but, except at the one point where it is injured, the vessel wall appears perfectly healthy.

On the left side there is a similar hæmorrhagic extravasation over the posterior half of the parietal lobe and over the external surface of the occipital lobe; no apparent source of this hæmorrhage could be found. It therefore appears probable that it arose from numerous minute points.

The pia arachnoid presents a smooth shining surface, engorged with fluid blood and intensely congested. In the pia arachnoid are many small hæmorrhages on the left side, chiefly at the anterior and posterior extremities of the hemisphere. It is slightly œdematous, very friable, but not thickened, leaving the cortex with difficulty, yet without tearing it.

There is very little speckling of the surface from bleeding points when the membranes are removed. The convolutions are but little wasted; on section the cortex is reddish brown, while the alternating areas of pallor are not so well marked. The white matter is only slightly congested, and of firm consistence. The ventricles are not dilated and the ependyma is normal; basal ganglia normal save for slight yellowish mottling of the optic thalami. The hemispheres are of equal weight.

The cortex presents a mottled appearance; areas of deep congestion alternate with areas of pallor, each being roughly of the size of a sixpence. One large patch of anæmia extends over the lower three quarters of the left motor area. Cerebellar cortex is congested. Medulla, pons, and basal vessels are normal.

Thorax.—Pericardium normal. Heart muscle firm, left ventricle slightly hypertrophied. Mitral valve slightly thickened; no vegetations.

Lungs congested and œdematous.

Abdomen.—Peritoneum normal. *Liver*, small patches of acute fatty change. *Spleen* normal. *Kidneys* normal. *Uterus* firmly contracted.

Microscopical Report.—Second left frontal convolution hardened in absolute alcohol and in formalin 10 per cent. Sections stained by Nissl's, Held's, Golgi's, and the Weigert-Pal methods, and with hæmatoxylin and eosin.

By Nissl's Method when hardened in Absolute Alcohol.—In the first layer of the cortex a few of the granule cells appear to be provided with longish processes, which are varicose and curly. In some preparations it is difficult to say whether or not these appearances are due to staining of the fibre of the tissue in the neighbourhood, but in others high magnification convinces us that these are genuine cell processes. The cells of the second layer show very marked degenerative changes, most of them presenting complete destruction of the chromophile elements. The nucleus generally shows a tendency to over-staining, and the perinuclear membrane is distinct. Held's method likewise reveals no structure where chromophile elements are absent. In many cells the nuclei have been destroyed, or dislocated, or dislocated and partially destroyed. It may be that these various lesions are due to faulty methods. In the third layer the destruction of the cells is less complete. Chromatolysis to a greater or less extent can be found in nearly all, and normal cells are only found with difficulty. Both layers likewise show cells or nuclei, which overstain and are shrunken, and also very thin, attenuated, and badly stained dendritic processes. Sometimes the cells are vacuolated.

In formalin specimens the methylene blue stain does not compare favorably with the alcohol-hardened, but in the former brings out the yellowish pigment, which is not at all conspicuous, and certainly not in excess.

In the hæmatoxylin specimens the cells are very badly differentiated from the surrounding matrix, but reflect the appearances of the Nissl method. In addition to this, however, they give a splendid picture of the axis-cylinders, which appear perfectly normal. The blood-vessels are distended with corpuscles, and there are a few capillary hæmorrhages. The walls are in many instances much thickened, and the nuclei do not stain normally, but

appear as somewhat lighter dots in the vessel wall (longitudinal section). Other appearances which suggest stasis are seen, such as the non-staining of the vessel contents, appearances like blood-plates, loss of distinctness of the corpuscles. In some of the larger vessels fibrin is distinctly seen spreading in threads among the corpuscles. The perivascular spaces are dilated, and in many instances granular *débris* can be seen in them.

The Weigert-Pal preparations stain very badly; the whole tissue appears speckled with minute blue dots resembling myelin, but too small to give a double contour. They are most common in the white matter, and gradually diminish in number toward the surface. The myelin sheaths scarcely take the dye at all when the fibres have left the white matter, and they appear broken and uneven; the usual varicose beaded appearance is never seen, probably because the myelin takes the stain so badly that it is not visible in so small a bulk. On the other hand, the vessels are stained exceedingly well, or rather the corpuscles in them are, and they stand out as clearly on the yellow background as the cells in a Golgi preparation. As in the case of the hæmatoxylin specimens, minute hæmorrhages are to be seen occasionally. The pia mater is infiltrated with corpuscles, which do not seem to be enclosed in vessel walls.

Golgi's method shows evidence of departure from the normal, the value of which it is more difficult to decide. There is a thick deposit of silver chromate in the first layer of cells and superficial part of the second one. Below this the second layer of cells on the sides of the convolutions is almost entirely unimpregnated, and impregnation gradually grows more perfect as the top of the convolution is reached, though even here it never reaches the same degree of perfection as the third layer. This layer, which is well impregnated, shows the following changes:—There are cells the bodies of which are swollen and rounded, giving off attenuated apical and other processes; there are other cells presenting a great diminution in the number and size of the processes. The absence of thorns is a common occurrence, and often renders recognition of the axis-cylinder no easy matter. Processes are often indicated merely by a series of fine dots, and in such cases no thorns or any appearance which suggests them are ever present. In other cases thorns may be represented by a row of fine granules at a distance from the processes corresponding with the end of a thorn; these dots in a few cases may have intermediate dots between them and the process; indeed, one finds stages between the complete thorn and the dot, and the dot may probably be regarded as the next stage to no thorn at all.

The changes so far described apply to the pyramidal cells. The next one we have seen only on the cells with the short or ascending axis-cylinder. This change consists of elliptical swellings or bulgings along the side of the dendrites. They are gene-

rally small, and may occur at the bifurcation of the process. In these cases the cell shows no thorns. They appear to be the same change, only less advanced, as that described by Berkeley in *Brain*, 1895, as occurring in the brains of alcoholic rabbits. Nearly all this type of cell show these changes. In a few instances pyramidal cells have been seen with a deep depression in their wall extending three quarters of the way across the cell; this appearance may possibly be due to defective impregnation.

Apart from cellular lesions, two other abnormal appearances have been shown by this method, and by no other. The one consists in globular swellings on the vessels like miliary aneurisms, and the other in large black globules like the ordinary amyloid corpuscle, but about twice their diameter. They look like osmic acid fat globules, but no osmic acid has been used in this method.

This completes the detailed account of the abnormalities found in this case, but we do not wish to suggest that all of them, more especially those seen by the Golgi method, are necessarily directly in relation to the disease.

To conclude, we find great congestion of the meninges, which has resulted in severe hæmorrhages. We note that the congestion diminishes in both directions as we depart from the arachnoid. The fact that the basal ganglia show no congestion to the naked eye is most interesting when it is considered how many high authorities consider them the seat of the disease. The yellowish pigmentation of the optic thalami is so constant that it cannot be regarded as having any causal relation to the disease. Microscopically we have noted severe degeneration of the cells and of the myelin sheaths of the axis-cylinders, a process also diminishing in intensity in relation to distance from the membranes. The appearances noted are, however, probably to be considered as a result rather than as a cause of the symptoms observed. Indeed, they bear a close resemblance to those reported when animals have been killed by depriving them of sleep. One change strikes us as unexpected, viz. the thickening, and that to no slight degree, of some of the blood-vessels. It is not confined to one coat of the vessels, but affects the media and externa chiefly. The appearances are those of a degenerative change occurring in previously diseased vessels, and the question arises as to the relation of this disease to the cause of death. Have these vessels, with their narrowed calibre, induced changes in inhibitory or regulating centres, which may have assisted in the provocation of chorea, or have they had no influence whatever?

The relation of rheumatism and chorea is one of perennial

interest. In the present case *we have no history of rheumatism, but a systolic murmur was present*, and we venture to state that, had this patient lived, the diagnosis would have been chorea with endocarditis. There was, however, no evidence of recent changes in any of the cardiac valves.

In conclusion, we draw attention to the acute fatty degeneration around blood-vessels of the liver, which may readily be overlooked. This points to a toxic cause, whether the toxin is introduced from without, or is produced by the body itself, or is manufactured by organisms within the body. If these latter had their seat in the cortex they would probably have been demonstrated by the methylene blue preparations, but we find no such appearances.

Our thanks are due to Dr. Gordon Russell and Dr. Wingrave for their kind assistance in endeavouring to obtain a complete history of the case.

Addendum on Methods employed.—In this work so many modifications of practical value have been introduced that it may be of interest to pathologists if I detail them as briefly as possible.

Nissl's Method.—Hardening in my own practice has always been accomplished by alcohol which is rapidly increased in strength till absolute.* The tissue is then fastened on a wooden block by melted paraffin, and cut under absolute alcohol on a sliding microtome as thin as possible. Paraffin embedding alone will give thinner sections than can be obtained in this way. As an alternative the alcohol may be washed out, the piece soaked for a few hours in dextrine, and then cut on a freezing microtome. After freeing the sections from alcohol or dextrine they are stained in the following fluid:

Methylene blue B. X. (patent Grübler) . .	3·75 grammes.
Green potash soft soap (Venetian) . . .	1·25 „
Water	1000 c.c.

The employment of soap is necessary for the cortex, though good results may be obtained from the cord without it. The special methylene blue is absolutely necessary.

For the cortex decolorisation is best accomplished by absolute alcohol alone. To facilitate mounting, the sections may pass from the dye for a few seconds into water. They

* 60 per cent. alcohol . . . 24 hours.
90 „ „ . . . 118 „
Absolute „ . . . till hard enough to cut.

are then decolourised on a slide, cleared with xylol, and mounted with Canada balsam.

The methylene blue stain gives results which are in my opinion unsurpassed by thionine or methyl violet, while the method with the correct dye is simple in the extreme. Formalin as a hardening agent gives poor and dubiously permanent results.

Held's method demands such thin sections that in general paraffin embedding is resorted to. Nissl long ago pointed out that this process destroyed or disorganised the chromophilic elements, and I have experimented in this direction with the same results. Much work has been published which loses a great part of its value because of this defect. By mixing equal parts of Nissl's blue solution with a ·75 solution of erythrosin a beautiful double staining is obtained: the Nissl granula are blue, the achromatic substance pink, the nuclear membrane and substance red, the nucleolus and intra-nuclear network purple. Decolorisation is obtained in absolute alcohol.

Golgi's Method.—After hardening for one or two months in formalin the pieces are placed in Müller's fluid for a week, and then with the usual precautions in 1 per cent. solution of silver nitrate (Bolton).

The silver is then thoroughly washed out by repeated changes of distilled water, the tissue soaked in gum (or dextrine) and cut on the freezing microtome. The embedding medium being washed out, the extraneous deposit of silver chromate is partially removed by strong potash (Bevan Lewis), which does not destroy these preparations as it does those hardened with osmic acid; they are then washed free from potash (at this stage, if desired, toning processes of various authors may be used), cleared with carbol-xylol (1—3), and mounted on cover-glasses in gum dammar. When thoroughly set these glasses may be turned upside down over a slide, the corners being supported by common glass beads fixed with gum dammar, for the slide must not come in contact with the mountant.

Weigert-Pal Method.—The method described by Bolton (*Journal of Anat. and Physiolog.*, Dec., 1897) has been followed, except that a mixture of bichromate of ammonia and chrome alum is used as the mordant, 1 per cent. of each, and that the sections are stained till very brittle, as short of this stage full impregnation of the cortical nerve-fibres is not obtained.

If the sections are supported throughout on small pieces of tissue-paper the fragility forms no obstacle to success.

The steps are, harden in formalin, cut sections on freezing microtome without embedding or washing, dye in Kulschitsky's acid hæmatoxylin, differentiation by Pal's fluids, washing, dehydration, &c.—by these means the tracing of fibres in the cortex is rendered very easy.

Discussion.

Dr. CLAPHAM asked upon what grounds was the patient sent to the asylum? He had a similar case in Sheffield, which he admitted into the Royal Hospital. It differed in the fact that it was not fatal, but there was no difficulty in treating the case in the ordinary wards of a general hospital.

Dr. FORD ROBERTSON, with regard to the use of alcoholic fixation, said that Continental observations upon nerve-cells had been made almost entirely with the sublimate fixation, and by those authorities alcohol was always said to be practically of no use. He himself did not see that the nucleus could by any probability be fixed, and he was sure that the post-mortem changes would be very great. He was entirely in favour of sublimate in the fixation of nerve-cells.

Dr. CLOUSTON desired to express great thanks to the reader of this paper. It made them realise how all-important pathological work was, and how much they were indebted to the younger members of the Association. In regard to the causation of such an acute case, his (Dr. Clouston's) choice would have lain in the diagnosis between acute rheumatism and the toxic effects of the dead fœtus. He was not aware that a dead fœtus could cause chorea. Such a cause might produce convulsions, and undoubtedly it could cause pneumonia, but it would be a new fact if poisons from a dead fœtus could cause chorea; while, on the other hand, they knew that rheumatism was intimately connected with chorea. If there had been a record of high temperature he would have favoured the diagnosis of rheumatism.

Dr. ALDOUS CLINCH said he stated expressly that it was only in the study of the cell that he regarded alcohol fixation as sufficient. He made no reference whatever to the complete study of the nucleus in his paper.

Clinical Cases. By F. GRAHAM CROOKSHANK, M.D.Lond., Assistant Medical Officer, Northampton County Asylum.

1. *Post-epileptic Hysteria.*

A MAN, E. C—, aged twenty-eight, is at present a patient in the Northampton County Asylum. This man has since childhood suffered from epilepsy, and although at one time the fits were for several years in abeyance, just now they are frequent and often severe. The attendants, who have known him for many years, state that while the severe fits are of the usual type, the lesser ones are often followed by "antics" and "playing the fool." In one of these less severe attacks, which I witnessed recently, the convulsions had all the characters of a genuine epilepsy, and were fol-