might be excited by flogging. If a drunkard could not of his own free will go out and do his morning work, that was, he held, the true therapeutic for criminal drunkards. It was said in the debate that harsh measures could not apply to the head of a family, but he had seen them effective even in the case of him who held the purse and dominated the household. With reference to what the President had said, some of his observations had expressed exactly what he (Dr. Wilson) desired to combat. The President said he had no doubt whatever that there were cases of marked hereditary alcoholism when the patient was foredoomed to drunkenness and failure in life. It might be so, but he (Dr. Wilson) held that that was not the attitude for them to adopt. To set forth a conception of the hereditary factor in disease which some authorities believed to be false, and to say here is a disorder which is due to devolution, and here is an unfortunate victim of abnormal degeneration, was wrong. He did not think they had any right to say to any man that he is born to be a drunkard.

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*The Normal Histology and Pathology of the Cortical Nerve-cells (specially in relation to Insanity).**

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IT was originally our intention to cover the whole ground of the pathology of the cortical nerve-cells in relation to insanity. But in the course of our more recent investigations we have been strongly impressed with the fact that there are certain as yet little known, but very grave fallacies, into which investigators in this field are in danger of running; and it seemed to us in the first place imperative to clear these up before formulating conclusions regarding the relation of cortical nerve-cell changes to insanity.

We shall therefore now deal only with these fallacies, with the occurrence of chromatolysis, varicose atrophy of the protoplasmic processes, and varicose hypertrophy of the axis-cylinder process in acute insanities.

We must first, however, briefly refer to present opinions regarding the normal structure of nerve-cells, and to the experimental production of the above-named lesions in these cells.

Normal Structure of the Nerve-cell.—The theory according to which each neuron or nerve-cell is a separate unit, communicating with other neurons only by contiguity of processes, and never by continuity of them, though it continues to be opposed by Golgi and others, is still maintained by the great majority of authorities. The question as to whether the

* Read at the Annual Meeting of the Medico-Psychological Association, Edinburgh, 1898, and illustrated by a microscopical demonstration.

protoplasmic processes subserve merely a nutritive function in relation to the remainder of the cell (as maintained by Golgi), or are also special receptive organs of nervous impressions, is one that is still in dispute. With regard to the appearances presented by nerve-cells in preparations stained with basic dyes, it is becoming clear that most other authorities are unable to accept Nissl's elaborate classification in all its detail as either of practical utility or warranted by the facts. Some of the terms he has suggested are, however, coming into general use. His division of nerve-cells into *somatochrome* and *karyochrome* is one that appears to have largely commended itself. In the somatochrome cells the protoplasm is well developed, and presents in preparations by Nissl's method numerous deeply stained bodies. In the karyochrome cells practically only the nucleus retains the stain, the protoplasm remaining clear. In the former group are contained the great majority of nerve-cells, including most of those of the cerebral cortex. The karyochrome cells have as yet been little studied. On the other hand, the somatochrome cells have during the last five or six years formed the subject of elaborate research by a very large number of investigators. It is now recognised that the protoplasm of somatochrome cells is composed of two different structural elements, namely, (1) the Nissl bodies (chromatic, chromatophile, or chromophile part), which stain deeply with basic dyes, and (2) the achromatic part, which is not stained by basic dyes. The chromophile part consists of elements which are generally spindle or rod-shaped. They occupy the greater portion of the cell-body, and in the large cells extend some distance into the protoplasmic processes. They are never observed in the axis-cylinder process, or in the cone from which this arises.

The achromatic part is in the processes composed of numerous distinct and exceedingly delicate fibrils; in the cell body of a network of similar threads, many of which are continuous with those in the protoplasmic and axis-cylinder processes. These fibrils lie embedded in an unorganised mass, which likewise does not stain with basic dyes. According to Lugaro and others the chromatic elements are lying in the spaces of the fibrillar network. Van Gehuchten, on the other hand, maintains that they are rather to be regarded as an incrustation upon the fibrils.

It is now universally conceded that the fibrils are the conducting portion of the neuron. Various views have been expressed regarding the function of the chromophile elements,

but the general consensus of opinion seems to be that they constitute a store of material which is utilised during the activity of the cell. The nucleus of the nerve-cell has lately been shown to have an exceedingly complex structure. As this matter is one that has no immediate bearing upon the changes to which we wish alone to draw attention, we shall not enter into it here. Suffice it to say that in sections from tissues fixed in corrosive sublimate and stained with a basic dye the nucleus of the nerve-cell presents a deeply-stained nuclear membrane, a comparatively pale intra-nuclear network, and one, or occasionally two, very dark nucleoli, situated generally about the centre.

Chromatolysis.—In 1894 Nissl described certain changes which he found to occur in the cells forming the nucleus of origin of the facial nerve after section of this nerve. To these changes, which, it has been found, can be similarly produced in other centres, Marinesco applied the name *chromatolysis*—a term which, though in certain respects a very unfortunate one, has since been so largely employed that it is not now likely to be replaced by any other. Chromatolysis implied originally merely disintegration of the chromatic elements of the protoplasm. When the term was first used the great importance of the fibrillar portion of the nerve-cell protoplasm had not been realised. Since this has been made the subject of careful study in normal and in pathological conditions chromatolysis has come to be employed in a much more extended sense, destruction of the fibrils, and also changes in the nucleus when accompanying or following disintegration of the chromophile elements of the protoplasm, being now regarded as part of the same pathological process.

Chromatolysis is seen perhaps in its most typical form in the corresponding cells of the anterior horn of the spinal cord after section of the sciatic nerve. The elucidation of the process we owe chiefly to the labours of Marinesco and Lugaro. About two days after the section the chromophile elements in the neighbourhood of the cone of origin of the axis-cylinder process begin to break up into fine granules, and to lose their affinity for basic aniline dyes. This change gradually extends to the remainder of the cell-body. In many of the cells it is followed by displacement of the nucleus to the periphery, and disintegration of the primitive fibrils of the protoplasm. In advanced stages the nucleus also disintegrates and becomes pale. The nerve-cells are not all affected equally by these changes. Many of them, indeed, remain perfectly

normal. Different degrees of chromatolysis may be seen side by side. The cells most severely affected become entirely disintegrated. Others, after three weeks or so, begin to undergo repair, and are restored to their normal state in from twelve to fourteen weeks from the time of section of the nerve.

Changes of an essentially similar kind, though often differing in many particulars, have now been shown to occur in the nerve-cells of the cord or brain in a very large number of different forms of poisoning produced experimentally. They have also been observed after ablation of certain organs, in experimental anæmia, inanition, artificial elevation of temperature, deprivation of sleep, &c., as well as in numerous affections of the nervous system in the human subject. In such cases chromatolysis may be partial or complete; it may be peripheral, perinuclear, or diffuse; it may involve the fibrillar portion of the cell, or leave it intact; and it may or may not be accompanied by changes in the nucleus, either in the form of displacement or disintegration. Lugaro, who has been the pioneer in the study of the morbid changes affecting the fibrillar portion of the nerve-cell protoplasm, believes that, while the alterations of the chromatic part are reparable, those of the fibrillar part are irreparable. Alterations of the nucleus are, he says, the last to occur, accompanying only the more grave alterations of the cytoplasm. He thinks it is probable that they are only determined when the resisting power of the cell has become exhausted. These conclusions, deduced from careful and laborious experimental observations, have, as we shall presently point out, very important bearings upon the pathology of nerve-cells in relation to insanity.

Varicose Atrophy of the Protoplasmic Processes.—The pathological value of many of the changes which have been described by various observers as recognisable by means of Golgi's method, has lately been seriously questioned. The observations of Hill and others have shown that the absence of gemmulæ in such preparations is not necessarily a pathological change. Lugaro,* who has all along expressed doubt as to the pathological character of the slight changes, such as swellings in the form of a rosary, recognisable by means of Golgi's method, has recently taken up a much stronger position in regard to the question. He says that personal experience has rendered him still more diffident regarding the

* *Rivista di Patologia Nervosa e Mentale,* 1897, f. 2.

value of these varicose atrophies. He states that he has been able to prove that such varicosities can be produced in enormous quantities by imperfect fixation, and that he thinks that it is also probable that mechanical maltreatment of the pieces of tissue, and even short action of the air upon them, are able to produce similar modifications. Even in normal preparations, treated with all possible precautions, he has sometimes found prolongations with the characters of the so-called varicose atrophy, changes which he thinks must be due to some cause which has escaped observation. In the face of this uncertainty of interpretation which the positive observation of protoplasmic varicosity presents, negative observations assume a greater value. In the course of his work upon the nerve-cell changes resulting from poisoning by arsenic and lead,* he has been able to establish the fact that even when the nerve-cell presents marked cytological alterations the external form of the element, as revealed by Cox's modification of Golgi's method, may appear quite intact. When alterations do appear in preparations by Cox's method, they affect specially the cell-body and large protoplasmic trunks, and, notwithstanding their presence, the fine branches and the gemmulæ may be preserved. He concludes that the methods of metallic impregnation do not reveal alterations except in their more advanced phases, when already it is possible to demonstrate distinct alterations by cytological methods. He is of opinion that it may be excluded that the alterations demonstrable with these impregnation methods begin in the fine protoplasmic branches, or that they are preceded by loss of the gemmulæ. It will thus be seen that Lugaro does not deny the occurrence of varicose atrophy as a pathological condition, but he recognises as such only a change which has characters of a somewhat different kind from those which have been described by many writers. It seems to us that these opinions regarding varicose atrophy expressed by Lugaro—than whom there is certainly at present no more reliable observer in the field of experimental neurology—are deserving of entire credence. We had ourselves long felt difficulty in accepting many of the views that were expressed regarding the significance of abnormal appearances to be observed in Golgi preparations, and even before reading Lugaro's paper above referred to we looked upon that form of varicose atrophy which he has observed in

* *Loc. cit.*

experimental lead poisoning as the only one that could be regarded as of a genuinely pathological character.

Varicose Hypertrophy of the Axis-cylinder Process.—With respect to this morbid appearance the matter seems to stand in much the same position. Little varicosities in the form of a rosary are certainly not exclusively produced by disease. We are inclined to recognise as pathological only a change of a much more gross character, consisting in a more general though still irregular swelling of the process, extending not infrequently to some of the collaterals.

Occurrence of these Morbid Changes in Cases of Acute Insanity; Histological Methods; Sources of Fallacy; Occurrence of Chromatolysis in Persons dying in General Hospitals.—We come now to the question of the occurrence of these changes in the acute insanities. That they do occur in the cortical nerve-cells in such cases has already been demonstrated, but we are not aware that any systematic research upon the subject has yet been recorded. We can scarcely include the recent work of Turner* in such a category, as it deals only with the giant-cells of the cortex; and we would further remark that the fresh methylene-blue method which he has exclusively employed is one upon which very little reliance can be placed for pathological research. It is capable of revealing with some distinctness the chromatic structure of the giant-cells, but we are certain that the same cannot be said of it with regard to the smaller nerve-cells. It is a noteworthy fact that very little work has been recorded upon the pathological changes in the nerve-cells of the cerebral cortex in comparison with that which has been published regarding the nerve-cells of the spinal cord. The principal explanation of this fact lies, we believe, in the circumstance that observers have experienced the greatest difficulty in satisfactorily applying to the small nerve-cells of the brain the staining methods which have proved so successful in the case of the large cells of the spinal cord and root-ganglia. Using Heidenhain's method of sublimate fixation, paraffin embedding, and staining with methylene blue, thionin, and toluidin blue, according to the technique now generally employed, we have seldom succeeded in obtaining clear views of the structure of the human cortical nerve-cells, more especially of that of the smaller cells. Moreover, in many instances we have found that the preparations are not permanent, fading to a serious extent even after a few days. Working for a long time

* *Journal of Mental Science*, July, 1898.

with both methods, we have become more and more thoroughly convinced of the superior value for the cortex of the methyl-violet method, which was first described by one of us in the *Journal of Mental Science*, last year.*

This method, when successfully carried out upon tissues fixed in sublimate, gives a view of the chromophile elements of the protoplasm which far exceeds in clearness and sharpness of detail any of the pictures which we have been able to obtain with the modified Nissl methods (Fig. 1). The smallest cells are as distinctly shown as the large ones. We have never seen the preparations deteriorate in the slightest degree. The method permits of the study of chromatolysis to very great advantage. It picks out with remarkable clearness ghost-cells and fragments of disintegrating cells, which for the most part remain quite invisible in Nissl preparations.

We have recently ascertained several important conditions upon which the success of this method seems to depend. In the first place methyl violet 6 B should be alone employed. The iodine solution must be fully saturated. The necessity of thoroughly drying the sections upon the heater has already been insisted upon; indeed, the reaction entirely depends upon the complete removal of water at this stage. Higher temperatures than 60° C. cause the methyl violet and iodine compound to decompose. With attention to these points we are now able to obtain practically constant results with this method. The following is a full description of the process as we now employ it for the cortical nerve-cells:

Fix very thin slices of tissue in saturated solution of corrosive sublimate in ·5 per cent. salt solution (Heidenhain) for twenty-four hours. Wash shortly in water. Place overnight in 80 per cent. alcohol to which has been added a sufficient quantity of alcoholic solution of iodine to give it a dark sherry colour. Change to methylated spirit (or alcohol of corresponding strength) with a similar quantity of iodine added. Renew this fluid next day. On following day change to methylated spirit without iodine. Cut sections preferably by the dextrine freezing method. It is essential that they should be very thin. Transfer the sections from alcohol to 1 per cent. methyl violet 6 B in water. Allow to stain for from five to ten minutes. Wash shortly in water. Place in saturated solution of iodine in 2½ per cent. potassium iodide in water for ten minutes. Wash sections in water. They may remain in this for an hour or so without suffering harm. Take a section up from the water on a perfectly clean slide. Carefully

* W. F. Robertson, "The Normal Histology and Pathology of the Neuroglia," *Journal of Mental Science*, October, 1897.

remove water from around it by means of a towel. Next, with a piece of smooth blotting-paper (folded double) firmly blot the section in the same way as one blots a sheet of wet manuscript. Immediately afterwards, without allowing the section to dry in air, pour over it some drops of a mixture of equal parts of turpentine and benzole. Place the slide upon a hot plate (described below), and thoroughly dehydrate the section at a temperature not exceeding 60° C. If the turpentine benzole tends to evaporate off the section, add more by means of a pipette. When dehydration is complete the previously black and opaque tissue assumes a dark blue and faintly translucent appearance. Generally from 10 to 15 minutes are required. When the section seems dehydrated remove the slide from the hot plate, allow it to cool, and then pour off the turpentine benzole. Decolourise with aniline benzole (1 to 2). The aniline oil must be perfectly anhydrous. Renew aniline benzole two or three times. When colour ceases to come out wash the section in several changes of pure benzole, and mount in balsam in benzole.

It is essential that the section should be completely dehydrated. Any spot in which moisture has been allowed to remain will be almost completely decolourised by the aniline benzole. On the other hand, it is important that the slide should be removed from the hot plate as soon as dehydration is completed, as the colour then begins to come out to some extent. While the preparation is being dehydrated on the hot plate the slide should rest on two parallel metal bars placed on the plate, so that the heat is transmitted only to the two ends of the slide. Such an arrangement will be found to prevent the turpentine benzole running off the section. A small spirit lamp placed below a metal plate resting on a tripod can be made to give a sufficient amount of heat to dry the sections satisfactorily.

We have also used Heidenhain's iron-hæmatoxylin method and staining with Delafield's hæmatoxylin, with a view to studying changes in the fibrillar portion of the protoplasm. They have not, however, been of much service to us for this purpose. Lugaro, who has chiefly advocated the use of these methods, has admitted that they do not succeed so well with the nerve-cells of the cortex as with those of the spinal cord and root-ganglia. We have also tried the method of chrome-oxalic fixation which Graf* has recently declared to be of such high value for the demonstration of the fibrillar portion of the nerve-cell. In our hands his solution has given results which are far inferior to those obtained by sublimate fixation. We notice that Graf has not recorded the results of any comparative observations of fixation by chrome-oxalic

* *State Hospitals Bulletin*, 1897, p. 368.

and by Heidenhain's sublimate, which is at the present day the reagent that is generally regarded as the best fixative for nerve-cells. After chrome-oxalic, as with sublimate fixation, normal nerve-cells stained by the iron-hæmatoxylin method present the chromophile elements so deeply coloured that the primitive fibrils are quite obscured except in the axis-cylinder process. It is only in cells that have undergone a certain degree of chromatolysis that these fibrils can be seen in the body of the cell by this method of staining. We are convinced, therefore, that the figure given by Graf as representing the appearance of a normal human nerve-cell stained by the iron-hæmatoxylin method, after chrome-oxalic fixation, must have been drawn from a cell which had undergone a degree of chromatolysis. It seems to us that this chromatolysis is sufficiently explained by the mode of death of the subject, *who was executed by electricity*.

Following the recommendation of Lugaro, of the many Golgi methods now in use we have employed solely the modification of Cox.

Before describing the morbid changes which we have found in the cortical nerve-cells in cases of acute insanity we have still to endeavour to explain the sources of fallacy to which we have referred. They depend upon the fact that there are certain causes which give rise to chromatolysis, or to conditions which more or less closely simulate it, in the cortical nerve-cells in all persons dying natural deaths. It is, therefore, essential to thoroughly understand the nature of these changes in order to be able to discount them, before attempting to draw any deductions as to the relation of acute insanity to chromatolysis. One factor which, it appears to us, we do not require to discount is that of structural modification due to functional changes in the nerve-cell. These have been shown by Lugaro to be of so slight a character that they may safely be neglected in pathological observations on the human subject. The alterations which it is essential to discount may be grouped under three headings:—(1) *post-mortem* changes; (2) senile changes; and (3) morbid changes which arise during the last few days of life in cases of death from natural causes apart from insanity.

It is only recently that *post-mortem* changes in nerve-cells have received the attention which they deserve. Several Italian neurologists* have recently made careful experimental inquiries into this subject. The results which they have

* A. Neppi, *Rivista di Patologia Nervosa e Mentale*, 1897, f. 4; O. Barbacci and G. Campacci, *ibid.*, 1897, f. 8; Giulio Levi, *ibid.*, 1898, f. 1.

recorded are in agreement as regards essential details, and it is therefore now possible to give a reliable description of these *post-mortem* changes. Our own observations so far as they have gone are entirely in harmony with the results obtained by these Italian observers. It will be readily understood that the rate of such changes depends largely upon atmospheric conditions, and will therefore vary considerably at different times. In the protoplasm the alteration takes the form of a gradual fragmentation of the chromophile elements, so that the cell assumes a powdery aspect (Fig. 2). Frequently there is a running together of the chromophile elements into several large masses. Before these changes have proceeded very far the chromophile elements begin to show diminished affinity for the basic dye, until after two or three days they entirely cease to retain the stain (Fig. 3). The most important change in the nucleus is that it stains deeply and diffusely. Only after three or four days have elapsed does it begin to disintegrate and become pale. The nucleolus retains its affinity for the stain for a still longer period. It will be seen that these alterations differ in some essential respects from chromatolysis. In *post-mortem* change the fragmentation of the chromophile elements is not in the first instance attended by diminished affinity for the stain. Indeed, Giulio Levi describes a preliminary hyperchromic phase. Further, the fragmentation and pallor always occur diffusely throughout the cell, and generally to an equal extent in all the cells. But the most important distinguishing feature, in the cortex at least, seems to us to be the deep diffuse staining of the nucleus. Chromatolysis in the cortex, except at a very early stage, is in our experience invariably attended by pallor of the nucleus. In their early phases at least, such as we commonly see in the human brains we examine, *post-mortem* changes in the cortical nerve-cells are, we therefore think, in most instances capable of being discounted without serious difficulty. We venture to suggest that some at least of the examples of "granular degeneration of the chromophilic material" recently described by Turner were of this *post-mortem* character. Two of the observers who have studied *post-mortem* changes experimentally have also used the method of Cox (Barbacci and Campacci). The results which they have obtained go to show that varicose atrophy, having the characters that we have referred to as being probably alone of an undoubtedly pathological character, is not simulated by such changes.

Hodge* observed in the course of his studies on the nerve-cells of honey-bees that with advancing age there are not only alterations in the nucleus and in the form of the cells, but at the same time a diminution in the number of existing cells. Lutzenberger† has found that in the healthy guinea-pig sometimes nearly one in every thousand nerve-cells shows evidence of disintegration, and he has suggested that in normal adult life a certain number of nerve-cells are always undergoing involution, or are in a regressive phase. It seems to us that there are the strongest anatomical grounds for believing that this theory is in accordance with actual fact. Probably the more advanced the age, the greater is the number of cells in a regressive phase, until in senility quite a high percentage is reached. We have recently had the opportunity of examining the brain of a woman who died at the age of ninety from senility uncomplicated by any serious organic disease recognisable at the *post-mortem* examination. Most of the cortical nerve-cells showed a large collection of yellow pigment in their interior, often replacing the greater portion of the protoplasm. A large proportion of these cells appeared otherwise perfectly healthy, showing very clearly marked and abundant Nissl bodies in the remaining protoplasm, and a normal number of processes. Very many of them, however, showed further changes of a disintegrative character, the stages of which appeared to be as follows. The protoplasmic processes slowly atrophy and disappear. At the same time the body of the cell gradually shrinks and loses its angular form. The Nissl bodies begin to break up and to lose their affinity for methyl violet. The nucleus begins also to disintegrate and to stain faintly. Finally there are seen only a few violet granules representing the remains of the nucleus and Nissl bodies, accompanied or not by some scattered granules of yellow pigment. Certainly not less than sixty per cent. of the cells in this case presented these disintegrative changes, and probably about ten per cent. had reached the last stages that can be recognised. It is further to be observed that there was an evident paucity of nerve-cells in the cortex, showing that many of them had entirely disappeared.

It is well known that pigmentary changes occur in the cortical nerve-cells in certain morbid conditions quite apart from senility. But to discuss this question would be to go beyond the limits that we have prescribed for this paper.

* *Journal of Physiology*, 1894.
† *Annali di Nevrologia*, 1897, f. 5.

We wish merely to direct attention to these senile regressive changes, and to insist upon the necessity of discounting them in studying the nerve-cells of the brain from any case in which senility is a factor.

We have made a careful study of the cortical nerve-cells of sixteen patients who died in one or other of the general hospitals of this city. In every instance we have found that chromatolysis was present, sometimes indeed in as many as from 10 to 15 per cent. of the cells. This may seem on first view a very surprising statement, but a moment's reflection upon some of the results which have been obtained in the experimental production of chromatolysis should, it seems to us, be sufficient to satisfy anyone that the occurrence of such changes in these cases is exactly what we should expect. An almost endless number of poisons, including many bacterial toxines, have been shown to produce chromatolysis in one or other of its forms, in a larger or smaller proportion of nerve-cells. Should we be surprised, therefore, that patients who die from such conditions as septic pneumonia, acute or chronic tuberculosis, exophthalmic goitre, or malignant disease, present a certain amount of chromatolysis in their cortical nerve-cells?

During the last few hours of life there is frequently a rapid invasion of the tissues by septic organisms. It has been shown that toxines such as they form are capable of producing chromatolysis with great rapidity. Chromatolysis has also been demonstrated to occur from inanition, want of sleep, experimental uræmia, and experimental anæmia; and Ballet and Dutil* found it in the cells of the spinal cord after occlusion of the abdominal aorta for only a few minutes. With the knowledge of experimental results such as these, we should certainly expect to find that a considerable percentage of the cortical nerve-cells of patients dying in general hospitals should show well-marked chromatolysis. But there is still in many cases another factor at work producing a similar change to which attention must be specially directed. Lugaro has recently† shown that experimental pyrexia causes complete disintegration of the chromatic portion of the protoplasm of cortical and other nerve-cells without producing any other very marked changes (Fig. 4). He found that all the nerve-cells were affected equally. Goldscheider and Flatau, who had previously studied these changes as they

* *Neurolog. Centralbl.*, 1897, p. 915.

† *Rivista di Patologia Nervosa e Mentale*, 1898, f. 5.

occur in the cells of the spinal cord, have observed that the condition is one that is capable of being repaired in the course of a few days. The important bearing that these observations have upon cortical nerve-cell pathology in the human subject must be evident to everyone. We have ourselves examined several brains, both from the insane and mentally sound, in which this diffuse change was a marked feature. It seems to us probable that the five cases described by Turner, in which he found the chromophilic material completely absent from the giant-cells, were cases in which this pyrexia change had occurred. It is particularly to be noted that in this chromatolysis from pyrexia the nucleus remains practically intact. It is therefore easy to distinguish the condition from chromatolysis of toxic origin, which in our experience is always, in the cortex at least, attended by marked changes in this portion of the cell.

A large number of careful observations upon the brains of patients dying in general hospitals is still required before it will be possible to fully discount in cases of insanity the cortical chromatolysis which is caused by the toxic substances generated in the course of other diseases. It is mainly the strong conviction that we have of this fact that has caused us to hesitate for the present to record the results of our observations upon the occurrence of chromatolysis in all the cases of insanity that we have studied. It is only in the acute insanities, and in general paralysis, that we have found a percentage of chromatolysis so high as to completely separate the cases off from those of the mentally sound.

The number of cases of acute insanity that we have been able to examine is six. All of them died from exhaustion, accompanied in some instances by hypostatic pneumonia. Three of them were acute manias, two acute melancholias, and the sixth was a remarkable case of severe recurrent mania in which an attack was followed by death from exhaustion. In the acute manias we estimated the number of cells affected by chromatolysis at about 50 per cent. in one case, 80 per cent. in another, while in the third every cell appeared to be involved. In the case of recurrent mania about 60 per cent. of the cells were affected. In the acute melancholias the percentage was much lower, being in each about 25 per cent. But the difference presented by the cortical nerve-cells in these cases as compared with the general hospital cases was not merely one of percentage of chromatolysis. There were also differences in the character of the

chromatolysis. It was in general far more advanced, cells in the last stages of disintegration being abundant (Fig. 7). At the same time the pale ghost-cells (Fig. 8), almost devoid of any stain, which are specially well brought out by the methyl-violet method, were present in far larger proportion in relation to the total amount of chromatolysis than in the general hospital cases. These features point distinctly to a much longer duration of the morbid process. It is further to be noted that, in some of the cases at least, there was an appreciable loss of a large proportion of the nerve-cells. We have already referred to the difficulty of studying the condition of the primitive fibrils of the cortical nerve-cells, owing to the want of a satisfactory method of demonstrating them. But the observations of Lugaro justify us in assuming that in all those cells which show distinct disintegrative changes in their nuclei the achromatic part of the protoplasm has also undergone disintegration. Such cells are irreparable and virtually dead. They cannot resume their functions, but must inevitably disintegrate and disappear.

We believe that in this complete disappearance of a large percentage of the cortical nerve-cells, and not in the mere loss of processes or in any peculiar morbid appearances of existing cells, we have the essential anatomical fact in the pathology of secondary dementia. We have certainly seen several cases of secondary dementia in which it could be demonstrated that at least 50 per cent. of the nerve-cells had entirely disappeared.

Regarding the causes of this very severe degree of chromatolysis in the cortical nerve-cells in these cases of acute insanity we hesitate to express any definite opinion. We would only point out that the form of the chromatolysis corresponds closely with that which has been found to occur in lower animals from the action of various toxic agents.

With regard to the occurrence of varicose atrophy of the protoplasmic processes of the cortical nerve-cells in the mentally sound and in the insane, the results of our observations have been exactly those that the experimental work of Lugaro would lead one to expect, viz. that in cases in which with Nissl's method, or with the methyl-violet method, there are found examples of very advanced chromatolysis, there are also to be observed examples of varicose atrophy of that form which, as we have already stated, can alone be relied upon as being of a genuinely pathological character (Fig. 10). We have found the condition in the brains of general hospital

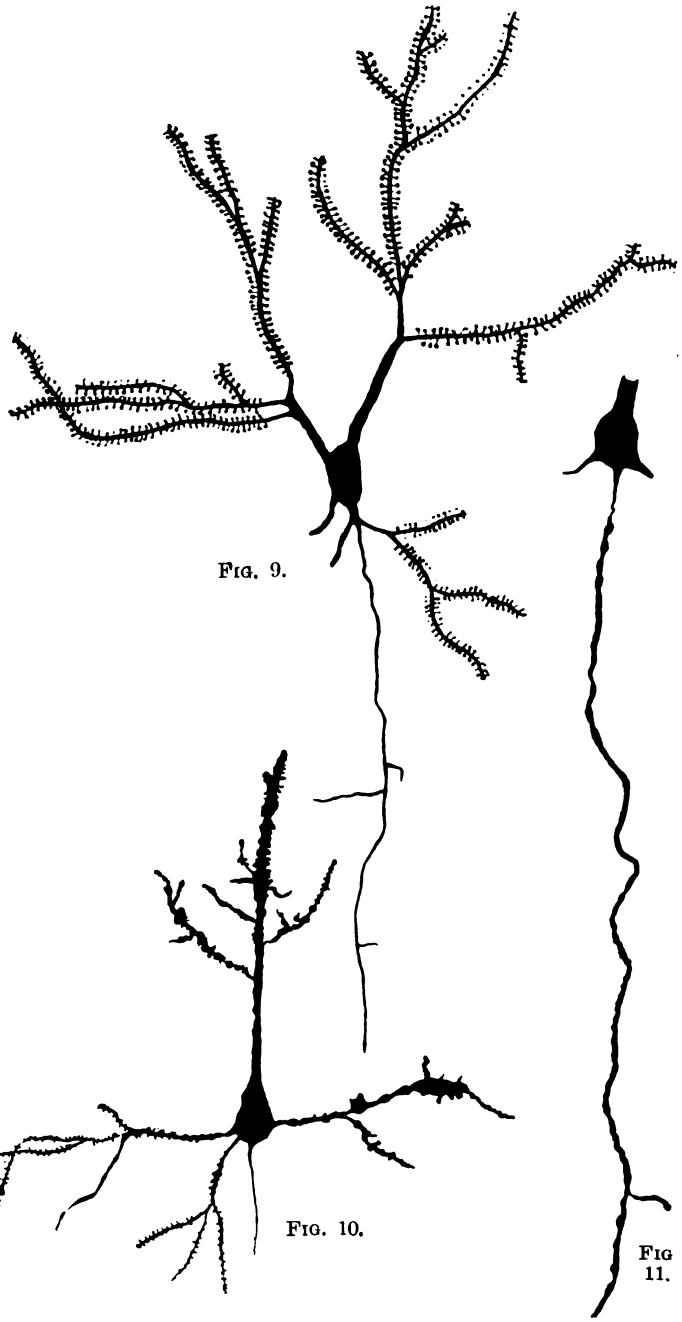

FIG. 9.

FIG. 10.

FIG 11.

To illustrate Article by Dr. FORD ROBERTSON and Dr. ORR.

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patients as well as in those of our cases of acute insanity, but to a far greater extent in the latter.

We have similar conclusions to record as to varicose hypertrophy of the axis-cylinder process (Fig. 11); but, regarding the significance of this change, we feel that it is necessary to speak as yet with still greater reserve.

Description of the Illustrations.

FIG. 1.—Normal pyramidal nerve-cell of human cerebral cortex. Methyl-violet method. (× 800.)

FIG. 2.—Pyramidal nerve-cell of human cerebral cortex, showing *post-mortem* changes. Methyl-violet method. (× 800.) The nucleus is stained deeply and diffusely. The chromophile elements of the protoplasm are partially disintegrated.

FIG. 3.—Pyramidal nerve-cell of human cerebral cortex, showing very advanced *post-mortem* changes. From a case upon which the *post-mortem* examination was made three days after death. Methyl-violet method. (× 800.) The chromophile elements of the protoplasm have entirely disappeared. The nucleus still stains deeply and diffusely. It shows slight vacuolation.

FIG. 4.—Pyramidal nerve-cell of human cerebral cortex, showing the type of morbid change that has been found to be produced by experimental pyrexia. Methyl-violet method. (× 800.) The chromophile elements of the protoplasm have disappeared, and the fibrils are abnormally prominent. The nucleus is stained deeply and diffusely, probably owing to *post-mortem* change.

FIG. 5.—Pyramidal nerve-cell of cerebral cortex from a case of acute mania, showing apical chromatolysis. Methyl-violet method. (× 800.) Note that the nucleus is involved in the morbid change.

FIG. 6.—Pyramidal nerve-cell of cerebral cortex from a case of chronic tuberculosis of kidneys and bladder, showing advanced chromatolysis. Methyl-violet method. (× 800.)

FIG. 7.—Group of three pyramidal nerve-cells of cerebral cortex from a case of acute mania, showing very advanced chromatolysis. Methyl-violet method. (× 800.)

FIG. 8.—Pyramidal nerve-cell of cerebral cortex from a case of severe melancholia, with death from exhaustion, showing very advanced chromatolysis. Methyl-violet method. (× 800.) This is a *ghost-cell*, or a cell which, while its original form is fairly well preserved, presents no affinity for stains. In many instances such cells are perfectly colourless in preparations in which other healthier cells in the immediate vicinity are deeply stained.

FIG. 9.—Nerve-cell of cerebral cortex of dog, showing protoplasmic processes with gemmulæ, axis-cylinder process, and collaterals. Cox-Mirto method. (× 500.)

FIG. 10.—Pyramidal nerve-cell of cerebral cortex from a case of chronic tuberculosis of kidneys and bladder, showing varicose atrophy of protoplasmic processes. Cox-Mirto method. (× 500.)

FIG. 11.—Axis-cylinder process of cortical nerve-cell from a case of exophthalmic goitre, showing varicose hypertrophy. Cox-Mirto method. (× 500.)