Section of Neurology.

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PRESIDENT'S ADDRESS.

The Pathogenesis of Cerebral Diplegia.

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THE Pathogenesis of Cerebral Diplegia, the subject which I have chosen for this Presidential address, is a very ancient subject, for it is eighty-one years since Dr. Little, Senior Physician to the London Hospital and founder of the Royal Orthopædic Hospital, commenced his writings which culminated in a monograph based upon a personal experience of 200 cases. This monograph is so complete in clinical detail, so free from error either of observation or deduction, and so truthful that it has completely withstood the test of time to the present day. Even modern writers repeat "he left but few details that can be added to his clinical description of the disease, and we may justly regard this as one of the first monographs on modern neurology." No malady more appropriately continues to bear the name of its recorder than does "Little's disease." His truthfulness of description and accuracy of deduction have not by any means been followed by all of his successors who have written upon this subject, some of whom seemed to have failed lamentably both in observation and in accuracy of deduction. And yet their conclusions have gained such universal acceptance, as to have led to a serious impairment of the progress of knowledge upon the subject, and to such confusion of the issue, that despite the excellent work and splendid monographs which have been published by many writers, the student of the present day, if he has gained a fair working idea of the pathology of this disease, will not have obtained this knowledge from any text-book of neurology written in the English tongue, whether translated from a foreign tongue or no.

I can best introduce my subject to you, and build up a conception—though perhaps a personal one—of the causation of cerebral diplegia by briefly reviewing the more important contributions which have been made to this subject.

Although some of the clinical features of cerebral diplegia were described in the early days of the nineteenth century, by Andry, Delpech, Heine and others, under the name of "cerebral spastic paralysis," and although Joerg, in 1828, stated that "too early and unripe-born children may present a state of weakness and stiffness in the muscles persisting until puberty or later," yet it was Little in the *Lancet* of 1841 who first called attention to "The influence of abnormal parturition, difficult labour, premature birth, and asphyxia neonatorum, on the mental and physical condition of the child, especially in relation to deformities." He saw at once the difficulty of making such widely dissimilar physical

conditions as premature birth with precipitate delivery on the one hand, and prolonged labour with asphyxia on the other hand, responsible for one and the same pathological condition. He did not think that gross injury to the brain was the cause of any of the diplegic forms of infantile spastic paralysis, though he thought it produced some of the hemiplegic forms, for how could the precipitate birth of a premature child in a multiparous woman give rise to injury to the brain? He pinned his faith to asphyxia as the cause of the lesion of the nervous system. In all prolonged labour and in breech presentations the cause for the asphyxia is obvious. In precipitate labour and in the case of premature infants he pleads again for asphyxia as the essential cause. Pressure upon the umbilical cord even for a very short time is likely to have a much more serious effect upon the immature than upon the mature. The prematurely born child may not have sufficient vitality for respiration to be established soon enough, or its vessels may not be ready for the change of circulation which should occur at birth. He actually found the same capillary congestion and minute petechiæ in the brain, heart and serous surfaces of the premature and precipitantly born, such as are well known to occur in children dead after obvious asphyxia; and he argued that widely spread fine lesions of this nature, in which—to use his own words—“decarbonization produced devitalization of the brain” and in which petechial hæmorrhages played a part, were the cause of spastic paralysis, which he attributed to these various abnormalities of birth.

The value of Dr. Little's contribution may be stated thus: He first established the incontestable fact that diplegia is often associated with abnormalities of birth, at the same time stating “it is obvious that the majority of apparently stillborn children whose lives are saved by the attendant accoucheur, recover unharmed from that condition.” He theorized the lesion as a widely spread fine lesion of the cerebral substance which could affect one part of the brain more than another. He showed that the less severe cases may progressively recover in the course of years, thereby proving that the slighter degrees of the lesion were reparable, and, lastly, he excluded gross injuries to the brain, and gross lesions generally, from the ætiology of the disease which bears his name, and pointed out its common association with microcephaly. Strictly speaking, the term “Little's disease” should be confined to diplegia which is associated with difficult birth. Actually, it is used by the French school for every variety of cerebral diplegia present from the time of birth. Brissaud strove hard to confine it to the paraplegic forms occurring in premature children.

In 1875, Erb and Charcot described the clinical picture of “primary lateral sclerosis,” which they attributed to a primary affection of the pyramidal tract in the spinal cord; and cases occurring in infants were soon discovered and described as “spastic tabes in infancy.” These were examples of the paraplegic form of diplegia, Little's work being apparently unknown both to Erb and to Charcot at the time of their earlier writings. But the subject of Little's work was soon brought into prominent discussion and a heated controversy was waged as to whether the primary spastic paraplegias of childhood were of spinal or of cerebral origin. The battle went against the supporters of the spinal theory, and in the end, owing to the excellent work of Wolters, and of James Ross, of Manchester, it became universally accepted that the lesion was cerebral in site. During this controversy much pathological material was collected, with the result that the anatomical finding was generally accepted to be an atrophy and sclerosis of the convolutions, remarkably symmetrical,

sometimes general, producing a walnut-kernel type of brain, sometimes local and incident upon any part or parts of the convexity, but most often affecting the Rolandic region and in the paraplegic forms most noticeable in the paracentral region, without any sign of vascular lesion or of meningeal involvement. This was the "Lobar Atrophic Sclerosis" of the French school. It was recognized as the end-result of some previous pathological process, no explanation of the nature of which was forthcoming. The important fact was also emphasized that the degree of the atrophic sclerosis present often did not correspond with the severity of the clinical picture; the paralysis might be severe and the atrophic sclerosis slight. The French authors agreed that the symptomatology was determined by other than the anatomical conditions as yet brought to light. In other words, the unknown initial pathological process may at the time of death, be much more extensive than the atrophic sclerosis which follows in its train. The correctness of this conclusion has been supported by all the subsequent evidence.

In 1885 Dr. Sarah McNutt wrote a thesis upon this subject which requires examination in detail, for it is important not only on account of the excellence of her clinical report and pathological examination, but also, and chiefly, on account of her false deduction, which, aided by the support given by Sir William Gowers, had the most amazing and inexplicable effect upon public opinion as to the pathology of the disease. It introduced a glaring error which has persisted to this day, and which, though pathologically untenable and resting upon no evidence whatever, seems to have defied all the attempts which writers during the past twenty-five years have made to eradicate it.

Dr. McNutt described a case of double infantile spastic hemiplegia in a child born with instrumental labour, which from the time of birth showed signs of very typical general spastic diplegia and which died at the age of $2\frac{1}{2}$ years. The pathological findings and the microscopic anatomy are beautifully described and figured, so well in fact as to leave no possible doubt as to the nature of the condition present. The brain was small and of the walnut-kernel type, the arrangement of the convolutions is primitive, and there is macrogyria. There was a deep wide groove on either side extending from the region of the orbital lobule, in the direction of the Rolandic fissure to the paracentral region, which almost separated each hemisphere into two parts. At the bottom of this groove the ascending frontal gyrus was buried and was atrophied almost to extinction, while the adjacent precentral and postcentral gyri were severely atrophied. No ganglion cells nor nerve fibres were to be seen in the atrophied cortex, and no nerve cells were to be found even in the grey matter of the convolutions, where the cortex was best preserved. Dr. McNutt's pathologist described the condition as one of a sclerosis commencing in the deeper layers of the cortex and invading the cortex from within outwards. The pyramidal tracts were degenerate above and wanting below.

One can have no hesitation in being positive that the pathological process in this brain described by Dr. McNutt had begun long before birth, from the primitive arrangement of the convolutions and from the condition of the pyramidal tracts. It was a typical condition of lobar atrophic sclerosis. Had Dr. McNutt remained content with her description of this case, no harm would have been done. But she proceeded to refer to another case which she had published and figured, of a child delivered by the breech with easy labour, who from the fourth day onwards had severe convulsions, and on the twelfth day began to develop left hemiplegia, which became complete. Death occurred on

the twenty-second day. Upon necropsy, the left hemisphere was found normal, but the right hemisphere was covered by a clot which had broken up the central convolutions, the optic thalamus, and the corpus striatum, and which was only separated from the lateral ventricle by the ependyma. Dr. McNutt then lays down the proposition that "it is legitimate to conclude that had this second child lived it would have developed by cicatrization the shrinkage of the central convolutions and the convergence of the neighbouring gyri, which was found in her first case, and which characterizes the most marked cases of this disease." She then generalizes meningeal hæmorrhage as the universal cause for infantile spastic states dating from the time of birth and associated with difficult labour. And this opinion expressed by her has gained the widest acceptance, so that one reads on every hand that meningeal hæmorrhage is a proved cause of diplegia. Yet her case of diplegia did not date from birth, for the anatomical findings showed that the disease must have been installed early in foetal life. And her case of meningeal hæmorrhage was not the result of difficult labour, for the birth was described as having been particularly easy. It was not a case of meningeal hæmorrhage but of a large intracerebral hæmorrhage which ploughed up everything from the basal ganglia to the cortex, ultimately bursting upon the surface. This cerebral hæmorrhage did not occur at the time of birth, but twelve days after birth, when the signs of the hemiplegia first appeared.

Yet this is the evidence upon which the case for meningeal hæmorrhage as a cause for diplegia rests. There is no other evidence. Freud in his excellent monograph published in 1897, sought clinics, museums and literature in vain for other evidence and found none, and that, too, has been my experience.

It is true that meningeal hæmorrhage is not uncommon after difficult labour, and doubtless it is a common cause of convulsion occurring after such births. Cruveilhier noted it a century ago. Wehje made 957 autopsies upon children from a few days to 6 months old, and found signs of undoubted meningeal hæmorrhage in 122 of them, though these cases had shown no symptom or sign whatever of damage to the brain. Similar results have also been obtained by Mraček in another large series of cases.

The evidence demands that meningeal hæmorrhage should be deleted as a causal factor for any infantile spastic state. Yet meningeal hæmorrhage is still the most striking among the proved factors of diplegia in most text-books of neurology. Strümpell, in 1885, brought forward indubitable cases of post-natal diplegia and infantile hemiplegia due to polio-encephalitis, and he argued this initial pathology for infantile spastic states in general. There does not appear to be much evidence in favour of foetal encephalitis, though Virchow described it and von Limbeck considered it to be the cause of lobar atrophic sclerosis, and much more recently the Longs have published some remarkable necropsies which seem to show that encephalitis may occur in intra-uterine life. So that it seems difficult entirely to refute this possibility. Though Strümpell's work received little support for many years except from Pierre Marie, yet most of it has stood the test of time. For now encephalitis is universally held to be a common cause of infantile hemiplegia, and of post-natal diplegia with severe initial symptoms.

In 1894 Brissaud started an entirely new conception of the origin of diplegia or rather of certain forms of diplegia. He considered it was prematurity of birth which was the essential causal factor and he avowed that birth before term arrested or retarded the essential functions of evolution of the fœtus.

In his words, "what takes the pyramidal tract three weeks to grow in intra-uterine life will take it three years or never in extra-uterine life in the prematurely born and thence arises the spastic paralysis." He confined this pathology to what he called "Little's disease," those purely paraplegic forms which show a tendency to amelioration or recovery. Now this is essentially picking and choosing, for there is every gradation between the purely paraplegic and the more severe forms of diplegia, and these cannot be separated pathologically. It is obvious that the immense majority of prematurely born children who survive complete the development of their nervous systems in good time and do not develop Little's disease. The major incidence of premature birth in connexion with paraplegic forms, though incontestably true, is not universal, and therefore it does not help Brissaud's argument; and there is the much more subtle explanation that the dyscrasia which produced the pyramidal trouble also caused the premature birth. In all autopsies upon paraplegic diplegia, some defect has been found throughout the pyramidal system from cortex to lumbar region. But on Brissaud's hypothesis we should find no abnormality of the cortex and upper parts of the pyramidal tracts. Notwithstanding this, Brissaud had many adherents, including Marie and van Gehuchten; indeed, van Gehuchten has gone so far as to say that premature birth at the end of the seventh month produces general rigidity because the pyramidal tract has only by then reached the medulla, whereas premature birth in the eighth month produces paraplegic rigidity because by this time these tracts have reached to the dorsal region. After birth some slow renewal of the arrested growth of the pyramidal system occurs, therefore these cases tend to improve and sometimes to recover. Meanwhile the steady accumulation of pathological evidence called for a conception of primary neuronc degeneration as the initial morbid process in diplegia. Cotard, as early as 1868, drew attention to the atrophy of the pyramidal cells out of all proportion to the shrinking of convolutions and sclerosis. Warda, in 1895, found absence or degeneration of cortical neurones in a case of pre-natal diplegia that was certainly not secondary to any sclerosis or other gross lesion. Mya and Levi, in 1896, found arrest of neuroblastic growth with degeneration of such neuroblasts as had developed their processes. In some of the most severe of the pre-natal cases there was found to be no macroscopic lesion at all but an almost universal degeneration of cortical cells, pointing to the advent of a rapid degenerative change shortly before birth. Cases of post-natal diplegia with insidious onset and clinically identical with the pre-natal cases, two of which I published in *Brain*, for 1900, were recorded as having their onset throughout childhood even as late as the twelfth year (notably a remarkable case published in *Brain*, by Campbell, with onset at the twelfth year), and in all these cases primary neuronc degeneration was the lesion found. Further, the occurrence of optic atrophy in about one-sixth of all cases made any other explanation than a primary neuronc degeneration difficult. Déjerine always supported a neuronc pathology and he very rightly contended for a clinical and pathological separation between the diplegias and the double hemiplegias.

In 1897, Freud, of Vienna, issued his monograph; this still remains the most complete and authoritative exposition of this subject. He seems to have been the first to use the term cerebral diplegia as indicating a bilateral symmetrical defect of the brain, not the result of gross lesions, in contradistinction to the hemiplegias and double hemiplegias which he considered always to be the result of gross lesions. He argued, and indeed

I think he proved, that all diplegia dating from birth, which had been attributed to abnormalities of birth, really had its pathological origin long before birth in intra-uterine life. He piled up statistics to show that every writer upon this subject had admitted that 40 per cent. of all cases of diplegia dating from birth were without any possible factor in connexion with birth. He analysed most carefully the circumstances attending the difficult birth in diplegia, and he sums up in these words: "Premature, precipitate and difficult births are not causal factors in the production of diplegia; they are only associated symptoms of deeper-lying influences which have dominated the development of the fœtus or the organism of the mother; the only cerebral paralysis which results from difficult birth occurs when the brain is lacerated and this takes the form of a monoplegia or hemiplegia or rarely of a double hemiplegia, and the anatomical result of this lesion is entirely different from the findings in the brains of diplegia."

Freud wished to link up prenatally installed diplegia with the cases of insidious onset during childhood at any age up to that of puberty, thus arguing a cause for primary neuronic degeneration of the brain which might be incident at any period of foetal life or during childhood, and he cites some remarkable cases, among which those reported by Feer are worthy of attention. Three cases of diplegia of the same clinical type occurred among the children of one mother. The first child was born with difficulty; the birth was accompanied by asphyxia and the infant was diplegic from the time of birth. The second child was easily born but again presented signs of diplegia of a severer type from birth. The third child was particularly well and strong till after seven months, when signs of progressive diplegia set in. Krafft-Ebing reported a similar instance in which one child was diplegic from birth while in two other cases the disease slowly appeared at the ages of three and five years respectively. Many cases of this nature have been reported by Schultze, Pelizain, Newmark and others. Surely the same cause was active in the post-natal cases as in the pre-natal cases in these families. Pelizain was anxious to bring all cases of familial spastic paralysis into the same causal group with congenital diplegia, for in the families reported there were children who were born paralysed after difficult birth and children in whom symptoms commenced, though apparently healthy, at any age up to the fourteenth year. The one distinction which at first seems to separate the congenital cases from the post-natal cases, and which caused Paul Simon to insist that they were separate diseases is neither a pathological distinction nor one of symptomatology, it is the course of the disease. Most of the pre-natal cases tend to improve, some of them to a remarkable extent. The post-natal cases never improve but progress more or less rapidly to a fatal issue, while some few become arrested. Yet progressive pre-natal cases are known and I have seen several of them; and both pre-natal improving cases and rapidly progressive post-natal cases have occurred in children of the same mother and often in members of the same family, and since in these examples the same cause must be acting there is no necessity to assume a different pathology for the two conditions. On the contrary, it seems to me that there is every reason, both clinical and pathological, for both conditions belonging to one class of diseases in which a primary degeneration of cerebral neurones may occur at any period during foetal and during adolescent life.

In 1909 Anglade and Jacquin reported a necropsy upon a case of spastic diplegia which was of great interest. Clinically the case was one of general rigidity of the common type. They found a neuronic degeneration of the cortex

of the cerebellum in addition to a similar but much more extensive condition in the cerebrum. This, I believe, was the first record of primary involvement of the cerebellum in diplegia. The late Dr. Batten many times expressed to me his belief that the cerebellum was extensively involved in the astatic and hypotonic type of diplegia, several examples of which he showed at clinical meetings of this Section; and the fact that definite involvement of the cerebellum has been found gives a definite basis to this conception. Smallness of the cerebellum has repeatedly been found but it has been regarded as secondary to pre-frontal lesions. Foerster long ago referred the astatic-atonie forms to an absence of the fronto-pontine projection, but I have been unable to discover upon what pathological or physiological evidence his statement was based.

I now turn to a consideration of the ætiological factors of diplegia, long lists of which will be found in all modern descriptions, with the remark that 40 per cent. of all the cases are without even the most slender causal antecedents.

Hereditary and Familial Influences.—These are exceptionally rare in the common types of the disease. Yet there are recorded instances in which a mother who was the subject of pre-natal diplegia has given birth to a child afflicted with the same disease, an example of which was reported by Oppenheim. Familial incidences in which pre-natal and post-natal cases occurred indiscriminately have been many times recorded as in the reports of Krafft-Ebing, Feer, Newmark and Pelizain already referred to. Post-natal cases of a progressive type with a heavy familial incidence have been recorded by Souques, by Pribram and by Hochhaus, while this ætiology is also very obvious in the type of amaurotic family idiocy and familial spastic paralysis. Diplegia may also in rare instances be coincident in the same families with other degenerative diseases of the nervous system, notably hereditary ataxy and myopathy, and certain facts showing this relation have been pointed out by Koenig, Strümpell, Bernhardt, Franz Schultze and by myself. Consanguinity of parents has been a by no means rare occurrence.

Maternal Ill-health during Pregnancy.—This factor has been placed in the most important position by many writers and I think without any justification, so rarely is it met with, so often are these diplegic children the first-born of healthy young mothers, so frequently are perfectly healthy children born of very sick mothers, so little is there which is definite and tangible about the nature of the maternal ill health even when this does precede the birth of a diplegic child. The cause seems rather to be individual to the conception rather than transmitted by the mother and I would remove maternal ill health from among the causal factors of this disease. There is, however, one important exception and that is the presence of syphilis. The influence of syphilis in causing diplegia has been hotly contested. Its incidence is admittedly rare. Naef and Feer examined 179 consecutive cases and were unable to prove the presence of syphilis in any one case. Dejerine insisted that syphilis was only a factor in that it caused premature birth. Yet I have seen diplegic children with the most obvious signs of congenital syphilis and so have many others. The most conclusive evidence is that in pre-natal diplegias a condition of the brain is sometimes found in which granular ependymitis, decortication and the general resemblance to the brain of general paralysis is so striking as almost to prove the point. What is needed is an examination of the Wassermann reaction in a long series of cases, and as far as I have been able to search the literature this work has not yet been done.

Abnormalities of Birth.—I have already excluded these conditions as

causal factors, and have treated them as common, but by no means constant clinical associates of diplegia, indicative of something wrong with the fœtus, or of something wrong with those mysterious relations between mother and offspring which determine a speedy delivery at full time. My authority for doing this is based on the inconstancy of these so-called factors, the insuperable difficulty of referring one and the same pathological condition to such widely different causes as premature, precipitate, and prolonged birth and to asphyxia, the absence of any reasonable explanations or pathological findings to show how such events could produce the disease, the opinion of modern writers upon the subject and the complete negation from the conditions of the brain found in every case.

Deductions from the Pathological Material.—It is remarkable that no lesions have been found in any part of the nervous system except in the cerebral hemispheres. Since the brain increases in size and develops during fœtal life by the evolution and development into complete neurons, of the neuroblasts of which it is originally composed, the terms which are so frequently met with in the literature of this subject, namely, "agenesia" and "arrested development," simply mean that some harmful process has affected the brain during its period of development. I have attempted to prove in my foregoing remarks that such arrest of development due to an affection of the brain during fœtal life and not to any event connected with birth, is to be found in the brains from all those cases of diplegia in which the symptoms are present from the time of birth. And I have further argued that the first signs of the affection are expressed in neuroblastic and neuron death or degeneration.

If we liken the brain from the commencement of its development to a garden in early spring, well sown with seeds—the neuroblasts, some of which germinate early, some meantime and some late, those germinating early perhaps of a hardier sort, those germinating late perhaps of a more tender kind, imagine what might be the effect of a noxious influence—a sudden sharp frost for example upon this garden. According to its severity and the time when it arrived, it might, if it caught all the seeds in a condition of germination and growth, leave this garden lifeless. Or it might spare those seeds as yet ungerminated and those seedlings which had attained sufficient growth and robustness to resist its influence and affect only certain kinds of the seedlings, perhaps according to the state of their development, to their death and destruction. Or the seedlings affected by the frost may not be all killed, some or all of them may be simply "cut" and their leaves for the time withered, and these may be able in some degree to renew their growth and attain a maturity in some cases perfect, in others stunted and imperfect, in all retarded. Lastly, this untoward weather may continue, and crop after crop may perish in a progressive destruction. Some such process as I have put before you in this homely simile of the seedlings and the frost will, I submit, best serve to explain both the ætiology, the symptomatology and the pathological findings in cerebral diplegia. This hypothesis will, in a measure, explain the restriction of the affection to the cerebrum, for this is the latest to develop, the highest and perhaps for these reasons the most vulnerable part of the nervous system. It will explain the tiny brain in cases of severe microcephalic diplegia, with no differentiation between grey and white matter and the most primitive type of convolutions, for here is to be witnessed widely spread neuroblastic death early in fœtal life, with no myelination, because no processes have been developed from the neuroblasts. It will explain the strangely symmetrical and even strictly systemic affection of the cerebrum;

the pyramidal region alone affected, the frontal and occipital regions alone affected, the parietal and frontal regions symmetrically involved, while the pyramidal and occipital regions escape, the corpora striata alone being affected as in the cases of choreic diplegia and congenital athetosis examined by Anton and Demange. It will explain those severe cases in which no signs of arrested development and little naked-eye change are found in the brain, for here the cerebrum has been hard hit at a time when its development is almost complete. It will explain the progressive improvement of the slighter cases with the possibility of regrowth in partially or temporarily damaged neurons and also those cases, both pre- and post-natal, which exhibit a progressive degenerative course.

This hypothesis is not altogether my own, though I claim originality for its development in this form. It was suggested to me by the writings of Brissaud on premature birth as the one and only cause of paraplegic diplegia. Premature birth was Brissaud's frost which cut the pyramidal seedlings. On my hypothesis it was the frost which caused both the premature birth and the pyramidal deficiency simultaneously.

The cause of the initial process is entirely mysterious, as is the case also in so many degenerative nervous diseases, as, for example, the hereditary ataxies, myopathies and progressive muscular atrophy. It may be of the nature of a toxic or of a deprivation process and is likely to be of more than one variety. If there is any difficulty in the conception of such a cause acting for a time only and subsequently allowing of regeneration of nerve elements, it is exactly paralleled by the neuronie affection of polyneuritis. If the action of the cause for a time only producing degeneration, followed by final arrest, is hard to believe, this is the invariable habit of the cause of peroneal atrophy where the degeneration commencing at a certain period of life, progresses for a time and comes always to a final arrest within comparatively narrow limits. The picking out of the systems of cerebral neurons by this disease may conceivably be due to the time of incidence of the essential cause; or to its physiological selective capacity for certain of the elements only, as occurs so commonly with poisons; or to a combination of these two events. And, further, the phylogenetic age of the several cerebral systems may be a factor. It would be fascinating if one could correlate the affection of the various regions of the cortex and the clinical types of diplegia with the times at which their neuroblasts were at their most active stage of development during foetal life, but I have sought in works on embryology and have not found details as to when the systems of cerebral neuroblasts develop. It is true that the neuroblasts which subsequently develop into the basal ganglia commence their growth long before those of the cortex and we have a clinical type corresponding to this region in congenital bilateral athetosis, and atrophy incident upon these regions as shown by the cases of Anton and others. The pyramidal system is comparatively late in commencing and in attaining its development, and we have positive pathological evidence to show that it is affected at different epochs in its development in different cases. For example the pyramidal tracts may be altogether undeveloped; or they may reach to the crus, or to the medulla, or to the cervical region of the cord. or they may have attained to the usual degree of maturity present at the time of birth but may be degenerated. Clinical evidence and pathological evidence show that the affection falls most heavily upon the pyramidal system in the majority of the cases and this major incidence has for many years and by great authorities been considered to be associated with an especial vulnerability of this system owing to its late period of development. But the pyramidal system has been found completely normal in

this condition of lobar atrophic sclerosis as in the cases recorded by Ganghofner and by Railton, although it may be argued against these results that modern methods of examination were not used. And Dr. Greenfield, a few weeks since, showed me a specimen of his in which the central regions of the cortex was comparatively intact, while the frontal and parietal regions were severely atrophied, the occipital region being also relatively unaffected. I seek to explain such cases on the grounds that the cause for the condition was active at a time when the pyramidal and occipital neurons were invulnerable owing to the stage of their development, while the parietal and frontal neurons were affected because they were in a more vulnerable stage of their development, or, alternatively, that there was a selective capacity on the part of the destroying agent for those neuron systems that were affected. I would put the following conditions forward in explanation of the universal affection and of the various local affections of the brain which are found in diplegia:—

(1) The severity of the cause, which may affect all the cerebral elements, indiscriminately, giving rise automatically, if acting early, to a small primitive type of brain, destitute of neurons, and causing clinically a condition of idiocy with diplegia and blindness. (2) The time of development at which the cause is active, which may determine those systems which are affected and those which are spared, in the local atrophies of the brain. (3) The physiological selective capacity of the cause to affect some systems and not others. (4) A cause which may be temporary in its action and which for this reason only picks out systems which are vulnerable at the moment. (5) A cause which may be continuous in its action and which results in a very progressive diplegia.

If my reasoning be legitimate then we must class together all the clinical results which primary neuron degeneration and its sequel, general or lobar atrophic sclerosis, produce, from microcephaly with idiocy alone, through the wide range of pre-natal and post-natal diplegias to the simplest forms of paraplegic rigidity.

The one anatomical lesion which has been found in all cases of diplegia since it was first pointed out by Cotard, in 1868, is disappearance of the neurons of the brain or their degeneration. I hold that this is a primary degeneration of the neurons and that it is the essential and primary lesion in all cases of diplegia.

Arrest of development of the brain and of its outgoing paths is often found. This is the natural consequence of the foregoing neuron degeneration when this occurs during the earlier periods of development of the brain and consequently it only occurs in pre-natal cases.

Atrophic sclerosis of the brain is the natural consequence of the neuron degeneration. It is more marked the earlier in life neuron degeneration occurs and the longer the patient has lived after the degeneration has been installed. In some varieties of diplegia, of which the Waren Tay-Sachs type is an example, no sclerosis follows the neuron degeneration and this is perhaps due to a peculiar nature resident in the cause.

Gross lesions are rarely found. In one of my cases there was a gross lesion of the nature of a scar in one parieto-occipital region, but the primitive type of brain and the general atrophic sclerosis on both sides, as well as the symptomatology, which was strictly bilateral, showed that this gross lesion was an accidental accompaniment. It is under such circumstances as these that all the gross lesions are found in diplegia. In this connexion I must briefly refer to porencephaly, one of the causes of which is certainly embolism, for I have

seen a porencephaly in which the detailed history of the occurrence of an embolism in the course of mitral stenosis many years before, was available. And if embolism can cause porencephaly, then thrombosis and arterial obstruction of any kind can produce it also, and this is, in my opinion, the usual cause of porencephaly. But there must also be other causes, for I have seen a porencephaly in an adult, who never at any time showed any signs of cerebral defect and who died of tuberculous meningitis. In this case the porencephaly must have arisen from a cyst formation, which neither interfered with the cerebral elements nor caused any rise in the intracranial pressure. In diplegia, small, and sometimes multiple, cyst formation is found, which is called porencephaly. I believe that these formations originate from the collection of fluid in degenerating and sclerosing tissue and that they are secondary to the sclerosis. In the few instances in which large porencephalies are found in the brains of diplegic subjects, I think that these are due to associated vascular lesions, as was proved in one of Freud's cases. The results of encephalitis do not for the most part resemble diplegia sufficiently to give rise to confusion between the two conditions. When the similarity is close, the history of an acute onset with pyrexia and perhaps convulsion, rapidly followed by a paralysis which is most marked at first, and thereafter tends to lessen, should leave little room for error in diagnosis. Finally, I submit that the essential anatomical cause of diplegia is a primary neuronc degeneration due to factors which are at present entirely elusive, with the exception of rare cases in which syphilitic infection of the brain is certainly the provoking agent. This conception of the pathogenesis seems to me to be compatible with all the pathological evidence which has been recorded and to explain best the symptomatology and clinical aspect of this class of diseases.

Pathological Findings in the Central Nervous System of a Case of Myasthenia Gravis.¹

By Dr. Y. A. BARRADA.

(Introduced by Sir FREDERICK MOTT, K.B.E., M.D., F.R.S.)

I AM greatly indebted to Sir Frederick Mott for kindly placing at my disposal the material of this case, and for many suggestions and valuable advice in the investigation of it.

The main object of this paper is to demonstrate some changes found in the central nervous system of a case of myasthenia gravis that may throw some light on the mechanism underlying the symptoms manifested in this disease.

The patient joined the Army on August 13, 1914.

Major Walshe's report from Orwa-el-Waska is as follows:—

" July 26, 1918.—While on the Palestine Front in June, 1918, he began to notice his legs were weak, so that he could not throw his leg across his horse, but had to be helped on. A very short walk "did him in completely"; he felt weak as a child. No pain or paræsthesiæ accompanied this progressive weakness of all his limbs. Two weeks later fluids began to return through his nose, his voice went, chewing his

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