ÉTAT MARBRÉ OF THE CORPUS STRIATUM FOLLOWING BIRTH INJURY

BY

R. M. NORMAN

From the Burden Mental Research Department, Stoke Park Colony, Bristol

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THE presence of myelinated fibres in aggregations of a density abnormal for that particular region of the nervous system constitutes état marbré. In the cerebral cortex of the adult such localized areas of hypermyelination may occur as an incidental feature of the pathology of cardiovascular disease or of carbon monoxide poisoning. Etat marbré of the corpus striatum, however, appears to be a phenomenon of infancy or, rarely, of early childhood, and its pathogenesis is still a matter of controversy, it being claimed on the one hand that the condition is a prenatal anomaly of growth, on the other that birth injury is the probable causative factor.

There are several lines of evidence giving support to the latter view. First, in a high proportion of the cases in which details of the birth and neonatal period are recorded there is found a history of prolonged or abnormal labour, or of severe asphyxia with difficulty in resuscitating the infant, or of the baby's weakness in early life associated perhaps with epileptic attacks (Meyer and Cook, 1936; Byers, 1942). Attempts to explain these events as the consequences of pre-existing malformation are hardly convincing. Secondly, as was shown by Schwartz (1924; 1926), the bleedings and softenings of fatal birth injury favour a periventricular distribution, the caudate nucleus and thalamus being sites of predilection, these central lesions following stasis in or rupture of the terminal tributaries of the great vein of Galen. This vessel is liable to damage or occlusion during birth by reason of its mode of termination in the straight sinus (Holland, 1920; Clark, 1940). Yagi (1930) has demonstrated that the elastic fibres in the wall of this vein are feebly developed even in fœtuses of seven months, a fact of significance in accounting for the well-known susceptibility of premature infants to birth injury. Furthermore, the experi-

mental work of Schlesinger (1939) showed that sudden occlusion of one small vein of Galen leads to hæmorrhage into the caudate nucleus of the same side. While it cannot be denied that necrotizing lesions of the basal ganglia may follow congestion or stasis in the Galenic venous system during parturition, it is not generally admitted that état marbré is a common sequela of such a process. The probability of such an assumption being correct is considerably increased by the findings in a case reported by Pfeiffer (1939) who described gross bilateral cavitation of the putamina with état marbré in the surrounding tissue. Moreover, in a case of undoubted birth injury recently published by myself (Norman, 1944) marbling of the caudate nucleus was associated with a small adjoining area of anæmic necrosis. Finally, état marbré of the corpus striatum is often combined with lesions of the cerebral cortex which themselves are highly characteristic late neuropathological sequelæ of birth trauma (Benda, 1945). Such, for example, are the hypermyelinated ulegyria or atrophic sclerosis overlying small foci of subcortical softening found with especial frequency in the parieto-occipital areas, and the more massive cerebral softenings represented by large cavities or the diffuse multiloculated type of polyporencephaly described by Juba (1937).

Although the evidence outlined above seems to establish a causal relationship between état marbré and birth injury, this view has been rejected by Alexander (1942), who reaffirmed the original opinion expressed by the Vogts (1920) that the condition is a prenatal malformation, genetically determined. He has claimed that the abnormal myelinated fibre bundles and networks of the putamen are aberrant offshoots of the fronto-pontine tract, and has denied the reality of the coincident gliosis and nerve cell loss first observed by Scholz

(1924) and since confirmed by several other writers on the subject. In view of this conflict of opinion I have thought it profitable to describe the following three new examples of striatal état marbré. These cases support the thesis that the condition commonly results from vascular lesions sustained during birth, and also illustrate additional pathological features of interest to the student of mental deficiency.

Material

CASE I

B. V., a male, was admitted to Stoke Park Colony when 10 years old and died aged 25 years.

HISTORY BEFORE ADMISSION.—The mother, an intelligent woman, gave a good account of the circumstances of the birth and early life of the patient. She was in very good health throughout the pregnancy but had no medical antenatal care. It was her first child and she was in her thirty-ninth year. Labour lasted about fifteen hours and "as the labour pains did not increase the doctor gave me chloroform and brought the baby." The infant weighed nearly 10 lb. at birth and was "bluey purple" when the mother first saw him. The doctor in attendance was able to recall the case, for it was the only midwifery he had done since qualification six years previously. He confirmed that the baby was very blue and he "had to work hard for twenty minutes to get it to breathe." Apart from the asphyxia he did not think the case presented any difficulties. There was no history of jaundice in infancy. At the age of 6 months the baby was "quite intelligent looking and laughed and noticed us." He was not breast fed but artificial feeding was satisfactory. There was delay in his ability to sit up without support and as time passed it was noticed that he "never seemed to have control over his arms when he tried to feed himself." His father spent much time trying to teach him to walk, but the child never managed more than a few steps before falling down. He was able to learn the alphabet, and could count and spell short words.

FAMILY HISTORY.—There is no history of mental deficiency, epilepsy, paralysis, or stillbirths on either side of the family. There are two other children of the marriage, and they are mentally and physically normal save that the younger has valvular disease of the heart, discovered for the first time when she went to school.

EXAMINATION AFTER ADMISSION.—He was a diplegic imbecile with no educational attainments. A neurological examination made when the patient was 21 years old gave the following information. The cranial nerves were normal and there was no nystagmus. He was unable to stand or sit up. Muscle tone was markedly increased in arms and legs, the arms being held in the position of internal rotation with flexed wrists. The knees were contracted and flexed and the legs could not be extended beyond an angle of about 150°. Equinus deformity of both feet was present. Athetosis was

severe in the face and arms, and both arms showed a marked rebound phenomenon. Leg movements were handicapped by considerable synergic spasm which affected especially the left side. The tendon reflexes were equal on both sides of the body, the knee jerks being exaggerated and obtainable by striking the whole length of the leg. Both plantar reflexes were extensor in type, and Oppenheim's sign was also present bilaterally. Satisfactory sensory tests could not be carried out, but a marked failure in the ability to localize stimuli was noted. There was severe dysarthria. Measurements of the length and circumference of forearm, arm, thigh, and leg showed no asymmetry. Sphincter control was normal. There was no epilepsy. Subsequently examinations showed little change in the general condition apart from variation in the knee jerks, which were on two separate occasions reported as normal, and also a variable plantar response in the right foot, which was flexor at one examination.

Death occurred at the age of 25 from broncho-pneumonia.

PATHOLOGY OF THE CENTRAL NERVOUS SYSTEM

MACROSCOPIC EXAMINATION OF THE BRAIN.—The brain weighed 1378 g. of which the cerebellum and attached brain stem accounted for 205 g. The convoluted pattern was normal. Coronal section revealed état marbré in both putamina.

MICROSCOPIC EXAMINATION.—Blocks of tissue were taken from representative areas of the cerebral cortex and basal ganglia of both sides, from cerebellum, brain stem, and cervical spinal cord. Sections were stained by standard methods for nerve cells, neuroglia, axis cylinders, and myelin.

Putamina.—The myelin stain confirmed the naked-eye impression of état marbré, densely myelinated fibres in the form of interlacing strands occupying mainly the dorsal three-fourths of the caudal portions of both putamina (Fig. 1). On the right side, more anteriorly, these abnormal bundles appeared as a narrow laterally placed fasciculus (Fig. 2). The normal darkly staining and compact fibre bundles of the putamen were intact and showed up clearly even in areas involved in the more diffuse hypermyelination of the marbled state. In sections stained by the method of Holzer for fibrillary neuroglia a dense network of gliosis was demonstrated in the areas of marbling, a rough correspondence as regards intensity being noted between adjacent sections stained for myelin and glia respectively (Figs. 3, 5, 6). Gliosis was more marked around the blood vessels, and shrinkage of the tissue had caused considerable dilatation of the perivascular spaces. A mild fibrillary gliosis was also present in the normal myelinated fibre bundles of the putamen traversing the areas affected by état

marbré (Fig. 6). A conspicuous loss of nerve cells had occurred in the regions showing état marbré, although the larger nerve cells sometimes survived in otherwise devastated areas (Fig. 4). Bielschowsky staining showed numerous axis cylinders of fine calibre occupying these affected areas.

Thalami.—Sections stained by cresyl violet revealed patchy and sometimes extensive areas of nerve cell loss, especially in the lateral nuclei. Such foci were characterized by an increase in glial nuclei, and often by small groups of "calcified" nerve cells (Figs. 7, 10). Holzer staining showed widespread gliosis, sometimes reticulate in pattern (Fig. 9), and in places of extreme density (Fig. 8). In myelin preparations an abnormal density of fibres was seen in parts of the medial and lateral nuclei, an effect enhanced by an occasional patchy poverty of fibres in adjacent areas (Fig. 2). In the nucleus of the left thalamus there was found an area of severe nerve cell loss and gliosis, associated with a conspicuous hypermyelinated plaque of quadrangular shape.

Other Parts of the Brain.—An abnormal gliosis, unassociated with nerve cell or myelin changes, was present around the aqueduct, beneath the floor of the fourth ventricle, and also in the central raphe of the dorsal pons. Elsewhere in brain and cerebellum no pathological features of note were discovered. In particular it may be remarked that the caudate nuclei showed no état marbré, that the pigmentation of globus pallidus and substantia nigra was normal, and that the myelinated fibres of the fronto-pontine and pyramidal tracts were intact.

CASE 2

C. G., a female, was admitted to Stoke Park Colony when 8 years 4 months old, and died aged 13 years 9 months.

HISTORY BEFORE ADMISSION.—The mother, a healthy farmer's wife, gave a good account of the birth and early life of the patient. The pregnancy was uneventful. It was her first confinement and the baby was full term. Labour started at 6 a.m., and at 12 noon that day the family doctor delivered the infant by forceps. There was some difficulty in getting the infant to breathe, and she was held upside down and smacked. Breast feeding was started, but for the first week or two the child was too feeble to suck properly. The mother noticed when the child was about 8 months old that she "was holding her left hand closed most of the time and was not using it with the other one", also that the left leg appeared to be weak when she started to crawl. At the age of 10 months convulsions were observed. At first "they were more like holding her breath for a few seconds, then gradually became worse as she grew older, occurring two or three times a day." During the fits the left arm and leg

became stiff. When the patient was 18 months old daily massage and electrical treatment were instituted, and she began to learn to walk. The arm and hand were useless, however, and she never learned to talk.

FAMILY HISTORY.—Father, mother, and grandparents were normal physically and mentally. The patient has a young sister who is also normal.

EXAMINATION AFTER ADMISSION.—At the age of 8 years the child was found to be an idiot with severe epilepsy, speechless, noisy, and excitable. She was incapable of performing even the simplest tests of the Merrill-Palmer Scale. Her weight and standing stature were normal, but she was small-headed. The blood Wassermann reaction was negative. A neurological examination at the age of 11 years gave the following information. The left arm and leg were stunted (2 inches and 1 inch shortening respectively). Both hands and feet were cold and blue, the left foot being the more affected. The patient was able to rise from the recumbent position with difficulty and could walk quite well with an obvious hemiplegic limp. The left arm was quite helpless, wrist drop was present, but there was no spasticity and no contractures. There was slight contracture of the left Achilles' tendon, but no evidence of increased muscle tone was found on passive movement of the limb. The left knee jerk was exaggerated, and was obtainable by striking the inner side of the left leg over a wide area. The right knee-jerk was also somewhat brisker than normal. The left plantar reflex was doubtfully extensor, with marked fanning of the toes. The abdominal reflexes were present. The cranial nerves and pupillary reactions were normal. There was no athetosis.

During the last year of her life the patient became feebler, and finally was scarcely able to walk without assistance. Muscle tone became more obviously spastic in the left limbs, and the left plantar reflex was definitely extensor in type. The epileptic fits, never properly controlled by sedatives, had recurred with greater frequency and severity and death from status epilepticus occurred in her fourteenth year.

PATHOLOGY OF THE CENTRAL NERVOUS SYSTEM

MACROSCOPIC EXAMINATION OF THE BRAIN.—The brain weighed 850 g., of which cerebellum and pons accounted for 142 g. A large cystic cavity was present in the right cerebral hemisphere, the greater part of the third frontal and superior temporal, and the lower portion of the central gyri having been destroyed. The adjacent parietal convolutions showed marked distortion of pattern and felt sclerotic to the touch. The outer wall of the cyst was composed of a smooth membrane which followed the main convex contour of the hemisphere. Coronal section of the brain (Fig. 11) showed that the cavitation extended deeply into the white substance, being separated by a narrow boundary from a somewhat dilated lateral ventricle. The cortex of the insula had been destroyed. Fine trabeculae

filled the interior of the cavity. The right hemisphere was about 2 cm. shorter than the left at its occipital extremity. The cerebellum showed slight contralateral atrophy.

MICROSCOPIC EXAMINATION

Cerebral Cortex.—The thin external wall of the cavity in the right hemisphere was shown on section to consist of a gliotic membrane derived apparently from compressed and atrophied white matter and distinct from its leptomeningeal coverings. Small islands of sclerosed grey matter, sometimes containing a few nerve cells, were present on the surface of this membranous wall (Fig. 13). In the parietal cortex adjoining the cavity extensive sclerotic hypermyelinated ulegyria was present, as illustrated in Figs. 15 and 16. Abnormal myelinated fibres, in the form of plaques, whorls, or reticulated strands, occurred at the edges of areas of total atrophy and heavy glial scarring, a cluster of bizarre microgyric convolutions often sprouting from a common stem of non-myelinated, densely gliotic tissue. The outer surface of such gyri were frequently mammillated, presenting the appearance of "granular atrophy", and on section they showed islands of nerve cells separated by a heavy network of fibrillary neuroglia (Fig. 14). The small distorted convolutions sometimes gave the impression of having adhered and fused at points of contact with one another (Fig. 16). The left side of the brain appeared intact; and neither cornu ammonis showed pathological change.

Basal Ganglia.—Well marked état marbré was present in the right caudate nucleus and in the dorsal quarter of the right putamen (Fig. 12). Gliosis could not be demonstrated except in the putamen, where, after prolonged search of phosphotungstic acid hæmatoxylin preparations under the oil immersion lens, a few fibrils were seen in an area of état marbré. In the outer segment of the anterior part of the right globus pallidus, two small foci characterized by dense gliosis and absence of myelin were visible by the naked eye. Microscopic examination revealed masses of "calcified" débris with occasional "calcified" nerve cells in these situations (Fig. 17). No conspicuous increase in Hallervorden-Spatz pigment was seen. The right thalamus was shrunken and showed marked retrograde degeneration of nerve cells. The basal ganglia of the left side appeared to be normal.

Other Parts of the Brain.—In the medulla the right pyramidal tract was very small, but contained thinly distributed myelinated fibres. The left pyramidal tract at this level was of fully normal adult size and appeared somewhat hypertrophied compared with

those from other defective brains with which comparison was made. In the cerebellum the cortex and white matter appeared normal, no microscopic differences between the two halves of the cerebellum being observed apart from a slight hypoplasia of the folia of the left hemisphere. The cells of the left dentate nucleus were smaller and often stained less deeply than those of the right.

CASE 3

L. W., a female, was admitted to Stoke Park Colony when 9 years 10 months old, and died aged 18 years 7 months.

HISTORY BEFORE ADMISSION.—Information as to the patient's early life was scanty since the mother had died from tuberculosis before the child was sent to the Colony, and the father, an unemployed collier, was unable to recall many details. The patient was one of twins and was born at home before the arrival of an ambulance to take the mother to hospital. When in her third year the child began to suffer from epileptic fits, and it was then that her father realized that she was not a normal child and was not using her right arm and leg properly. More precise evidence as to the infant's condition before this date was furnished by observations made in the Sheffield City General Hospital when she was 18 months old. Dr. Clark, the Medical Superintendent, kindly provided the following notes. "The child was sent in as a case of pneumonia but proved to have bronchitis. There was a slight internal strabismus of the left eye, but no other paralysis. She was well nourished, and there was no history of any previous illness. She remained in hospital about three weeks and was discharged well. There was no history of fits."

FAMILY HISTORY.—The parents, grandparents, and two older brothers were mentally and physically normal. The twin sib of the patient was found dead in bed when six months old but the father could not say what was the cause of death.

EXAMINATION AFTER ADMISSION.—The patient was an idiot with a mental age of two years nine months as estimated by the Merrill-Palmer scale of tests. Speech was limited to a few poorly articulated words. She was often noisy and destructive and took little interest in her surroundings. She was small-headed, and about three years retarded as regards standing stature. The blood Wassermann reaction was negative. Neurological examination gave the following information. The fundi and discs were normal. The pupils were equal and reacted to light and accommodation. There was a left convergent strabismus. A right-sided hemiplegia was present with shortening and wasting of the limbs, the forearm being contracted in the pronated position. Muscle tone was spastic, and the tendon reflexes were exaggerated on the right side, the left knee jerk also being abnormally brisk. The abdominal reflexes were absent. Both plantar reflexes were reported as flexor. She was able to walk but was unsteady. Sphincter control of bladder and bowel was defective. She was a severe

epileptic, the fits being incompletely controlled by phenobarbitone and bromide. Death resulted in her nineteenth year from pulmonary tuberculosis.

EXAMINATION OF THE CENTRAL NERVOUS SYSTEM

MACROSCOPIC EXAMINATION OF THE BRAIN.—The weight of the brain was 825 g., cerebellum and pons accounting for 135 g. The transverse dimension of the left cerebral hemisphere was markedly shorter than the right, slight shortening also being present at the occipital pole. The gyri of the left side were generally somewhat smaller and of more variable diameter than those of the right hemisphere, this difference being most noticeable in the parieto-occipital area (Figs. 18, 20). The convolutions in this part of the cortex were more complex and irregular, and sometimes their crowns at points of narrowing appeared sclerosed. The cuneus was markedly stunted. Viewed from the surface the brain showed no evidence of a destructive process, but on section the basal part of individual gyri in the parieto-occipital area often showed considerable shrinkage, and varying degrees of destruction were seen in the walls of the convolutions. The left lateral ventricle was generally dilated, the subcortical white matter in the roof of the posterior horn being reduced to a few millimetres in depth. The frontal part of the body of the left caudate nucleus was considerably thinned and elongated in a lateral direction (Fig. 19). In the white matter of the left frontal lobe, immediately superjacent to the outer and upper angle of the dilated ventricle, a small area of cavitation and rarefaction was present beneath the intact ependyma. The cerebellum showed slight hypoplasia of the right hemisphere.

MICROSCOPIC EXAMINATION

Cerebral Cortex.—The shrunken parieto-occipital gyri of the left hemisphere showed, in the main, the same microscopic features as those in Case 2, though the numerous small convolutions of bizarre shape were not encountered. Hemiatrophy of individual convolutions was frequently seen, with abrupt transitions between mural areas of destruction and overhanging intact crowns. The anterior wall of the left precentral gyrus, and also the left post-central gyrus in part of its course, were affected in this way, the latter narrowing at its upper limit to an atrophied leaf-like structure. The basally constricted, club-shaped convolutions showed hypermyelinated plaques, gliosis, and conspicuous nerve cell loss in their shrunken portion (Fig. 24). The left visual cortex was atrophied in the depths of the

calcarine fissure. In the transitional zone between degenerated and normal portions of the visual area, *état marbré* was present in the form of narrow strands of hypermyelinated fibres running at right angles to the stria of Gennari (Fig. 22). Linear streaks of gliosis, corresponding in myelin preparations to similar streaks of demyelination, were often seen radiating upwards from the thinned white matter into the central cores of the overlying gyri. This phenomenon was also observed in the small area of cavitation adjoining the frontal horn of the lateral ventricle (Fig. 23). The central white matter of the left occipital lobe was devoid of myelin and showed heavy gliosis (Fig. 22). There was a conspicuous loss of pyramidal cells in the Sommer sector of the left cornu ammonis. No pathological change of note was found in the right side of the brain, with the exception of a small area of complete cortical devastation associated with gliosis, and irregularly arranged hypermyelinated fibres present in the anterior wall of the pre-central gyrus in its upper portion.

Basal Ganglia.—The attenuated part of the body of the left caudate nucleus showed complete disappearance of nerve cells, heavy fibrillary gliosis, and a conspicuous strand of coarse, myelinated fibres running parallel to the ventricular surface. At a point where this atrophic portion expanded frontally to form the head of the nucleus there was an area of typical *état marbré* in the form of a large triangular hypermyelinated scar having within it an island of normal tissue (Fig. 21). In the thalamus of the left side there were several areas of nerve-cell devastation and gliosis, more particularly in the lateral nucleus, of the type commonly associated with retrograde degeneration following cortical lesions. In the dorsal part of the lateral nucleus, near its ventricular surface, there was a small necrotic focus, characterized by absence of myelinated fibres and a dense undergrowth of fibrillary neuroglia.

Other Parts of the Brain.—The left half of mid-brain, pons, and medulla were noticeably smaller than the right. A small focus of tissue destruction, similar to that described in the thalamus, was present in the left side of the midbrain at a point dorso-lateral to the decussation of the superior cerebellar peduncles (Fig. 25). The pyramidal tract of the left side showed marked degeneration, though scattered fibres were fairly numerous in the medullary pyramid, the total volume of which, however, was grossly reduced (Fig. 26). The lateral columns of the right side of the spinal cord were similarly affected throughout their course. The right cerebellar hemisphere and dentate nucleus showed mild hypoplastic changes, as in Case 2.

FIG. 1.—Case 1. Coronal section of basal ganglia of the left side. Note the état marbré in the dorsal part of the putamen and in the anterior nucleus of the thalamus. Anderson's modification of the Kultschitsky-Pal method, $\times 2.2$.

FIG. 2.—Case 1. Coronal section of basal ganglia of the right side. Note the état marbré in the outer part of the putamen and the abnormal mottled appearance of the thalamus (due to areas of myelin poverty in juxtaposition with areas of increased fibre density). Stain as in Fig. 1, $\times 2.6$.

FIG. 3.—Case 1. Left putamen showing état marbré. The normal compact fibre bundles are intact. Anderson's modified Kultschitsky-Pal stain, $\times 12.8$.

FIG. 5.—Case 1. Left putamen. Fibrillary gliosis in an area of état marbré. The field corresponds to that shown in Fig. 3. Holzer stain, $\times 12.8$.

FIG. 4.—Case 1. Left putamen showing gliosis and loss of small nerve cells in an area of marbling. The larger nerve cells are preserved. Toluidine blue, $\times 100$.

FIG. 6.—Case 1. Left putamen. Fibrillary gliosis in an area of état marbré. On the left is seen part of a normal compact fibre bundle. Holzer stain, $\times 360$.

FIG. 7.—Case 1. Left thalamus showing extensive loss of nerve cells and increase of glial nuclei in the lateral nucleus. Toluidine blue, $\times 36$.

FIG. 9.—Case 1. Left thalamus. Same area as in Fig. 7. Showing reticulate arrangement of the gliosis. Holzer stain, $\times 36$.

FIG. 8.—Case 1. Left thalamus. Dense fibrillary gliosis in lateral nucleus. Holzer stain, $\times 360$.

FIG. 10.—Case 1. Left thalamus showing loss of nerve cells and glial proliferation in the area of marbling seen in the anterior nucleus. Note the "calcification" of many of the remaining nerve cells. Cresyl violet, $\times 80$.

FIG. 11.—Case 2. Coronal section of brain showing maximum extent of the cavitation of the right hemisphere.

FIG. 12.—Case 2. Etat marbré of the caudate nucleus and dorsal putamen of the right side. The cortex of the insula has been totally destroyed. Anderson's modified Kultschitsky-Pal stain, $\times 2.8$.

FIG. 13.—Case 2. Section through part of the thin external wall of the cystic cavity in the right hemisphere. Note the island of grey matter in membrane and the distortion and splitting of the gyri on the right. Mallory's phosphotungstic acid haematoxylin, $\times 3.4$.

FIG. 14.—Case 2. Cerebral cortex overlying an area of rarefaction in the right occipital region. Note the islands of nerve cells separated by network of gliosis and the mammillated surface of the gyri ("granular atrophy"). Cresyl violet, $\times 24$.

FIG. 16.—Case 2. Sclerotic hypermyelinated ulegyria adjoining central cavitation of right hemisphere. Note basal constriction of some of the gyri and apparent fusion of adjacent microgyric convolutions. Stain as in Fig. 15, $\times 5$.

FIG. 15.—Case 2. Occipital gyri adjoining the hemispheric cavitation. Note the état marbré of the ulegyria and the absence of myelin in the basal part of the convolutions. Anderson's modified Kultschitzky-Pal stain, $\times 3.5$.

FIG. 17.—Case 2. Focus of nerve cell loss and gliosis in the right globus pallidus with abundant "calcified" debris and nerve cells. Toluidine blue, $\times 100$.

FIG. 18.—Case 3. Medial surface of left occipital lobe showing narrow gyri of complex arrangement (cf. Fig. 20).

FIG. 20.—Case 3. Medial surface of right occipital lobe for comparison with Fig. 18.

FIG. 19.—Case 3. Coronal section of brain through middle of thalami. Note dilated lateral ventricle, thin central white matter of left hemisphere, atrophy of left caudate nucleus and thalamus.

FIG. 21.—Case 3. Etal marbré of head of left caudate nucleus. Anderson's modified Kultschitsky-Pal stain, $\times 24$.

FIG. 22.—Case 3. Coronal section through left occipital pole showing absence of myelin in much of the central white matter. Note hemiatrophy of a gyrus and the atrophy of the basal part of the calcarine cortex. Anderson's modified Kultschitsky-Pal stain, $\times 2.7$.

FIG. 23.—Case 3. Subependymal cavitation with surrounding poverty of myelin found adjacent to the frontal horn of the left lateral ventricle. Note on the left the "Y"-shaped area of necrosis with thin prolongations entering the central cores of the frontal gyri. Stain as in Fig. 22, $\times 2.9$.

FIG. 24.—Case 3. Ulegyria of left occipital lobe. Note the very thin and poorly myelinated subcortical white matter, the basal atrophy of gyri with thin central streaks of non-myelinated tissue, and the hypermyelinated plaques in the transition zone between atrophied and normal cortex. Stain as in Fig. 22, $\times 3$.

FIG. 25.—Case 3. Midbrain. Note hypoplasia of left side and small round area devoid of myelin at the left side of the decussation of the superior cerebellar peduncles (not an artefact). Stain as in Fig. 22, $\times 2.1$.

FIG. 26.—Case 3. Medulla showing small left pyramid which is not completely degenerate. Stain as in Fig. 22, $\times 2.7$.

Comment

The pathological findings in the first case give no support to Alexander's (1942) theory that *état marbré* is a prenatal malformation due to aberrant fibres from the fronto-pontine tract ramifying in the corpus striatum. The obvious nerve-cell devastation of the areas of marbling, the associated fibrillary gliosis, the widespread implication of both thalami with frequent "calcification" of nerve cells and patchy neuroglial sclerosis, point rather to a vascular pathogenesis as postulated by Scholz *et al.* (1938). According to this view, hypermyelination of nerve fibres is the expression of a disturbance of glial function conditioned by the partial anoxia of the tissues of the area concerned. When, moreover, the regions affected by *état marbré* correspond to the periventricular drainage area of the vulnerable Galenic vein, when there are found associated with this marbled state lesions of a grosser kind compatible with the theory of a vascular pathogenesis, and when the clinical history records the infant's severe asphyxia after abnormal parturition, it would seem perverse to seek further than birth injury for the primary cause of the condition.

The association in Case 1 of an intact cerebral cortex with gross reduction in intelligence is a seeming paradox. While an accurate estimate of mental ability is difficult to make in an individual with severe dysarthria and in whom mobile spasm makes performance tests impracticable, it is well known that, given appropriate training, or sometimes even without this, some of these unfortunate patients are able to surmount their physical handicaps in an astonishing way and show a pertinacity of effort incompatible with the presence of mental defect. One such patient of normal intellect at present at Stoke Park, with arms entirely useless on account of severe athetosis, and unable to climb stairs because of spasm of the thigh muscles, is nevertheless able to use his toes for writing, manipulating a spoon, and for lighting and holding a cigarette. Perhaps in such persons the nerve cell loss is minimal and confined to the extra-pyramidal motor system, whereas, in the present case, the poor development of cortical function implicit in the patient's imbecility may be attributed to the coincidental widespread lesions of the thalami and the consequent interference with their cortical projection systems.

In the second case, the history of the birth is highly suggestive of trauma, forceps having been applied in a primipara six hours after the onset of labour and the infant's apnoea having been treated by a crude and now obsolete method likely to aggravate venous congestion in the head. The

postnatal story of the baby's apathy and weakness, epilepsy and hemiplegia subsequently becoming manifest, is also typical of birth injury. The survivors of such tragedies of domiciliary midwifery are collected together in colonies for mental defectives and doubtless form a considerable proportion of their paralysed population. From the pathological standpoint, the large trabeculated cystic cavity involving much of the central white matter of the hemisphere is typical of the late consequences of multiple confluent hæmorrhages or anæmic necrosis due to venous congestion and stasis during birth (Schwartz, 1924; Benda, 1945). The bizarre hypermyelinated ulegyria seen at the edges of this central porencephaly is of the same type as that previously described in cases of birth injury (Norman, 1944) and need not be discussed again in detail here. The *état marbré* found in the putamen and caudate nucleus of the porencephalic hemisphere resembled the variety described by Alexander in that an accompanying gliosis was virtually absent, or, at least, was not effectively demonstrated either by the Holzer or Mallory methods. Yet the association of striatal marbling with obvious destructive lesions of the cortex and globus pallidus of the same side surely discounts the possibility of a double pathology. It would seem that only by an exclusive preoccupation with examples of *état marbré* confined to the striatum and unaccompanied by gliosis may the theory of primary malformation be seriously entertained. The small focus of necrosis in the globus pallidus containing ferruginous débris is of interest, since demyelination of part or all of the globus pallidus, sometimes with excessive deposition of the Hallervorden-Spatz pigment has not infrequently been encountered in conjunction with *état marbré* of the basal ganglia. In the present instance the lesion was a minimal one resembling those found in the thalamus and midbrain of Case 3, and was probably due to a small hæmorrhage. The combination of cortical softening with *état marbré* of the basal ganglia accounts for the frequent occurrence of some degree of athetosis in the affected hand of some young hemiplegics, infantile hemiplegia differing in this respect from the adult form. That athetosis was not observed in the present case is not surprising considering the extent of the damage to the cerebral cortex, preservation at least in part of the pyramidal tract being a necessary prerequisite for the exteriorization of mobile spasm.

In the third case the pathological findings were diverse: a stunted left hemisphere with relatively narrow and tortuous gyri showing widespread hypermyelinated lesions in the parieto-occipital region, unilateral dilatation of the whole of the latera

ventricle of the affected side, atrophy of the body of the left caudate nucleus (état fibreux of the Vogts) merging into état marbré in the region of the head of that nucleus, small foci of necrosis in the left thalamus and midbrain, and, most important of all from the standpoint of pathogenesis, paraventricular softening of the central white matter in the left frontal lobe. The latter finding, in the light of Schwartz's observations, may be regarded as pathognomonic of the terminal vein lesions of birth injury and was present also in the first of three cases of birth injury recently published by myself (1944), where the distribution of lesions closely resembled those of the case now under consideration. Yet from the clinical history it would appear that the onset of hemiplegia was delayed, certainly until after the age of eighteen months and probably until about the age of three years, when epileptic fits commenced. Such a history is not usually regarded as suggestive of birth injury, and a hypothetical inflammatory cause, the so-called encephalitis of Strümpell, is often invoked to account for the subsequent hemiplegia. The fact, however, that the onset of infantile hemiplegia is more common the nearer the age of the infant approaches one year and becomes much rarer after the age of six (Taylor, 1905) points to a causal factor operative with maximum intensity in early infancy, and it is likely that birth injury plays some part in the undoubtedly complex ætiology of this group of encephalopathies. It may be supposed that in these delayed forms of birth palsy the original lesions spare sufficient cortical tissue to mask for the time being the inherent instability of the infant's motor apparatus. As time passes, however, sclerosis occurs in the damaged parts of the brain, epileptogenic foci are formed, convulsions begin, and the associated vascular changes wreak further permanent injury upon the cortical inhibitory centres, with resulting hemiplegia which may be either ingravescent or sudden in its mode of development.

Summary

The clinical and neuropathological features presented by three mental defectives whose brains showed the common feature of état marbré of the

corpus striatum have been described. It has been shown that a conspicuous fibrillary gliosis and nerve-cell loss may be present in the areas occupied by the hypermyelinated fibres of the striatum. Etat marbré of the corpus striatum may be associated with widespread destructive lesions elsewhere in the brain, particularly in the cerebral cortex where hypermyelinated ulegyria occurs at the margin of areas of cystic degeneration of the subcortical and central white matter. Lesions of thalamus, globus pallidus, and midbrain, suggestive of a vascular pathogenesis, were also found in these cases. A form of delayed hemiplegia following birth injury has been described. It is concluded that in these cases the vascular lesions set up by abnormal parturition have been inflicted mainly upon the venous side of the cerebral circulation and that état marbré of the corpus striatum and elsewhere is only one of the many possible sequelæ of partial anoxia of the tissues conditioned by birth trauma.

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