2. *Dutch Retrospect.*

By J. Pieterson, M.D.

(Concluded from January, 1889, p. 614.)

An experiment of great importance has lately been demonstrated by Unverricht: when at the commencement of a seizure one, or, perhaps better, more, motor centres are quickly extirpated the muscles of these areas thus innervated take no part in the universal contraction-phenomenon. Munk succeeded by the simple extirpation of a single centre from the cortex in eliminating from the general convulsion the contractions corresponding to that centre; Rosenbach succeeded in this only when he had destroyed all the motor centres of one hemisphere.

Contrary to results thus obtained, he instances the experiments of Albertoni and of Pitres and Franck. The former found that after extirpation of the motor centres of one hemisphere he obtained universal muscular contractions by irritation of the other; the two latter also found that the contractions caused by irritation of the cortex were uninfluenced by the extirpation of one or more motor centres. On the other hand, Bubnoff and Heidenhain consider that the cortex is the true seat of origin of these contractions, and Luciani has contradicted Albertoni's experimental results.

Of importance, too, are the later investigations of Rosenbach as to the action of bromides on the convulsive seizure. He found that after administering a certain dose of bromide it was impossible by irritating the cortex with an induction current to awaken these convulsive attacks. The influence of bromides on the subjacent white matter was minimal; by irritation thereof contractions could again be induced without the occurrence of any universal convulsion on strengthening the irritation, and, moreover, the seizures ceased directly the current was interrupted. It is without doubt an important fact that after the exhibition of bromides, the most active anti-epileptic we know of, the contractions caused by irritation of the brain-cortex should no longer evince themselves. We have no doubt that if these experiments of Rosenbach are repeated they will be verified. Unverricht claims to have induced in the subjects of his experiments by continued cortical irritation, or where the cortex showed a marked susceptibility thereto, a condition conformant with the status epilepticus observed in man. Rosenbach repeated the old experiments of Nothnagel, and irritated the floor of the fourth ventricle before and after section of the medulla oblongata. He found universal contractions to ensue, which, however, in point of time coincided directly with the duration of the irritation, and did not, as in irritation of the cortex, commence some time after the onset and continue

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some time subsequent to the cessation of the irritation. The assumption is not too hazardous that this difference in result between irritation of the capsular and subjacent white portions of the cerebrum must be explained by the fact that the ganglion cells exercise a specific function whereby an irritation must first accumulate before its action proceeds. In the physiology of the reflex centres analogous phenomena are to be found in great number. Golz, who in Pflüger's "Archiv," Bd. xxxvi., p. 479, disputes the cortical origin of epilepsy, is thus disposed of :— "Golz here communicates the phenomena he observed in dogs from whom on both sides the whole so-called motor bulb had been removed. These animals could for months remain in good condition, and would then die with symptoms of universal epileptic convulsions. From this he draws the deduction that there is no foundation for considering the so-called motor centres in the cortex the starting point of epileptic contractions. Against this opinion forwarded by Golz may be placed what in general may be summarized against his methods of argument, viz., that the direct results of his experiments are more exact than his inferences therefrom. When these animals had lived for months in good health there must undoubtedly have ensued an adoption of function by the still remaining intact cortex, and a certain amount of readiness of action must again have come to the muscles. Then there is also afforded the possibility of the appearance of epileptic contractions especially because there existed at the same time a palpable brain lesion. It would prove much more if Golz could bring forward a case in which universal epileptic contractions were to appear *during the period of existence of degenerative symptoms*, and thus shortly after the operation and when the residual cortex had not yet assumed the degenerated functions." The above is a short *résumé* of the most important and best confirmed facts on which the theory of the cortical origin of epilepsy is built. It will be interesting now to examine in how far pathological anatomy and clinical observation tend to support or subvert this deduction.

"In post-mortem examination in cases of epilepsy there are in some cases to be found lesions most varying in their nature, in others no noticeable deviation from the normal. This latter is probably the rule in all recent epileptic cases, and from this must directly be inferred that the changes found in cases of longer standing must be regarded rather as the result than as the cause of this malady. In the first place I wish to establish the fact that even in the long-standing cases of epilepsy, where the affection has progressed even to the furthermost imaginable stage of dementia with obliteration of all the higher intellectual faculties, where the speech even is lost and life is reduced to a condition of pure vegetative existence, that in these cases even any trace of anatomical digression from the normal may be absent. Such cases

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are, however, greatly in the minority, and I have met with only two. One for years confined in this asylum (Meerenberg, Bloemendaal) had frequent epileptic attacks up till the day of his death with secondary dementia. At the post-mortem examination neither macro- nor microscopic change could be demonstrated. I made numerous sections of the cortex in every conceivable direction, staining and colouring them after every known method, but it was not granted me to discover any pathological divergence. The other was admitted here with the diagnosis idiocy, and to this, in fact, his symptoms directly pointed. He was a young man of three-and-twenty, who could neither stand nor sit upright, who never spoke, and who evinced no sign of imaginative faculty or intellect, whose limbs were drawn up and contracted, and who was continually confined to bed, and fed artificially. His history showed that until his ninth year he had exhibited no physical or mental abnormality, but that subsequently epileptic attacks had made their appearance. His affection undoubtedly makes one suspect, and points to 'idiotia atrophica,' and causes one to regard the epileptic seizures as a consequent symptom. After treatment lasting about six months, patient died. At the post-mortem the brain, though slightly œdematous, was found to be otherwise altogether normal; neither coarse nor microscopic change could be positively demonstrated; the sections through the cortex were treated and examined in every possible way, but neither in the ganglion cells nor in the fine network of nerve-fibres in the cortex could any change be discovered. The most natural conception of this case is that in a child in good health up to the age of nine epilepsy made its appearance, and that this led to an unusually severe degree of dementia, and that this was not an instance of 'idiotia atrophica.' It occurs to me that many cases which are described in works as of long-standing idiocy, and where after post-mortem no pathological change can be found, that these are cases such as the above-mentioned. For true cases of atrophic idiocy one usually finds a pathological substratum or a congenital deficiency of brain-substance; for an epileptic dement this need not by any means be the case. During life both affections can in every way be characterised by the same symptoms.

"Bourneville claims to have found a pathological distinction between epileptic and other forms of dementia, especially the paralytic. He maintains that epileptic dementia demonstrates its presence in the lower layers of the cortex, and that it causes changes there, while paralytic dementia produces change in the upper layers, and that then it is as a rule accompanied by a chronic meningitis. Both the above-mentioned cases, however, controvert this statement. Equally in the lower as in the higher cortical layers have I failed to demonstrate any pathological change notwithstanding the extreme degree of dementia. There remains, therefore, no other conclusion for us to draw but this, that epilepsy

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can proceed to a strongly-pronounced degree of dementia without it being necessary to find a consequent anatomical lesion. These cases of epileptic dementia without pathological divergence are, however, rare."

Another class of epileptics to consider are the epileptic idiots. It is a fact universally recognized that idiots are considerably prone to the development of epilepsy, inasmuch as epilepsy so frequently appears in conjunction with idiocy, and that as the latter is a primary affection one must naturally suppose some bond to exist between these two maladies. In a large proportion of these cases anatomical changes extremely varied in their nature are to be found in the cerebral tissues. Epilepsy must not, therefore, be made answerable for these lesions, but we must suppose that in consequence of such changes there have ensued both idiocy and epilepsy. These lesions concern in the first place the cortex and the white matter of the cerebral hemispheres, but in addition there are also to be found the secondary lesions which appear in the cerebral base and in the medulla oblongata. But it is just by reason of this secondary change that epileptic idiots give us so little that is decisive to draw conclusions from as to the seat of lesion of epilepsy; the secondary as well as the primary pathological change might be made responsible for it, and we might thus pronounce a medullary lesion, as Nothnagel formerly did, to be the primary seat of an epileptic attack. We are hence led to the conviction that the lesions which are found in cases of idiocy may rank as causes of the simultaneously existing epilepsy, which, to judge by the phenomena it presents, runs a normal retrograde course. This fact is important, not because it teaches us aught as to the seat of lesion of epilepsy, but because it refutes the opinion that an epilepsy which finds its origin in material brain-change must *per se* run an *ab*normal retrograde course. In reference to this, hemiatrophia cerebri deserves some consideration. Here, while a wholly atrophied cerebral hemisphere with its fellow in a perfectly normal state are to be found, an epilepsy will co-exist which shows no digression from the ordinary form. He instances two cases undergoing treatment in the asylum in whom this diagnosis of cerebral hemiatrophy has been made who are subject to a concurrent epilepsy. In one of these the peculiar character-degeneration, which Samt has described so aptly, and which differs so materially from the character-deformity observed in hysteria, has evinced itself. Here, then, we have a pure epilepsy existing coincidently with an organic brain-lesion. He cites a third case in which an extensive fracture of the skull, the depressed bone having at the time of accident been removed from the left frontal region, was followed some years after by epilepsy and consequent dementia. The epilepsy differs in no way from the ordinary form; the attacks are not frequent, are of the *grand mal* type, and of long duration. No motor or sensory degenerative symptoms are evident.

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By the side of these instances of organic brain lesion in which a normally retrogressive epilepsy existed there are arrayed the numerous cases of organic cerebral affection in which there is to be found not a true epilepsy, but an epileptoid condition. Here we do not find a single convulsive attack, but a condition in which one or more of the prominent signs are in abeyance—either that the unconsciousness is only more or less complete, and a recollection less or more pronounced of the attack exists, or that the muscular contractions have an abnormal onset, confining themselves to one or more of the extremities, exhibiting only a clonic or a tonic character, displaying first a clonic then a tonic contraction, etc. He adduces two cases out of a large number for purposes of illustration—one of a woman who, during the latter years of her life, had been subject to advanced dementia, and who had had frequent attacks of an epileptoid nature with partial unconsciousness. These attacks would follow one another in rapid succession, giving rise to a condition of stupor; further than this there were no other recognizable degenerative symptoms. Post-mortem revealed bilateral accumulation, especially in the frontal lobes, of numerous small "granulation tumours" (? syphilitic) varying in size, the largest being about $\frac{1}{16}$ inch in diameter, and lying especially around the perpendicularly-running arterioles in the cortex. The other case, an old right hemiplegic with aphasia and complete infranuclear facial paralysis. The epileptoid condition is here marked by attacks of very slight nature, their duration being only a few seconds, with at times partial, at others total, loss of consciousness. Instances such as these may be multiplied indefinitely. A passing reference is made to the epileptic condition which so frequently appears in paralytic dementia. The presence of these epileptoid attacks is an important diagnostic symptom in organic brain-change, without its bearing any direct evidence as to the localization of such lesions.

"A further change which is often found associated with epilepsy (by some writers regarded, indeed, as constant) is sclerosis of the pes hippocampi (cornu ammonis). This may be uni- or bilateral. Dr. P. van Brero found four instances of sclerosed cornu ammonis in fifteen cases of epilepsy in which post-mortem examination was made in 1886 here." [This sclerosis of the pes hippocampi can be so extreme that van Brero came across a case in which even the fimbria and corpus mamillare were diminished in size. One can easily surmise that here a secondary degeneration had taken place along the tracts described by von Gudden.] "Other and extended statistics demonstrate the more frequent occurrence of this change in chronic cases of epilepsy. In recent cases not yet combined with psychical change there exist no data, and so long as it is not with certainty confirmed that the affection of the cornu ammonis precedes the advent of epilepsy, it is not justifiable to regard this sclerosis as a causative influence. Over

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and above this too little importance has been attached to another circumstance. Sclerosis of the pes hippocampi has been especially demonstrated in chronic cases in which a remarkable degree of dementia has been existent, and in which this sclerosis may have been but the part of a sclerosis affecting the greater part of the cerebrum. When in like cases close notice of the condition of the superjacent cortex is not taken, these observations and deductions will have but little value. The conclusion Sommer draws that the hippocampal affection can rank as the cause of epilepsy must, therefore, certainly be regarded as unproved. The theories which have been proposed in connection with epilepsy as to the functions of the cornua ammonis overstep all experimental principle. The only trustworthy data which can be adduced in support of this are to be found in comparative anatomy. From this we gather that in primates and other anosmatic mammals (the dolphin, etc.), the whole of the pes hippocampi is very ill-developed, while the osmatic mammals exhibit an extraordinary development of this portion of the brain. There is a good deal of likelihood, therefore, that the development of the cornua ammonis stands in some relation to the sense of smell. The frequent appearance of hippocampal sclerosis in chronic cases of epilepsy renders it desirable that collections of data as to recent cases be made. It is most likely that epilepsy frequently is the cause of this change in the pes hippocampi. Lastly, sclerosis of one or both cornua appears in other cases than epileptics. In other forms of insanity I have been able, though rarely, to demonstrate its presence. Whether it can be found in subjects afflicted with non-mental disease I cannot decide."

In the above summary the changes which may occur in the cortex in so far as they may in a greater or less degree rank as likely causes of epilepsy have been noted. [It will be observed that the author makes no mention of a series of phenomena to which Gowers ("Diseases of the Nervous System," Vol. ii., p. 698) has drawn special attention—the fact that the different auræ give us information as to the functional region of the cortex in which the process of the fit begins. The rarity, too, of olfactory auræ might have been cited to controvert the theory of the hippocampal origin of this disease.]

Epilepsy, following the universal cycle of nature, causes in its turn also changes in the cortex cerebri. These changes are usually diffuse in their nature, but may also be local, *e.g.*, the above-mentioned cornual sclerosis. To decide whether a lesion is to rank as consequence or cause in cases of epilepsy we must take note of the time of its commencement. The under-mentioned anatomical changes occur only after the prolonged existence of epilepsy and must therefore rank as its effect.

The pathological anatomy of chronic epilepsy agrees almost wholly with that of chronic dementia, and in all likelihood is but

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the expression of that simultaneously existing dementia. We find in the first instance chronic meningitis, which is distinguished from the meningitis of general paralysis in that the thickened meninges are not adherent to the cortex, but can be separated with ease, by a less rich arterial anastomosis and with a less free development of the structural elements in the walls of the vessels which are also less dilated—it is the ordinary meningitis of chronic dementia. This meningitis may have occasioned secondarily an atrophy of the different cerebral convolutions, or this convolutional atrophy may exist independent of a chronic meningitis. Cases of atrophied cerebral convolutions with a normal condition of the meninges are relatively not so rare. This atrophy is a simple diminution in thickness of the grey matter, no apparent external abnormality being observed, and a narrow cortex being only demonstrated on section, or the whole convolution, including the white substance, may be atrophied and its condition then recognized as such externally. In all probability these are two distinct developmental stages of the same pathological process, and in the latter the change has passed over to the white matter in the form of a secondary degeneration. Coarsely we find, as a rule, an increase in the structural tissue, both in the white as well as in the grey cerebral matter. The vascular system is most frequently altered pathologically, but sometimes not at all, and, as a rule, the number of ganglion-cells in the cortex is largely diminished. As to the nerve-fibres in chronic epileptic dementia, a diminution of these is possible, and even most probable. It is, however, difficult to determine whether in an atrophied convolution there is to be found a proportionate or disproportionate decrease in the nerve fibres. It is usually easy after examination of a satisfactory number of sections to make a differential pathological distinction between ordinary and paralytic dementia. In the latter, one usually finds many spindle cells, the blood-vessels are mostly markedly changed, the walls of the vessels are dilated with free development of their structural constituents, the number of blood-vessels also is increased, while, as has lately been demonstrated by Tuczek with certainty, the number of nerve fibres is greatly reduced. All these changes are either not to be found at all, or at most but in a small degree in epileptic dementia.

When epilepsy has persisted for so long a time that distinct anatomical change has supervened in the cortex, and that there thus exists a more or less considerable degree of dementia, we, as a rule, take it for granted that there is a corresponding diminution in the number and intensity of the epileptic seizures compared with the degree there existed at the time of onset of the malady, or the length of time during which it had prevailed. It is a fact for a long time well recognized by practical psychologists that with the advent of dementia the number of epileptic seizures declines. This must be regarded as pathological evidence

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strengthening the already experimentally established principle that the epileptic attack, especially as regards the muscular contraction stage, is dependent on the integrity of the cortex. As soon as diffuse anatomical change appears in the cortex, then the epileptic accessions diminish in frequency and intensity. As has already been mentioned above, Unverricht found that the contractions were absent after cortex irritation when the motor centres were extirpated, and the fact that the seizure is less severe when there is an established cortical lesion is a pathological point wholly in agreement with this experimental investigation.

"When in a patient subject to epilepsy the seizures have remained numerous up to the time of decease, we have grounds for concluding that few anatomical changes will be found in the cortex cerebri, while over against this in decidedly distinct cases of dementia where the attacks have diminished during the later years in number and severity there exists great probability that at a post-mortem examination some anatomical digression will be discovered. I regard this as an important argument in favour of the cortical origin of epilepsy. . . . On the ground, then, of experimental investigation, and also in part by reason of pathological evidence, it occurs to me that the statement of Nothnagel's according to which epilepsy is made to originate by reason of a medullary lesion cannot at present any longer be defended. With greater justification can we accept the proposition that epilepsy depends on an affection of the grey superficies of the cerebrum, and while fully cognizant of its speculative nature, we introduce into our declaration an unknown quantity, designating the change of the ganglion cells in the cortex (a change with which we are not yet acquainted, but of which the symptoms are the epileptic seizure and the epileptic mental disturbance) *the epileptic lesion*. The epileptic lesion of the cortex can exist without our being able to find for it any anatomical evidence. Such are the cases of ordinary uncomplicated epilepsy which is thus a purely functional affection. For this epileptic lesion of the cortex, however, an anatomical causation can also exist, as we find in many cases of idiocy, in cerebral hemiatrophy, and in some instances of definite localized pathological digressions of the cerebrum. These localized lesions, however, do not usually give distinct epileptic changes in the residual intact cortex, but only a condition which more or less approaches thereto. These are the so-called epileptiform states which are so richly represented in organic brain change. Strictly regarded, it is thus not proper to speak of cortical forms of epilepsy, and by such to indicate the conditions where, owing to organic brain perversion, anomalous forms of epilepsy exist."

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