Section of Neurology

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Observations on the Pathology of Cerebral Diplegia (*Abridged*)

PRESIDENT'S ADDRESS

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DIPLEGIA is one of the commonest causes of crippling in children.

Collier (1924) did not denote the types of cases to be admitted under the title "Cerebral Diplegia", but it is clear from his address that his conception of diplegia embraced conditions of bilateral spastic weakness, congenital or acquired, both progressive and non-progressive and of all degrees of severity, ranging from generalized rigidity of the four extremities to the mildest cases which show only slight spasticity of the legs.

Sachs (1926) regards the exact form of the paralysis as relatively unimportant. In his view, it is of more practical value to group the various cases according to their time of onset and to the morbid lesions which have been found to be the chief cause of one or other forms of paralysis. But in making this choice the difficulty arises that very often we have only the history of the case to guide us, and important facts relevant to the condition may have become forgotten in the course of time.

Moreover, since the normal activities of the newborn infant are probably all reflexes mediated by the brain-stem and spinal cord, signs of pyramidal involvement are seldom evident at birth and, hence, separation of the congenital from the acquired types of cerebral diplegia will often be a matter of some difficulty. Frew (1936) states that, of sixty-two cases of cerebral birth palsy, fifty-two showed no sign of paralysis at birth, stiffness of the limbs not appearing until between the second and fourth month after birth. In my series of fifty cases, wholly satisfactory histories were seldom obtained but there was reasonable evidence of a congenital or early post-natal origin in all but five.

[For further discussion on cases of diplegia the reader is referred to the bibliography.]

Before discussing the pathological changes which may be encountered in the diplegic's brain, a few words may be said about current views on their mode of production.

PRIMARY DEGENERATION OF THE CEREBRAL NEURONES

Collier lent all his eloquence and weight of authority to support the theory that primary neuronal degeneration is the essential cause in all cases of diplegia whether incident in fœtal life or in childhood. From the pathological material available, he deduced that the morbid process begins long before birth and is in no way related to birth injury or meningeal hæmorrhage. The arrest of neuronal development he compared to the blighting effect on germinating seeds of a frost which, according to the severity and time of arrival, causes an interference varying from complete death and destruction to retardation and stunting of growth. The nature of this frost affecting the neuroblasts is unknown. In support of his view, Collier stressed the following points: The remarkable symmetry of both the paralysis and the atrophy and sclerosis of the motor convolutions. The lack of correspondence between the degree of atrophic lobar sclerosis when present and the severity of the clinical picture—the paralysis may be severe and the atrophic sclerosis slight. The presence in some cases of atrophy of pyramidal cells out of all proportion to the shrinkage of convolutions—some of the severest cases of prenatal diplegia having no gross lesion at all. The presence in amaurotic idiocy of a ubiquitous degeneration of ganglion cells unaccompanied by sclerosis, this disease being considered by Collier to belong to the general class of diplegias. The occurrence of optic atrophy in many cases of diplegia. The occurrence of familial diplegia, including instances where one child is diplegic from birth and the other siblings healthy until the onset of paralysis in the early years of childhood; the close resemblance of the symptoms of congenital and postnatal cases. The implication of the cerebellum in one case of congenital diplegia described by Anglade and Jacquin (1909). The failure to discover even the most slender causal antecedents in 40% of all cases, and, lastly, the difficulty of referring one and

the same pathological condition to such widely different causes as premature, precipitate and prolonged birth and to asphyxia.

All gross lesions, according to Collier, are an accidental accompaniment and he concludes that the evidence demands that meningeal hæmorrhage should be deleted as a causal factor of any infantile spastic state.

Great importance was, at one time, attached to the communications of Dr. Sarah McNutt (1885) who made the generalization that meningeal hæmorrhage is the usual cause of spastic states dating from the time of birth. A case of cerebral diplegia which showed bilateral cortical atrophy did much to strengthen her in this belief.

There can be little doubt, however, that McNutt misinterpreted her observations. In the first place, she failed to show that subarachnoid hæmorrhage could cause cerebral diplegia, for her two patients in whom she found hæmorrhage were not diplegic; and, secondly, she failed to establish any relationship between subarachnoid hæmorrhage and the pathological condition described by the two pathologists who examined her material.

It is, of course, not disputed that subarachnoid hæmorrhage is a frequent finding in infants' brains. Extensive extravasations are often found in infants dying within a few days of birth but such cases afford no proof that lesions of similar magnitude exist in infants that survive. Nor is it disputed that approximately 12% of all newborn infants exhibit blood in the cerebrospinal fluid, but the ultimate fate of such cases is unquestionably favourable and, even in those in which fairly extensive subarachnoid hæmorrhage over the convexity of the brain is found, it seems likely that complete absorption without damage to the underlying cortex is the rule. We know, too, that in the adult, subarachnoid hæmorrhage, if diffuse, may do little damage.

Ford (1926) stated that he had been unable to find a single report of a case of true cerebral diplegia in which the occurrence of an intracranial hæmorrhage at birth was established. Frew (1936) mentions the case of two babies that lived for a fortnight with extensive cortical hæmorrhage but the general condition of the infants was quite unlike what one finds in cerebral birth palsy. The same writer also examined the post-mortem records of seventeen cases of intranatal cerebral palsy. In no single instance was there any evidence of a cortical hæmorrhage, recent or old.

The late results of birth injury have been studied by Roberts (1939). Sixty-six cases of intracranial hæmorrhage due to birth injury were followed up for varying periods of time up to eight years. Forty infants—approximately 60% of the entire group—developed in a perfectly normal way. Only nine, showing both motor disturbance and mental retardation, could be classified as examples of cerebral spastic paralysis. Of four infants with motor disturbance only, two were monoplegias, one a paraplegia and one a case of generalized spasticity. This investigation does seem to suggest that intracranial hæmorrhage is responsible for a certain number of infantile spastic palsies but it does little to advance the view that cerebral diplegia is conditioned in this way.

However, it is not only hæmorrhages of large size which have been assigned an important role in the production of cerebral diplegia. In recent years attention has been focused on the part played by extravasation of microscopic dimension.

Schwartz (1924) was among the first to demonstrate in children, stillborn, or dying during the first six months of life, the frequency of petechial hæmorrhages and minute necrotic areas in the central white matter surrounding the third and lateral ventricles. He stressed the frequency of hæmorrhage, especially in premature infants, in the territory drained by the vena terminalis, the vena lateralis ventriculi and the vena basilaris.

Frew goes further than Schwartz. In his opinion, hæmorrhage in the parts drained by the vena terminalis is responsible for all types of cerebral birth injury, including cerebral diplegia. The parts principally affected are the lateral nuclei of the optic thalami. He suggests that hæmorrhage in this situation, by cutting off the sensory impressions which normally pass through this region, robs the cells of the motor cortex of sensory impulses on which their postnatal development is claimed to depend.

Patten and Alpers (1933) in a study of thirty infantile brains, removed either as a matter of routine or because there was some suspicion of disease, found petechial hæmorrhages in twenty-six.

It is significant that most of the capillary hæmorrhages in these cases were under the ependyma of the ventricles, in the so-called germinal centres, where one finds foci of neuroblasts and spongioblasts destined to become sources of supply for the cortex itself. They suggest that hæmorrhages into the subependymal region destroy the spongioblasts from which the oligodendroglia are derived and so interfere with the capacity of the brain to form myelin. The essential basis of cerebral diplegia is therefore defective myelinization.

Patten and Alpers conclude by stating that the hæmorrhages occur prenatally and that they have no relation to trauma; their cause is unknown.

If we adopt this conception of the relationship of myelinization to the development of motor function we are pursuing a theory which has some affinity with that advanced by Brissaud (1894). It may be recalled that he emphasized the not infrequent association of prematurity with the paraplegic forms of diplegia and avowed that birth before term arrests or retards development of the pyramidal tracts which, under normal conditions, are pictured as growing out from the cortex from the fifth month onwards. In an infant born at six months the tracts will not have developed below the medulla and the child will be diplegic; in an infant born between the eighth and ninth month the tracts will have reached the cervical region; in such a case, only the lower extremities will be deprived of their regulatory influence, and thence arises a paraplegia. His theory is open to obvious objections. In the first place, the immense majority of infants born prematurely do not suffer from paralysis nor is the proportion of diplegic infants born prematurely, large.

Again, though it is true that in the human fœtus the process of myelinization follows a definite pattern, it has not been established beyond dispute that the deposit of myelin is coincident with the development of function in the neuron. Nor does recent research suggest that this phase of maturation proceeds in such an orderly cephalocaudal manner. Orthello Langworthy (1932) has shown that in the human fœtus of six months there is a considerable amount of myelin in the cervical region of the spinal cord though at this time there are no medullated tracts rostral to the midbrain. He claims that the process of medullation extends from the medulla in a cephalic direction and it is not until the second month of postnatal life that myelin is found on fibres beneath the cortex. In the cord the spread of myelinization is from the cervical regions downwards.

Asphyxia and Anoxæmia

Though eighty years have elapsed since the appearance of Little's classical paper in which he stated "capillary apoplexies are the cause of general spastic rigidity" there is still no unanimity of opinion on this problem. Obviously, during its progress through the birth canal the fœtus undergoes special risks to its vital oxygen supply and these are increased by various accidents or incidents common in parturition. Asphyxia is inevitable when the cord is compressed as may happen in the course of podalic version and is common in breech presentations but these factors are too inconstant to afford a reasonable explanation of the origin of diplegia.

Stress has lately been laid on the possible part played by oxygen want. Such varied conditions as carbon monoxide poisoning and nitrous oxide anæsthesia are known to exercise the gravest effects on the central nervous system and, in particular, on the cerebral cortex and basal ganglia. Brander (1940) records an instructive case of a pregnant woman who attempted suicide by carbon monoxide poisoning. When seen at the age of 4½ years, her offspring was an idiot with spastic quadriplegia.

Courville (1938) has drawn attention to the special risks of nitrous oxide gas when used for the induction of anæsthesia in the second stage of labour. According to Schreiber (1938) the use in parturition of sedative drugs such as the barbiturates may so heavily narcotize the newborn infant that its respiratory centre is depressed to the point of producing anoxæmia.

Faber (1942) claims that insufficient attention has been paid to the possibility of anoxæmia occurring in earlier periods of gestation. Among the conditions which may interrupt the fœto-maternal circulation he mentions degrees of placental separation, placenta prævia, attempts at abortion, the toxæmia of pregnancy—itself a recognized cause of placental separation—and congenital syphilis which may cause placental changes sufficiently severe to interfere with normal oxygen supply to the fœtus. In a case of cerebral atrophy in Frew's series, maternal pneumonia during pregnancy appeared to be a factor of importance.

That the effects of oxygen want are especially injurious to the nervous system is clearly indicated by experimental work on animals by Gildea and Cobb (1938), Weinberger, Gibbon and Gibbon (1940), Thorner and Lewy (1940).

A few words may be said about the pyramidal tracts whose involvement is held responsible for the cardinal feature of this syndrome. It has become an almost ineradicable belief that in all mammals the pyramidal fibres are derived exclusively from the giant cells of Betz in the fifth lamina of the precentral convolutions. This belief rests largely on the observation that the anatomically conspicuous Betz cells exhibit a retrograde chromatolysis when the fibres of the pyramidal tracts have undergone transection or damage in some part of their course, but we cannot assume that the axons of small nerve cells do not share in the response to injury of the pyramidal tract, for such cells do not ordinarily show chromatolysis.

Campbell (1905) estimated the number of Betz cells in each precentral convolution to

be in the neighbourhood of 25,000 and more recently Lassek counted rather more than 34,000 in similar areas. There seem to be few exceptions to the histological arrangement whereby large cells possess large fibres and small cells small fibres and on this basis it follows that if the giant Betz cells are the sole source of pyramidal bundles the constituent fibres should be predominatingly large. Yet in the human pyramidal tract the contrary obtains: by far the greater number are fibres of small calibre. Just rostral to its decussation each pyramidal tract contains roughly two-thirds of a million medullated nerve fibres of which nine-tenths can be classified as small; in other words the large fibres derived from the Betz cells are enormously outnumbered and hence it follows that, unless the axons of Betz cells dichotomize extensively before reaching the spinal cord, the greater proportion of pyramidal tract fibres must originate from cells of small size.

In the present state of our knowledge it is not possible to say with any degree of certainty where these cells of origin are to be found. Both Economo (1929) and Fulton (1938) have expressed the view that small pyramidal cells of the precentral areas contribute to the corticobulbar and corticospinal projections.

Here it may be observed that it is by no means easy to decide what exactly constitutes a Betz cell. Size, by itself, affords no criterion. Lassek (1940) found cells with the morphological appearance of Betz cells of a size varying between 900 and 4,100 sq. μ; the diminutive type predominated in all regions of the motor cortex while 75% of the giant cells were congregated in its upper third. Giant cells may also be found in the posterior parts of the second and third frontal convolutions.

It seems evident that, if the fibre content of the pyramidal bundles receives a substantial contribution from the immense number of small pyramids, their implication in the upper motor neurone disease could only be demonstrated by making serial sections of the entire motor cortex with counts of the ganglion cells in at least three laminæ and a task of this magnitude has yet to be attempted.

A review of the voluminous literature of cerebral diplegia conveys the impression that speculation on its pathogenesis has outstripped the concrete task of examination of pathological material. Yet, obviously, assembly of pathological data should precede speculation. Here it must be confessed that the reports of the last century are of limited value, many of them being concerned solely with macroscopic appearances while others dealing with microscopic findings labour under the handicap of inadequate histological methods.

Material from Leavesden Hospital

The present study is based on material derived from diplegic aments. In the series are fifty brains and thirty spinal cords. Table I gives an analysis of the clinical types included in the series.

TABLE I

Cerebral diplegia	36
Cerebral triplegia	3
Cerebral quadriplegia	4
Double athetosis	5
Cerebellar diplegia	2
	50

Four patients exhibited congenital syphilis, in one tuberous sclerosis accompanied the diplegic syndrome and in six there was a familial incidence. The ages of the patients at death and their distribution according to mental age are given in Charts 1 and 2. It

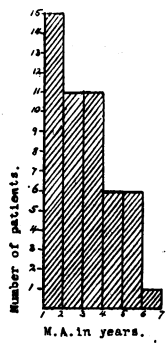

CHART 1.

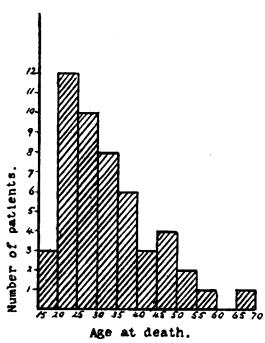

CHART 2.

will be observed that three-fifths of the patients had reached adult life, that all were mentally defective and, with few exceptions, in the ranks of low-grade amentia.

In Chart 3 the total brain weights are shown. It will be seen that fourteen patients

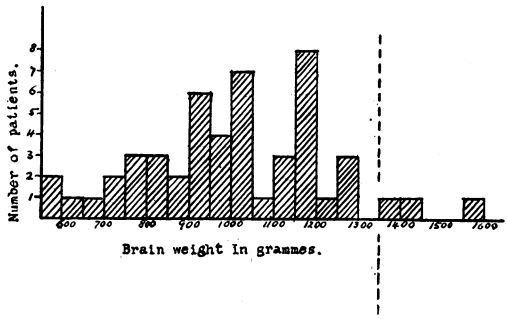

CHART 3.

exhibited a marked degree of microcephaly, while only three reached the average normal brain weight.

Description of Lesions

TABLE II

Macroscopic appearances

Normal appearances	9	Cerebellar atrophy	5
Atrophic lobar sclerosis	6	Developmental anomalies	1
Microcephaly	16	Optic atrophy	2
Micro-hydrocephaly	3	Small pyramids	12
Cortical atrophy without obvious sclerosis	6	Thickening and opacity of pia-arachnoid on vertex	13
Marked abnormal convolution pattern ...	13		

Table II brings out the wide variations in the naked-eye appearances. They include brains which, apart from their undersize, showed no departure from the normal to those which were typical examples of atrophic lobar sclerosis. Ford claims that atrophic sclerosis is the commonest pathological finding in cerebral diplegia. In this series it was present in only six cases.

Rather more than a quarter of the brains showed a marked degree of thickening of the pia-arachnoid, usually most marked in the neighbourhood of the longitudinal fissure. Beneath the thickened membranes the convolutions were usually narrow but seldom definitely sclerotic.

Two of the cases were examples of cerebellar diplegia and in both the cerebellum showed a very marked atrophy. But cerebellar atrophy of a striking degree was also present in three cases of spastic diplegia who, during life, gave no signs of cerebellar involvement. Moreover, milder degrees of atrophy of the cerebellar hemispheres were encountered in a good many other cases, even in microcephalics who usually show a relatively large cerebellum. One other macroscopic appearance calls for remark. In the normal brain the pyramids form two conspicuous rope-like strands on the ventral aspect of the medulla. In the fifty diplegic brains a normal degree of development was seen in ten instances only.

Disturbance of the internal configuration of the cerebral hemispheres was noted in two instances. In one, sclerosis with cavity formation was found in the mesial thalamic nucleus of one cerebral hemisphere and in a second case the appearances were those of status marmoratus.

Microscopic appearances.—The wealth of material, now amounting to more than three thousand slides, makes the task of presenting a comprehensive picture of the histological findings one of some difficulty and here it is possible to present only the barest outline.

At the outset it may be said that degeneration of the pyramidal tract was by no means a constant finding. In four cases (8%) no abnormality could be found in any part of the corticospinal path. In these Betz cells were present in their normal number with no evidence of demyelination of their fibres, nor was there any apparent loss of the smaller pyramids in the motor area.

In five cases only was it possible to trace degeneration from the motor cortex through the internal capsule, the peduncles and brain-stem to the lumbar region of the cord. In other cases where abnormality existed, degeneration could be demonstrated only at certain levels. Thus, in twenty-two cases a full complement of Betz and smaller pyramidal cells was present although in more than half marked demyelination of the pyramidal

tracts existed at lower levels. In eighteen cases there was moderate loss and in ten complete absence of Betz cells. In three cases, although the giant pyramidal cells were apparently nearly or entirely absent, degeneration of nerve fibres did not become visible until they had reached the pons or the medulla or the spinal cord. These topographical differences were striking. Of the thirty spinal cords examined, fifteen appeared entirely normal, three showed moderate degeneration and twelve marked degeneration of the pyramidal tracts. Another point to be emphasized was the frequency with which there was concomitant involvement of other pathways, particularly in the lateral and posterior columns of the cord. Sclerosis strictly limited to the pyramidal tract occurred in but one instance.

In all cases in which pyramidal degeneration was present it was possible to demonstrate varying degrees of astrocytic gliosis. Such a finding ill accords with the conception of a primary arrest of myelinization in cerebral diplegia.

In the cerebral cortex various other changes were noted. Apart from the general poverty, irregular alignment and defective development of nerve cells, so often seen in the brain of the low-grade ament, one could often note small areas in which no nerve cells could be seen. In extent these varied from mere cell gaps only visible under high-power microscopic examination to larger and more easily seen areas of complete devastation. Sometimes oval and sometimes linear in outline, almost invariably they were limited to the third and fourth laminæ.

Demyelination, either limited to the subcortex or widely spread throughout the white matter was another not infrequent finding. It appeared to be a characteristic feature in cases of familial diplegia and was invariably associated with a fibrillary gliosis readily demonstrable by the application of Holzer's stain.

Ganglion cell lesions of the basal ganglia are somewhat difficult to evaluate, requiring constant comparison with normal tissue, and further study is required but it may be said here that, in the striatum, loss of the large or of the small nerve cells or of both was a fairly frequent occurrence. An outfall was found in twenty-three cases—almost half the total.

Status marmoratus was found in one case. Changes in the pallidum were seldom noted.

Cerebellar changes.—When Collier addressed this Section he was able to refer to only one case of cerebral diplegia in which there were cerebellar changes. In the present series, they were extremely common. A completely normal cerebellum could be found in twelve instances only.

The microscopic appearances showed every gradation from localized loss of the Purkinje cells in one or two lamellæ to complete and universal atrophy of the cortex of both the vermis and lateral lobes.

Gross atrophy all layers	8
Total or marked loss of Purkinje cells	7
Moderate loss	5
Slight loss	9
Proliferation of Bergmann's cells only	9
Normal	12

The elements most constantly involved were the Purkinje cells; their degree of involvement varied from an outfall limited to one folium to a complete disappearance in all areas and this cell loss showed no predilection for the neocerebellum.

The layer of Bergmann's glia cells was usually conspicuous wherever cell atrophy could be detected. In more advanced cases the molecular and granular layers shared in the atrophy.

The cause of this frequent implication of Purkinje cells is obscure but there is no doubt that these cells are exceptionally vulnerable, for Scherer (1931) mentions at least thirty pathological conditions in which these elements are affected. Degeneration secondary to involvement of the cerebral cortex is not a feasible explanation and it is obvious that birth injuries of a gross character can play no part.

Ellis (1918) stated that a deficiency of Purkinje cells is a characteristic finding in the cerebellum of the mentally subnormal and in large measure affords an explanation of the deficiency in motor co-ordination found in such individuals. This has not been my experience. Some years ago, W. Ross Ashby and I made a quantitative study of the Purkinje cells in the brains of sixty-two mental defectives. Counts below the normal density of 300 to 400 cells per sq. mm. were found in but five instances and, of this number, four were examples of infantile cerebral palsy. More serious consideration must be given to the claim of Spielmeyer (1930) that, in the epileptic, changes in the cerebellum are frequent and equal to those seen in Ammon's horn. He describes as characteristic proliferation of the fibroglia in the molecular zone, increase in the number of Bergmann's glia cells and, above all, loss of Purkinje cells. Of the sixty-two aments referred to,

roughly one-third were epileptic, but normal Purkinje cell counts were the rule, except in the brains from diplegic cases. Forty-four per cent. of my diplegic patients were epileptic but the loss of Purkinje cells bore no constant relationship to the presence or absence of convulsions and it would seem, therefore, that the presence of epilepsy cannot afford a satisfactory explanation of the frequency of these changes.

The possibility that anoxæmia plays some part in their production is suggested by the animal experiments of Gildea and Cobb (1938), Weinberger, Gibbon and Gibbon (1940), Thorner and Lewy (1940) which give convincing proof of the disastrous effects of oxygen want on the cerebral and cerebellar cortex. Changes varying from minute patchy areas of cell loss to larger areas of cortical destruction are typical findings in cerebral anoxia while in the cerebellum the Purkinje cells are hardly less susceptible.

Now, as we have seen, these changes are frequently encountered in the brain of the diplegic and though similarity of lesions is not a sound basis on which to build claims for identity of cause, the hypothesis of cerebral anoxæmia operating at or before birth would appear to offer a reasonable explanation of the pathological findings in certain cases of cerebral diplegia.

To suggest the hypothesis that nutritional deficiency may help to explain the origin of cerebral diplegia is to theorize entirely beyond the known facts, yet the lesions I have described have so many points of resemblance to those observed in avitaminosis that the following comment seems permissible.

In the first place, attention may be drawn to the undisputed fact that in the past a not inconsiderable proportion of the population of this country lived on the borderland of vitamin insufficiency and that clinical experience has shown that many of the disturbances so common in the early stages of pregnancy are almost certainly due to a low level of maternal nutrition.

Secondly, recent experimental work on the effects of vitamin deficiency has indicated that many of the lesions produced have the distribution and character of those described in cerebral diplegia. Swank and Prades (1942), for example, have shown that thiamine deficiency exercises its effects first on the distal part of the axon with myelin changes secondary to these, that degeneration proceeds centralwards, that large nerve cells and large nerve fibres degenerate first, presumably because their metabolic needs are greater and they are therefore more susceptible to nutritional deficiency, that marked degeneration is found in the cerebellum and, lastly, that widespread hæmorrhages of small size are present in regions containing degenerating neurones.

Thirdly, a study of the lesions in demyelinating diseases in man and animals indicates that many of these have their counterpart in the diplegic's brain. We have already seen that in cerebral diplegia disappearance of the large cells of Betz is inconstant and there may be apparently complete absence of demyelination at cortical, capsular or peduncular levels when obvious sclerosis is evident in the brain-stem and spinal cord. As Davison (1941) has shown, this peculiarity of distribution is shared by amyotrophic lateral sclerosis: in about two-thirds of the cases the giant cells of Betz are spared and degeneration of pyramidal tracts may not become visible until the pons, the medulla or even the spinal cord is reached. The ætiology of amyotrophic lateral sclerosis is unknown but Wechsler's (1940) studies on vitamin E therapy suggest that the question of nutritional deficiency cannot be ignored.

Then again there is a close analogy between the petechial hæmorrhages found by Patten and Alpers in the neighbourhood of the ventricles and those found in the periventricular grey matter in the Wernicke syndrome and the principal causative factor in the latter is almost certainly nutritional deficiency.

Several points of interest emerge from consideration of the peculiar disease in lambs known as "swayback". Innes and Shearer (1940) have shown that "swayback" occurs in the offspring of normal ewes and in most instances is present from birth. It appears to have its origin in a disturbance of copper metabolism which causes no obvious disturbance in the health of the ewe but exerts a pathological effect on the fœtus or young lamb. Clinically there is generalized inco-ordination, marked spasticity and occasional blindness. The microscopic appearance of the affected brain is characterized by the constant presence of cortical nerve cell degeneration, severe demyelination and cavitation of the white matter with astrocytic glial proliferation. In a recent communication, Winkelman and Moore (1942) have provided an almost perfect human analogy to "swayback". An infant with progressive spastic diplegia, convulsive seizures and marasmus died when twelve weeks old. Microscopic examination showed complete diffuse demyelination of the hemispheric white matter with symmetrical cavitation and an astrocytic gliosis. These authors express the opinion that their case may help to strengthen further the viewpoint of those who believe that antenatal factors may explain some of the clinical syndromes often attributed to birth trauma.

Conclusions

Although much investigation has still to be undertaken, a number of facts stand out sufficiently clearly to justify certain generalizations.

First, there is no evidence in this series of fifty cases of cerebral diplegia of any morbid change in the nervous system which is invariable and specific.

Secondly, it may be observed that the lesions encountered in cerebral diplegia are of a character so diverse as to indicate that the hypothesis of a single cause common to all cases cannot be sustained.

Thirdly, the high proportion of cases born normally at term exhibiting marked degrees of microcephaly afford clear proof of the prenatal origin of the condition and suggest that birth injury has in the past been assigned far too large a part in the pathogenesis of cerebral diplegia, and, lastly, many of the lesions encountered in this investigation can best be explained on the basis of Collier's conception of a primary degeneration of the cerebral neurones. The ætiological factors concerned in this degeneration are likely to be numerous. The possibility that anoxæmia and nutritional deficiencies are among those concerned deserves serious consideration.

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