of middle and lower thirds, than on the opposite side. The lateral ventricles are dilated; within them the choroid plexuses, also enlarged, are seen. *cal. f.*, calcarine fissure. Other letters as in the preceding figure. × ¾.

FIG. 4 D.—Horizontal section of the brain, made in the plane D D, Figs. 2, 3, 4 A, 4 B, 4 C. The section passes through the area of defect. The anterior portion of the left island of Reil still persists, covered by the posterior extremity of the third left frontal gyrus, which passes much farther backwards than on the right side. Posteriorly the splenium of the corpus callosum is seen, with a portion of the lateral ventricle, *l. v.*, containing the choroid plexus, bounding it on each side. In front of the splenium is a portion of the velum interpositum, in which the two veins of Galen lie; and anterior to this, in the middle line, the cavity of the third ventricle is seen. Externally, on each side, lie the optic thalami, the left being smaller than the right. Outside the thalami are the lenticular nuclei; the left is slightly smaller than the right. The caudate nuclei, which lie more anteriorly, are of equal size. The anterior limbs of the internal capsule are well developed on both sides; the left posterior limb is smaller than its fellow, and its anterior end is indistinct. The basal ganglia are somewhat distorted on the left side. Between the caudate nuclei lie the anterior horns of the lateral ventricles, separated by the anterior pillars of the fornix and the septum lucidum, in front of which is the genu of the corpus callosum. × ¾.

Concerning the Significance of Central Chromatolysis with Displacement of Nucleus in the Cells of the Central Nervous System of Man.

By JOHN TURNER, M.B., Senior Assistant Medical Officer, Essex Asylum.

A LARGE amount of both experimental and clinical work has now accumulated around this subject. I need only briefly mention the main results of the former, as they have been so often referred to by others that they are now probably familiar to all workers in this field.

Nissl, in 1894 or thereabouts, showed that shortly after section or injury of the axons of the hypoglossal cells, these cells showed alterations in their appearance. These were—swelling, then dissolution of the central chromatoplasm, and displacement of the nucleus towards the periphery of the cell. After reunion of the axis-cylinders restitution occurred; if reunion was prevented the cells, or many of them, degenerated beyond repair. Further experiments showed that section of *any* motor axons resulted in a similar change in their cells of origin. Marinesco and others have amply confirmed these results. As regards sensory cells, an important difference was noted. Lugaro (1) claims to have been the first to demonstrate that section of the peripheral branch of the posterior

root-ganglia sets up this change in their cells, but that section of the central branch fails to produce any such change. He now explains this on the assumption that the sensory neurons, in common with other peripheral neurons, have great power of repairing peripheral mutilations, and therefore they react when their peripheral branch, but not when the central, is injured.

Van Gehuchten (1897) and Warrington (1898) affirm that by depriving cells of the influence of the afferent impulses with which they are normally affected the change can also be produced,—as, for example, when after the severance of the posterior roots certain of the cells in the anterior horn become affected.

I have not seen Warrington's account of his experiments published in the *Journal of Physiology* (vol. xxiii, pp. 112—129), but Barker (*The Nervous System*, p. 299) gives a fairly full notice of them, and reproduces some of the figures, and it is from this source that I take my information. The alteration was found especially to affect the dorso-lateral group of cells, one of which is figured. This particular group is apparently very prone to present such a condition; so common is it in the cords which I examine (from the insane) that very few fail to show it. As will be referred to later on, the same condition seems to be very general in the cells of the cuneate and gracile nuclei and Clarke's column.

Lugaro (1) has recently questioned the truth of this last view; he does not believe that the typical picture of *réaction à distance* can be produced in the way that van Gehuchten and Warrington suggest. He regards central chromatolysis with peripheral nucleus as a form of rejuvenescence of the cell in association with regenerative activity in the injured nerve-fibre. This is the view of van Biervliet and van Gehuchten, the former of whom points out the resemblance the reacting cell has to an embryonic nerve-cell. Lugaro states that types of cells corresponding to the phases of reaction and repair are found in certain stages of phylogenetic development.

So much for the experimental side of the question. Clinically these cells have been met with in the cortex in a large number of cases, which present both on the psychical and physical aspects very varied symptoms. The reader should consult the articles published in *Brain*, vol. xxiv,

pp. 47—114, by Adolf Meyer, for full particulars regarding these, where also he will find a bibliography of the subject; and also the article published in the autumn number of *Brain*, 1902, by S. J. Cole. This latter writer deals with the relation of alcohol to this cell form. I have myself met with between forty and fifty, and the large number which presented psychically symptoms of depression led me to suggest that one of the causes which is capable of setting up the change might be a lack of sensory impressions passing to these cells from the periphery, in accordance with the hypothesis that I, some years ago (*Journal of Mental Science*, vol. xlvi), advanced, that states of depression depend on defects in the afferent or sensory side of the nervous reflex arc.

I have recently re-examined my cases with reference to (1) the precise character of the cell change; (2) its incidence in other parts of the central nervous system besides the cortex cerebri; (3) the locality and nature of the degeneration, if any, in the axons in their passage along the cord; and (4) the nature of the psychical disturbances associated with these changes; and as this has led to some modification in my views I herewith give a short account of the conclusions I have arrived at.

At the outset I would remark that I have never maintained that the cell change is a cause of the melancholic condition—quite the reverse; I hold that the melancholic condition is the cause (one of the causes) of the cell change, or, more precisely, that the physical changes underlying the melancholic condition are accountable also for the alteration in the nerve-cells.

In a communication to this JOURNAL (October, 1900) I drew attention to the occurrence of this cell change in imbeciles, and suggested that in these cases also this was the result of paucity of normal impressions impinging on the cells. Its occurrence here is difficult to explain, either by the direct toxic theory or the axonal reaction theory. In this class of cases the cells, so far as my experience goes, do not show an advanced condition of the change; they are large, plump, and still retain well-developed chromophilic flakes, peripherally and in the dendrites, and the nucleus, although displaced, presents an entirely normal appearance. In earlier communications I referred to this form as an early stage of *réaction à distance*. This I now believe to be incorrect.

It seems to me highly improbable, for example, in Case 3,

an imbecile who died at the age of 35, referred to later on, that these cells were in a transition stage towards a more grave and irreparable lesion. I see no reason to suppose if this man had died at a much earlier date, or if he had lived many years more, that any other than this condition of cells would have been met with. Fifteen days in the case of injury to axons (as by hæmorrhage) is long enough for advanced changes to manifest themselves (shrinking, complete absence of chromatoplasm, and very pronounced nuclear changes), and therefore a lesion of the axons in these imbeciles is improbable; a direct toxic action on the cells themselves is also highly improbable. I believe that it can be most feasibly explained here as the result of a state of defective development. It may be, as Lugaro suggests, that these cells represent phylogenetically an immature form. I prefer to regard them as immature, owing to unfavourable conditions of cell environment. The greater development of the efferent nerve-cells usually found in man is in all probability associated with the wealth of sensory impressions they receive. In imbeciles there is unquestionably not only a lack of afferent impressions from the periphery, but also an even greater lack of impressions of an associative nature—impressions from one cell to another.

I have divided my cases into two classes, in one of which the cells are similar to those just described; and these I term the imbecile type. In the other class are placed those cases where the change is much more pronounced, so that the nucleus is more or less affected; and these I term the genuine axonal reaction type.

A. *Imbecile Type.*

The chief characteristics of the Betz cells in this class are—

1. Large size with rounded outline. In many the border of the cell has an indefinite or frayed-out appearance, such as is often seen in animals.

2. Well-formed Nissl bodies are present in the apex, dendrites, and at the periphery of the cell body, while the centre has a pale, finely granular appearance.

3. The nucleus is markedly displaced, and may even bulge out the cell border; but it is large, round, and clear, and presents a normal appearance.

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Vortex cells are common (noted in six out of sixteen cases).

Meynert's columns are always well defined.

The cortical arterioles are generally thickened, or show an increase of nuclei in their walls, or have a hyaline appearance (noted in fourteen out of sixteen cases).

I will now give a short account of the cases in which I have found this type of cell.

No. 1.—A. S—, female, was never very bright; got worse at age of 19. When admitted was fairly nourished; palate high, narrow, and asymmetrical; pasty complexion; imbecile aspect; smiled and displayed her gums when spoken to; was very taciturn; speech fairly clear. Very little information could be elicited from her. She could tell the number of her brothers and sisters. Obstinate and perverse. Remained dull and inanimate, sitting all day unoccupied. Habits dirty; rarely speaking. Died, after five years' residence, of tubercular enteritis, æt. 27.

Autopsy.—Body fairly nourished. Beyond the ulcers of cæcum, colon, and ileum, and an adherent (organised) clot in the superior longitudinal sinus, nothing was detected to call for notice in the viscera.

Microscopical examination showed small tubercles and caseous deposits in the lungs, and the liver showed advanced fatty degeneration; the kidneys were natural.

No. 2.—R .T—, female, an imbecile incapable of looking after herself. Mother a drunkard; father died of phthisis. Is eldest of seven; the others show no mental defects. On admission was thin, with a rather narrow and highly arched palate. Very childish and amiable; sits and plays with a doll, and chuckles when spoken to. Speech very indistinct. She does as she is told. Beyond having to be dressed and kept clean, she gave no trouble. Died after seven years' residence, æt. 24, of general tuberculosis. At the autopsy the body was emaciated. Tubercular ulcers were found in the intestines and a small cavity in one lung. The brain was firm, but otherwise appeared natural. The kidneys and liver appeared natural, but were not microscopically examined.

No. 3.—T. E—, male, imbecile suffering from epilepsy; sufficiently intelligent to work in a jute factory before his

admission here. He was 16 years old when admitted, had frequent and severe fits, and prior to and after them was often maniacal and violent. He was very impulsive, and on several occasions had bitten other patients very badly. He was active and in good health until several months prior to death, during which time he was confined to bed suffering from phthisis, of which he died at the age of 35. At the autopsy the body was fairly nourished. The upper lobe of the right lung was solidified, and contained many caseous areas. The brain was firm, but otherwise natural, as also were the other viscera.

No. 4.—S. M—, female, congenitally defective mentally; mother of eight children, one of whom was imbecile. She became worse (mentally) after the birth of her first child, and since then had been obstinate, sulky, and troublesome. Kept her bed for some time prior to admission. On admission was thin and badly nourished, had a surly, forbidding aspect, and lay huddled up in bed. She would not reply to questions, and was very resistive. Refused food, and struggled without making any noise when she was fed through the nasal tube. Was dirty in her habits; often very noisy at night. Later on she began to talk a great deal in a childish, querulous way; now ate ravenously. Her legs became contracted, and she developed a bedsore, and died of pneumonia, æt. 45, three months after admission. At the autopsy nothing was found in the viscera to call for remark beyond the pneumonic condition of the lungs, degenerated coronary arteries, and some shrinking at the vertex of the brain. The kidneys and liver were examined microscopically: the former showed some thickening of the capsule and the arteries, and a small cyst was found; the latter was in a well-marked state of fatty degeneration. The posterior spinal ganglia were examined, and the cord for tract degeneration. The cells of the ganglia did not present the appearance of axonal reaction. In the cord there was very slight (practically negligible) Marchi reaction in the posterior columns, and crossed pyramidal tracts in both the cervical and lumbar regions. The posterior nerve-roots at their entrance to the cord were markedly degenerated in the lumbar region, not at all in the dorsal or cervical regions. The anterior nerve-roots in the lumbar region also showed considerable Marchi reaction.

No. 5.—M. F—, an imbecile woman, but with sufficient intelligence to be an useful house worker. When admitted in 1888 was maniacal and troublesome, but quieted down after ten months, and remained for ten years a fairly intelligent and very industrious woman, but weak-minded, flighty, and talkative. At the end of this period she developed acute melancholic symptoms, refused food, and emaciated. For the last year of her life she was a deplorable, miserable-looking creature, sat all day in a chair, unoccupied, and died at the age of 49 of pneumonia. At the autopsy there was found consolidation of both lungs posteriorly. The heart, as is usual in imbeciles, was very small (139 grammes). The intestines showed commencing colitis. The brain showed some shrinking at the vertex, and the lateral ventricles were dilated. The liver and kidneys were examined microscopically; the former showed some increase of interlobular tissue and thickening of the capsule; there was some increase of interstitial tissue in the kidneys. Besides the brain cortex the cells of the cuneate and gracile nuclei and Clarke's column were affected, but not the anterior horn-cells of the cord or those of the posterior root-ganglia. The cord showed insignificant recent degeneration of the crossed pyramidal tracts in the cervical and dorsal regions, and none in the lumbar.

No. 6.—F. B—, female, chronic melancholia with probably congenital defect. Always more depressed at night. She had a high, narrow, and asymmetrical palate. After four years' residence as a quiet, industrious woman, she developed (result of a fall) cellulitis of one leg with extensive suppuration. She rapidly became demented and depraved in habits, and died. At the autopsy the brain, thoracic and abdominal viscera appeared fairly healthy. On microscopical examination of the kidneys a slight increase of interstitial tissue was noted, and the liver showed slight fatty changes. Osmic acid preparations of the cortex (ascending frontal) showed a natural condition of the tangential fibres and of the fibres of the medullary portion.

No. 7.—A. E. B—, female, æt. 36, suffered from agitated melancholia. She had a high, narrow, and V-shaped palate. At the autopsy no evident changes were noted in the viscera. Microscopical examination of the kidneys and liver showed

that the former were healthy, and that there was very slight fatty degeneration of the cells of the liver.

No. 8.—E. S—, female, æt. 52, suffered from agitated melancholia passing into dementia; palate rather high and narrow. At the autopsy no very evident cause for her death was found.

Besides the Betz cells those of the cuneate and gracile nuclei and Clarke's column were affected, whilst those of the anterior horns of the cord and the posterior root-ganglia were not. Practically there was no evidence of tract degeneration in the cord beyond one or two scattered fibres in the crossed pyramidal tracts of cervical, dorsal, and lumbar regions.

No. 9.—E. E—, female, suffering from agitated melancholia, died of pneumonia and pleurisy at the age of 40. There was a history of alcoholic intemperance in this case. Her kidneys were tough and contained cysts; microscopically they showed increase of interstitial tissue, especially marked just beneath the capsule, and some fatty degeneration of the renal cells. The liver showed fatty infiltration. Besides the Betz cells some of the fore-horn cells of the cord, especially in the lumbar region, and also some of the posterior root-ganglia cells, were affected.

Nos. 7, 8, and 9 were more fully described in the *British Medical Journal*, October 26th, 1901, "The Physical Basis of Melancholia."

No. 10.—H. H—, female, suffering from an acute attack of agitated melancholia subsequent to influenza. Was only a few days in residence when she died, æt. 60. Her kidneys were small and granular.

No. 11.—J. C—, female, senile melancholia; died after a month's residence, æt. 67. Had large granular kidneys.

No. 12.—E. H—, female, chronic melancholia of several years' duration; died æt. 73. Had small granular kidneys.

No. 13.—J. P—, male, admitted in an acutely melancholic condition; constantly groaning and ejaculating that he is the

most miserable man in the world. Died after five months' residence, æt. 68. His kidneys were in a state of chronic interstitial nephritis, with numerous small cysts. Liver natural.

No. 14.—M. A. F—, a female, senile melancholia; died of chronic Bright's disease, with small granular kidneys, æt. 73.

The last two cases I shall refer to did not present symptoms of depression: both were demented, the man apparently a recent case, but no history could be obtained; the woman probably congenitally defective, with very bad family history.

No. 15.—F. R—, male; was admitted in a dazed condition; faulty in habits, sitting in one posture all day. He died after a month's residence, æt. 38, of bronchitis.

No. 16.—H. R—, female, admitted in a maniacal condition, ultimately passing into a state of secondary dementia. Her father and father's sister had been insane, and one of patient's sisters was imbecile. Her palate was rather high and narrow. She died æt. 35, and at the autopsy her stomach was completely filled with pieces of blanket, sheeting, and hair. Her kidneys were healthy to the naked eye. Besides the Betz cells, many of the posterior ganglia-cells were affected, but not those of the anterior horns of the cord nor the Purkinjë cells of the cerebellum. Her cord showed well-marked old degeneration in the posterior columns in cervical, dorsal, and lumbar regions, but the crossed pyramidal tracts were apparently unaffected.

In the above list of cases five were undoubtedly imbecile, and eleven (including one of the former) were melancholic. Nos. 10 to 14 inclusive occur in old people.

It is interesting to note that the ill-formed palate, Clouston's deformed type, one of the physical stigmata of congenital defect, is very commonly met with in those not classified as imbecile (*vide* Nos. 6, 7, 8, and 16). We shall, however, point out that this type of palate is not unfrequently associated with the second class of cases.

I have noted the condition of the kidneys and liver, because disease of these organs, especially the former, is very commonly

met with. Although it would seem to be a factor predisposing to the condition of nerve-cells, yet it is not an essential one, for in Nos. 1, 2, 3, 7, 15, and 16 these organs were natural (1 and 7 examined microscopically).

B. *Genuine Axonal Reaction Type.*

The second type of cell is met with under very varied conditions both physically and mentally. As I believe that lesion of the axon is a factor in all these cases, I have termed them the genuine axonal reaction type in contradistinction to the first class, in which, probably, the axon is not at fault, and which are therefore not instances of axonal reaction at all, although the form of cell simulates it. Whether this condition of the axon is a secondary result following a lesion of the cell is a moot point. The weight of evidence, in my opinion, is in favour of the view that the cell is implicated secondarily to the axon.

These (Betz) cells present the following features:

They are in the majority of instances small, angular, stain very lightly, and show practically no Nissl flakes. Very often a large mass of pale yellow pigment lies all along one side of the cell—the side most remote from the nucleus. The nucleus, beyond being much displaced, is generally shrunken and denser than usual; in some cases, however, it may be large and ruptured.

I have notes of eighteen cases which correspond to this type. It will not be necessary for my present purpose to give details of them, as the form of cell change seems to have no definite connection with the mental aspects of the cases.

Eight of these had an undoubted alcoholic personal history. In five the palate was badly formed. The kidneys were granular in five, and in one large and pale.

The cord was examined for tract-degeneration in two—one with an alcoholic history, the other without. In both cases very marked signs of recent degeneration were found in the crossed pyramidal tracts.

In one case the condition was undoubtedly due to lesion of the axons; in this, after a hæmorrhage of fifteen days' duration, which had destroyed one internal capsule, the cells on the side of the hæmorrhage alone were affected. This case is

interesting as showing the length of time which is sufficient to set up very advanced changes when the axons are affected. The cells on the side of the lesion were pale, shrunken, without chromatoplasm, and the nuclei were profoundly affected.

As regards the incidence of the change in other nerve-cells, I may say that in this class, as in the first, the hypoglossal cells are rarely affected, whilst those of Clarke's columns and the cuneate and gracile nuclei almost always are.

I am very doubtful whether this condition of these cells has any pathological significance, at all events when the nucleus is merely displaced and the peripheral and dendritic Nissl flakes are well formed, for I have rarely examined any cases in which these regions, especially the two latter, do not show it more or less marked; and I am inclined to think that a peripheral nucleus and finely granular central chromatoplasm is a condition normal to these localities. Dr. J. J. Douglas (*Brit. Med. Journ.*, September 14th, 1901) has drawn attention to the common occurrence of this condition in the cells of Clarke's columns.

It is not usual to meet with the alteration in the Purkinjë cells of the cerebellum in either class.

The conclusions I would draw are that we must not class together as similar all cases of central chromatolysis with displacement of nucleus.

It may be due to two (perhaps more) different causes; and whilst in one of these classes the affected cells seem to bear a definite relation to the mental symptoms of the cases in which they occur, in the other they do not seem to have any such relation.

The first type of cell is found in imbeciles and some melancholiacs, especially senile melancholiacs. There is no evidence in these that the axons are at fault, and they are met with under conditions which are opposed to the view that they are in an early transition state, tending towards a more marked degree of cell change. In the case of the imbeciles there are reasons for regarding them as a peculiar form of cell associated with this defective mental state; they represent immature cells which have not fully developed owing to unfavourable environmental conditions, *viz.*, a lack of sensory innervation. In the case of the melancholiacs it seems probable that they are also the result of defective innervation, especially liable to manifest

itself at an advanced period of life, when the metabolism is at a low ebb. They would therefore represent a degradation or dissolution of the cell whereby it reverts to an immature form.

The melancholic condition does not depend upon the presence of these cells, but the cell condition is due to the cause which on the psychical side manifests itself in depression.

Although both in imbeciles and melancholiacs, therefore, it is supposed that the immediate factor which acts on and affects the cells is similar, there is no necessity to postulate any psychical parallel between the two conditions. Whether the above-mentioned factor operates on a fully developed nervous system, or on one which is not fully developed, will determine the respective psychical results following this change in the cells.

In the other class the cell change is due either to direct lesion of the cell bodies or to a lesion of their axons. I am inclined to think that, at any rate in the cases with an alcoholic history, the second alternative is the correct one. And as we are able to definitely assert that lesions to the axons will set up the change in their cells of origin, I prefer to accept this explanation in those cases where we find such a condition rather than invoke another—a problematical cause about which we have no certain knowledge.

Reference.

(1) Lugaro, 'Riv. Speriment. di Freniatria,' 1902, f. i, p. 981 (account taken from abstract by W. Ford Robertson, *Review of Neurology and Psychiatry*, vol. 1, No. 1).

On the Action of the Rolandic Cortex in Relation to Jacksonian Epilepsy and Volition.

By A. B. Kingsford, L.R.C.P.Lond., M.R.C.S.Eng.

The feature of Jacksonian epilepsy to which I wish to call attention is the periodicity of the discharge. Whether we regard the lesion as "irritative" or "discharging," it is, at all events, *chronic;* and whether we regard the discharges as going