with insanity,—to this extent at least, of having the work of the superintendent made too departmental, and too little that of the practical physician. The departmental notion would be the ruin of their position and of their usefulness if ever it were carried out. It had been detrimental to the insane in every country where it had been adopted. There was a similar tendency threatening France—an apparent desire to make the superintendents of asylums stewards or managers, to insist on them concerning themselves with "beans and bedsteads" rather than with the cure of the insane. He sincerely hoped that this tendency would be resisted to the utmost by their Association as a body and by themselves as individuals.

Dr. A. E. MACDONALD, of New York, said that he had the honour of presenting his credentials as representative of the Medico-Psychological Association of America, and had further to thank the meeting for having conferred upon him the high distinction of election as an honorary member. He had listened to the President's able and broad-minded address with very great pleasure, and could endorse what he had said in reference to the Elmira Reformatory. In his opinion the efforts made to reclaim young criminals in that admirable institution had been largely successful. Elmira had given many a chance of becoming useful citizens, and he strongly supported further development of Mr. Brockway's work in America.

The resolution that the thanks of the meeting be given to Dr. Urquhart for his presidential address was then put by Dr. Rayner, and cordially adopted.

A New Nissl Method.—Normal Cell Structure and the Cytological Changes terminating in Fatty Degeneration. Some Remarks on Cell Physiology and its Relation to Insanity. A Note on the Use of Picro-formol generally, and in Bevan Lewis's Fresh Method. Being the Essay which gained the Bronze Medal and Ten Guinea Prize of the Medico-Psychological Association, 1898; by J. R. LORD, M.B., London County Asylum, Hanwell.

I. *General Remarks.* — It has frequently appeared to me that a rapid and easy method of staining according to Nissl would be of great advantage. It has been my routine practice

to cut a fresh section and to stain according to Bevan Lewis in every case of insanity in which an autopsy had been obtained, and from that to record a few microscopic notes. A fairly complete description of neuroglial changes could thus be recorded, but only in a minor degree the changes which had occurred in cell protoplasm, *i. e.* cytological changes and various degenerations. For this one has to stain according to the method of Nissl, a method which stands out supreme for this purpose. But even Nissl's method is by no means perfect, and there are many drawbacks and imperfections. Hardening in alcohol causes considerable shrinkage; in fact, the main part of the cell is occupied by the nucleus. Alcohol also largely dissolves out fat, and therefore fatty degeneration cannot be shown. Again, it is not every asylum laboratory that has equipment for Nissl's method, but every asylum has the means of making a Nissl preparation according to a way I am about to describe.

II. *Advantages of the New Method.* — (*a*) Sections quite freshly cut with an ordinary freezing microtome are used. This allows of large unshrunken cells being examined in place of the small cells, the result of hardening. (*b*) Alcohol not being used as a hardening medium, fat is not dissolved out. As a result I have been enabled to trace more completely the changes that a cell undergoes prior to fatty degeneration. (*c*) Simplicity of the process. There is no need for embedding. (*d*) Rapidity of the process. A good Nissl preparation can be obtained within thirty minutes of death. (*e*) This method shows more accurately the degree of separation of the tissue, an important point in cerebral pathology. (*f*) Neuroglia and blood-vessels are better stained.

III. *Picro-formol as a Fixing Agent.* — It was found impossible to subject a fresh section to Nissl's method without shrinkage and disintegration of the section. I therefore looked about for a suitable fixing agent. After trying many things (amongst which was osmic acid), a mixture of picric acid and formol was found to be the most suitable. Solutions of various strength were tried, and the best one was found to be—

A saturated aqueous solution of picric acid .	50 per cent.
Six per cent. formol solution in water . .	50 „

This solution is a good general fixative for all processes, and a good Nissl preparation can be obtained after some weeks' immersion, the pieces being taken, frozen, section cut and stained. For other methods the fixative can be washed out,

and in my experience I have never found it to interfere with future staining. This applies to all tissues, whether brain or not, and there is no more suitable medium for the preservation of tissues when found necessary to send them away for examination. It is to Dr. Graf that I owe the idea of a mixture of formol and picric acid.

IV. *The Method.*—A piece of fresh brain is taken (the fresher the better) about 2 c.c. from the central convolution with pia adhering, and frozen on a freezing microtome (pia towards the operator), one of the best being Fraser's modification of Cathcart's microtome. A little gum on the plate facilitates freezing. Sections are cut and immediately floated into water. They are then taken up on a slide and some picro-formol allowed to flow on. Care should be taken that the section floats on the fixative. The section is subjected to this for five to fifteen seconds, and then it is floated back on water. It is next taken up on a slide, and a ·5 per cent. aq. sol. of Nissl's methylene blue (Methylenblau patent B) is pipetted on just in the same way as was the picro-formol. It is now heated until the first bubble appears, and allowed to cool. The excess of stain is washed off, and a solution of aniline oil in absolute alcohol (10 per cent.) is allowed to flow on until no more stain leaves the section. Dry the section by pressing with blotting-paper, taking care to see that the surface of the latter is smooth, or the section will be torn. Origanum oil is next dropped on and removed, after clearing, in a similar way. Benzine removes any traces of oil left. It was usual to mount in a solution of colophonium in benzine in order to obtain a permanent specimen. The benzine was burnt off by firing. Others have recommended evaporating the benzine gradually by gentle heat. Neither of these plans is satisfactory. The following is better:—Melt some colophonium in a porcelain capsule, only adding a little benzine. Smear the melted colophonium over the section with a glass rod used horizontally. Now put on a cover-slip and heat until the cover-slip is in a satisfactory position. For this purpose use a thin sheet of asbestos mounted on wire gauze, and supported on a tripod over a Bunsen flame.

V. *Normal Structure of a Large Pyramidal Cell according to this Method.*—The cell consists of a mass of protoplasm of a roughly triangular shape. This is not constant, as many are distinctly stellate. The less the brain is hardened the fewer cells appear pyramidal. It has numerous processes, the main one being that which passes up to the outer layers of the

cerebral cortex. Staining by methylene blue reveals a fine fibrillation. Throughout the cell are small spindle- or rod-shaped bodies, which take on the stain deeply. The protoplasm about the nucleus appears to be deeper stained, but this is due to the greater thickness of protoplasm in this situation. The nucleus appears to have a capsule, and stains less deeply than other parts of the cell. An intra-nuclear network is easily made out. The nucleolus takes the stain deeply, and a clear endonucleolus can be frequently seen. I ought to mention that this is a more or less ideal account of structure, founded not merely on the microscopic appearances of human nerve cells, but also on those taken from monkeys, dogs, cows, pigs, cats, &c. In man, although one frequently sees cells which completely bear out this description, yet even in an apparently sane cortex the large pyramidal cells commonly show a mass of yellow material unstainable with ordinary aniline stains—a material which I have succeeded in demonstrating to be of a fatty nature. (See Section VIII.)

VI. *Some Further and less Definite Points of Cell Structure.*—Examination of the kitten's brain, fixed and stained immediately after death, shows points which I have never seen in human brain tissue. These may modify our views in some respects. The nucleus is not rounded, but irregular, in some almost stellate in shape. It takes the stain deeper than the main body of the cell. The latter is seen to contain an irregular coarse network with apparently clear interstices. Frequently two or more deeply stained nucleoli are present. The great majority of the cells are irregularly stellate. The structure of the outermost layer of the cortex is beautifully revealed, showing the occurrence of large stellate and spherical cells with cytological structure differing from all other nerve cells which I have examined. This will form the subject of another paper.

VII. *Changes in the Cell in Fatty Degeneration.*—One of the first changes is an enlargement of the nucleus. It becomes darker and granular. The ovoid bodies break down into smaller ones of varying shape. These are usually found about the proximal part of the cell. This is not constant, however, as sections show that any part of the cell may undergo the same change. These smaller bodies break down into smaller ones still. The nucleus loses its distinct shape, and cannot be distinguished from the degenerate cell protoplasm. The finer granules shade gradually into fat. As they change the stain affects them differently; at first

dark blue, then dark green, then light green, and finally yellow. Finally the cell breaks down completely and bursts. The contents escape, and there is nothing left but the stumps of the processes. Usually in any section all these changes can be noticed, sometimes one and sometimes another predominating. The earliest stages are the most difficult to recognise. Examination of a large number of sections shows that fatty degeneration is the common fate of nerve cells in insanity. This view is supported by the most recent results of chemical investigation.

VIII. *The Nature of this Yellow Material.*—I have been at some trouble to ascertain the nature of this yellow material. So far, in this paper, I have assumed that it is of a fatty nature. A difficulty (more or less imaginary) arises when we consider the fact that very few large pyramidal cells in thehuman cortex are without it, and the question arises, is it normal? I am of opinion that there is a degree of fatty change in an otherwise normal cell due to ordinary katabolism or natural gradual decay, but we never find in a normal cell all the series of cytological changes above described. These changes are distinctly pathological. I do not maintain that they occur only in insanity, because, as will be pointed out, there is every reason to believe that these cells are not the source of nervous energy, but are merely trophic centres. It is elsewhere that the origin of nerve impulse must be sought. Thus gross changes might occur in these cells and the person be quite sane; while, on the other hand, we know that such changes are commonly concomitant with insanity.

I believe that the essential pathological change which causes or accompanies insanity will, in the future, be demonstrated to occur in the outermost layer of the cerebral cortex, a region to which great attention has of late been paid, and justly so. But to come back to this yellow material. I had till quite recently failed to stain it with osmic acid, but lately have succeeded, the green stain ending where the black begins. After fixing in picro-formol for three days, sections were cut and placed in ·25 per cent. osmic acid for twelve hours. They were then counterstained with methylene blue, and the black staining of the yellow material was clearly shown. The whole of the degenerate material was, however, only partially stained, and thus I conclude that it is an intermediate product between normal protoplasm and fat. Moreover the degenerate material found in early stages of cell degenera-

tion is not affected by osmic acid. Ether and alcohol dissolve out a portion only, and thus confirm my opinion. From these considerations I am convinced that the protoplasm of these nerve cells ultimately breaks down into fat, which can be stained with osmic acid and dissolved in ether and alcohol, the intermediate products yielding negative results to these reagents.

IX. *Some Remarks on Cell Physiology and its Relation to Insanity.*—A most important question in cell histology is the question as to whether the minute fibrillæ of the nerve communicate directly with the nucleus, or pass independently through the cell, taking departure through another process. The enormous and far-reaching change the acceptance of this latter opinion would cause in our ideas on the function of these cells has largely hindered this opinion from being accepted, but there can be little doubt as to its correctness. I think that it has been clearly demonstrated that these fibrillæ neither end in nor have any direct communication with the nucleus. On examining these cells with the high power the fine fibrillation before noted is seen not to be interrupted by the nucleus, but to pass (at all events in the peripheral parts) straight through the cell. What, then, is the function of the nucleus? We can no longer hold the view that it has anything to do with the impulse (sensory or motor) passing along the nerve-fibre. We have no proof whatever that it either originates or receives an impulse. We can assign no function to it except a trophic function, having some nutritive influence on the nerve cell and the fibres in connection with it. We know that the first evident signs of active degeneration occur in the nucleus, and this may point to a trophic function. Otherwise there is no necessity to ascribe to the nucleus any function whatever. We might, indeed, look upon it as a relic of development, its function having ceased when the cell separated from its parent neuroblast after having performed its duty in karyokinesis. On first beginning these investigations I thought that a certain arrangement of chromophile granules might be associated with certain forms of insanity; but this has failed. Further investigation and experiment may show that certain forms of degeneration are associated with certain forms of insanity, but at the present I can only affirm that the commonest form of degeneration terminates in fat.

The ovoid bodies have excited much interest, but I doubt very much, after examining very fresh specimens, whether

they are not really the result of the splitting up of a general protoplasmic network of the cell. On this point I am still undecided.

If nerve cells are not the seat of nerve impulse, what is? This is a difficult question, and its solution is not within the power of the author. But, as before stated, I think that it will be found in the outermost layer of the cerebral cortex. Many considerations support this view. Everyone knows that gross lesions may affect large portions of the brain, and that the person may still retain undamaged mental powers. Also that most of the pathological changes said to occur in insanity are found in the brain tissue of perfectly sane people, with perhaps one exception, *i.e.* those changes affecting the membranes and the subjacent layer of grey matter. Even in slight cases of meningitis delirium is soon apparent. This is probably due to the spread of the inflammatory process to the layer immediately below the meninges. Further, if we grant that the nervous processes associated with mentalisation and consciousness occur in the outermost layer of the cerebral cortex we correlate these with a vast area, an area not only anatomically continuous, but also connected with every part of the brain. Thus I would account for sanity persisting in spite of wide-spread coarse brain lesions. Processes certainly pass outwards from the nerve cells in the deeper layers, and it would appear that the minute fibrillæ pass straight through the nerve cells to the outermost layer and there split up. The manner in which they end has not been demonstrated. Do they come in contact with cells there, or do they end in the matrix? As before stated, I have noticed peculiar cells in this layer in the kitten's brain, but have not yet demonstrated them in the human brain because of the difficulty in obtaining pieces immediately after death.

X. *Picro-formol in Bevan Lewis's Fresh Method.* — Experience shows that picro-formol can take the place of osmic acid as a fixative in Bevan Lewis's method. It should be used exactly in the same manner as osmic acid, and of the same strength as for Nissl's method. It is cheaper and less difficult to keep. The stain takes quicker, and neuroglia stains more deeply. Otherwise it has no advantage over osmic acid.

XI. *Concluding Remarks.* — Thus within a short time of the patient's death, and with very little apparatus, a complete account of microscopic appearances can be recorded. The piece of brain is taken, frozen, sections cut and stained according to Bevan Lewis and Nissl, and from these two sets

of sections changes in all the constituents of the cerebral cortex can be fully described.*

Description of Drawings illustrating these Changes.

FIG. 1 represents the appearance of a normal cell. The nucleus (*N*) stains lighter than the cell body. *N O* is the nucleolus with a clear endonucleolus. The ovoid bodies (*O B*) are stained deeply.

FIG. 2 represents an early stage of degeneration. The nucleus is enlarged and granular, while one of the processes shows the breaking down of the ovoid bodies into intermediate granules before becoming fatty.

FIGS. 3 and 4 represent later stages with the appearance of fat (*F*) and the different staining of granules (*G*) and intermediate granules (*I G*). The nucleus is scarcely distinguishable.

FIG. 5 represents a later stage still. The cell has burst, and nothing remains but the processes and *débris*.

The Specific Gravity of the Insane Brain.†

By FRANCIS O. SIMPSON, L.R.C.P.Lond., M.R.C.S.Eng.; Senior Assistant Medical Officer, Govan District Lunatic Asylum, Hawkhead.

THIS paper is only intended to be a preliminary note upon the specific gravity of the brain in the insane, and contains the results of experiments upon thirty cases conducted at the West Riding Asylum, Wakefield, during the early part of this year. Over 1400 investigations have been made upon these brains, and as the inclusion of data from different parts of the country might cause scientific inaccuracies, it has been thought advisable to publish the present results separately, prior to the initiation of a further series of experiments.

The most important work upon the subject undertaken in this country was performed by Sankey between the years 1846 and 1852, the material used being obtained from the London Fever Hospital. The paper in question appeared in the *British and Foreign Medico-Chirurgical Review* of 1853, vol. xi; it is of a most exhaustive nature, and is accompanied by numerous valuable tables.

The present series of investigation were conducted upon

* Since writing this paper I have had my attention directed to a method by Dr. Robert S. Cook, in which osmic acid was used as a fixative, and have repeated my experiments with osmic acid, which has failed as before to produce a good Nissl preparation.

† Prepared for the Annual Meeting of the Medico-Psychological Association, Edinburgh, 1898.