ILLUSTRATIVE CASE III

Woman, aged 65, seen on November 19th, 1931, with a history of feeling run down and "poorly" since November, 1930. In August, 1931, she had an attack of bronchitis, associated with pain in left side of chest and shoulder; pain becoming much more severe. Physical examination was negative.

Radiological examination showed a tumour extending outwards from the mediastinum (Fig. 5). The lateral view showed this tumour to be occupying the region of the costo-vertebral groove. Malignant disease was diagnosed, and operation was carried out on November 26th, 1931. A portion of the eighth rib was resected, and the growth was found in the costo-vertebral groove. It was attached to the lung, and had spread out from it. A small portion was excised, and fifteen 1.5 millicurie radon seeds were inserted as evenly as possible throughout the growth. The chest was sutured. The post-operative reaction was slight, and convalescence uninterrupted.

Histological examination of the growth showed that the tumour was a squamous-celled carcinoma. Further x rays showed the growth to have largely disappeared (Fig. 6). Pain has now completely gone, and the general condition of the patient is improved, while there has been a gain in weight.

OTHER MALIGNANT CONDITIONS

Endothelioma appears to arise as a more peripheral growth, and it has been possible on two occasions completely to extirpate the growth by removing the lower lobe. One of these cases is still living and well three years after operation.

Sarcoma is more rare in the lung itself. Only one case has been encountered, and in this the sarcoma was ossified. It was removed, but the patient unfortunately succumbed from pneumonia in the opposite lung nine days later.

Secondary malignant disease will rarely justify operation, as in the majority of cases the secondary deposits in the lung are multiple and bilateral. However, one patient, in whom a partial pneumectomy was performed for a secondary deposit, has survived for four and a half years without further symptoms.

CONCLUSIONS

Modern methods of investigation enable a much earlier and more correct diagnosis of intrathoracic growths to be made, and often assist one to determine the exact nature of these tumours. These methods entail:

1. Careful radiological examination of the chest from the antero-posterior, lateral, and oblique aspects.
2. Further radiological examination after the induction of artificial pneumothorax, or gas replacement of effusions.
3. The delineation, where indicated, of the bronchial tree by lipiodol.
4. The introduction of the thoracoscope into a pneumothorax cavity, where this is possible, for visual examination of the superficial surface of the lung and pleura, and determination of the superficial characters of the tumour—projection into the pleura.
5. Bronchoscopic examination where lipiodol gives evidence of bronchial obstruction, or in cases where haemoptysis is a prominent feature, and in which the sputum is negative for tubercle bacilli after several examinations.

In spite of these methods exact diagnosis will be impossible in certain cases, and it is in these that exploratory thoracotomy should be advised with certain precautions.

The operation is of no greater severity than exploratory laparotomy, and, in fact, the convalescence is often shorter. By this means tumours which were apparently malignant have been proved to be benign, and have been successfully removed, while others, definitely malignant, have been found operable.

The hope of satisfactory treatment of all types of intrathoracic new growths, benign or malignant, depends upon early diagnosis.

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A CASE OF PORENCEPHALIC IMBECILITY

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STOKE PARK COLONY, STAPLETON, BRISTOL

(With Special Plate)

There recently died in Stoke Park Colony an adult female imbecile, whose case presents some interesting features, apart from the developmental errors revealed in the nervous system at the post-mortem examination.

CASE RECORD

R. B., born in or about the year 1905—exact date unknown—was admitted to this institution on October 26th, 1920. She was certified as a "macrocephalic feeble-minded patient of low mentality, unable to settle down for any length of time to any occupation, and not to be depended upon to do any work properly." The certifying medical man returned her physical condition as "normal," and, as she was a guardians' case of apparently unknown parentage, was unable to furnish any family or social history. The then medical officers of this institution regarded her as a "retrograde imbecile, quiet, well-behaved, dull, apathetic, without any interests." The matron in charge stated that she was small for her age, of pale, unhealthy complexion, with no signs of wasting or paralysis of any of the limbs, and with no deafness or dimness of vision. She was stated to be lively at times, with occasional attacks of bad temper. She had practically no educational attainments, and was only able to do a little simple sewing under supervision.

The patient's health remained generally good until January 27th, 1930, when, during drill in the afternoon, and coincident with a menstrual period, she was suddenly taken ill, and had a fit of twitching and jerking of the face and arms. She was put to bed; whereupon she had a second attack, with loss of consciousness. On examination the same night she was found to have a flaccid paralysis of the right arm and leg. The next day, while still unconscious, the patient was removed to hospital, and apparently recovered consciousness the day after admission. The notes state that six days after admission she was restless, excited, and sometimes incontinent, but was now able to move her right leg, though not her right arm. The urine was loaded with albumin, and continued so throughout the illness. The patient was treated in hospital for chronic nephritis until April, 1931, but as she had been walking with a special boot since January, 1931, she was then returned to the care of her own house matron, but remained under regular medical observation.

In September, 1931—that is, about twenty months after her seizure—she came under the care of the present medical staff of the institution. She was then found to be suffering from advanced renal disease, with a systolic blood pressure of 150, and signs of renal failure. She was therefore readmitted to hospital. The old right hemiplegia was still apparent, and there had been very little improvement in the upper limb. She complained of dimness of vision in the right eye, and examination of the fundi showed that the optic disks were pale and the retinal blood vessels greatly engorged. The urinary output was diminished in amount, and in December the patient had three uraemic convulsions. The general condition became steadily worse, subcutaneous and submucous haemorrhages appeared in the beginning of January, and the patient died on January 21st in uraemic coma. Clinically, therefore, the case appeared to be one of imbecility complicated by chronic nephritis. Post-mortem macroscopic examination seemed to confirm this, as the kidneys were reduced to half their normal size, and showed advanced chronic nephritis. There was also fibrinous pericarditis, and what appeared to be the remains of an old cerebral haemorrhage over the lower half of the central sulcus in, or about, the Sylvian fissure, as well as a cyst-like structure on the left cerebral hemisphere in the vicinity of the parieto-occipital fissure. Subsequent examination showed, however, that the

cerebral appearances were misleading, as they were due to porencephaly, the result of a partial developmental failure, and not to any gross visible haemorrhage.

COMMENTARY

Anatomical Considerations

At a very early stage of embryonic life the wall of the neural tube, from which the brain and spinal cord are developed, consists of a single layer of columnar cells, which quickly become multi-layered. In this latter form the now thickened wall of the neural tube consists, from without inwards, of the following:

- (a) An external limiting membrane.
- (b) A middle syncytium:
 1. Marginal layer (white matter).
 2. Mantle layer (grey matter).
 3. Ependymal layer (ventricular wall).
- (c) An internal limiting membrane.

In certain parts of the telencephalon (cerebral hemispheres), and possibly also of the metencephalon (cerebellum), the middle syncytial layer has, in this case, remained permanently in its embryonic state, and no brain cells have been developed therefrom. Developmentally, the telencephalon consists of three regional parts—the corpus striatum, the rhinencephalon or archipallium (olfactory brain), and the neopallium or true brain. The last two together form the whole of the externally visible hemispheres, and are collectively termed “the pallium.” Just as in any other part of the neural tube, the walls of the pallium are differentiated embryologically into ependymal, mantle, and marginal layers. The surface extent of the cerebral wall—that is, the thin grey cortex (pallial mantle layer)—increases more rapidly than the white medullary layer (pallial marginal layer) which underlies it. As a result, the originally smooth pallial wall becomes fissured and convoluted—a device of Nature to increase the area of the neurone-bearing cortical strata within a confined space. That portion of the pallial wall which overlies the corpus striatum expands more slowly than the surrounding areas, so that the adjacent portions of cortex, termed in the adult the frontal, parietal, and temporal opercula, come to overhang, and eventually to conceal, the insula or island of Reil, and by their apposition to form the lateral fissure of Sylvius. The formation of the opercula commences about the third or fourth month of intra-uterine life, and shortly after birth these opercula should finally have closed in over the insula. In the brain of this imbecile patient this cortical opercular formation has not taken place at all, with the result that there is no insula, no true lateral fissure of Sylvius, and no true opercula. Along an oblique line in the primitive pallial wall, coincident with the position of the future adult lateral fissure of Sylvius, the mantle layer has completely failed to form any cortical grey or white matter whatsoever. At the parieto-occipital end of this oblique line the developmental failure is even more complete, for there is no trace of either marginal or mantle layers, with the result that the wall of the lateral ventricle is plainly visible upon, and forms part of, the cortical surface, upon which it appears as a cyst-like structure filled with cerebro-spinal fluid. At the frontal end of the same oblique line microscopical examination shows that the syncytial embryonic tissue between the external and internal limiting membranes has persisted, and it is this tissue which has simulated the appearances of an old haemorrhage—a natural assumption in view of the history of the case. A similar developmental failure occurred in the right cerebral hemisphere, though to a much lesser degree.

Deficiency of Neurons

On both cerebral hemispheres there are other features of neurological interest, such as a diminution in size of many convolutions and cortical areas, imperfection of

cerebral fissuring, a retention—on the surface—of annectant gyri, a complete absence of certain parts of the cerebral hemispheres, and a gross diminution in the size of the corpus callosum, centrum ovale, projection and association fibres and areas, and of other macroscopic collections of white matter. The inferior surfaces of both cerebellar hemispheres also show an absence of cerebellar grey cortex in areas coincident with Bolk's “leg” areas, and this is most marked upon the right side.

The relatively large areas of totally undeveloped grey cerebral cortex sufficiently explain the patient's imbecility, and prove the association of mental deficiency with lack of cortical neurons. That this patient was devoid of such a sufficiency of neurons is shown by the cortical absence just referred to; by the striking reduction in thickness of the corpus callosum, which, it will be remembered, is entirely composed of the medullated axons of cortical cells, but in this case was no thicker than a stout piece of cardboard; by the almost complete absence, especially on the left side, of the centrum ovale, which again is normally composed of projection and other medullated axons which have their cell bodies in the grey cortex; and by the reduction of both grey and white matter to a thin sheet spread out over the wall of the lateral ventricle. The reduction in grey cortical matter is, in this brain, so pronounced that it can safely be asserted that von Economo's estimate of 14,000 million neurons must have been reduced by about a third, and the imbecility was thus due to this neuron reduction and to nothing else. This patient was originally returned by the certifying medical man as macrocephalic, whereas she was really strikingly microcephalic. Over-all head length was 176 mm., over-all head breadth 140 mm., and head height 120 mm., which gives a brain capacity of 1,188 c.cm., and a percentile placement of minus 1, representing a very high degree of microcephaly. As measured after death the fronto-occipital length of the cerebral hemispheres was 155 mm., and the greatest breadth 122 mm. The microcephaly is, in this case, a useful clinical suggestion of a paucity of cerebral neurons.

Interpretation of Hemiplegia and other Defects

Whilst the striking developmental failure of this brain fully explains the patient's imbecility it does not explain the hemiplegia. The clinical history is suggestive of a haemorrhage, and at the post-mortem examination the syncytial tissue already described was sufficiently like a blood clot as to be at first mistaken for one. That this was not, however, the cause of the paralysis is certain, and for two reasons: first, microscopical examination showed that the supposed blood clot was composed almost entirely of embryonic material; and, secondly, the syncytium was not over the Rolandic motor area, but altogether below it, so that even if there had been a haemorrhage it could not have produced a hemiplegia. Macroscopic cross-section of the left internal capsule, too, has so far failed to reveal any sign of haemorrhage, so that pending more careful microscopical examination it is as yet impossible to adduce any satisfactory evidence of the site or cause of the paralysis-producing lesion. The possibility of an embolus has not, of course, been overlooked, nor the fact that the patient was menstruating at the time of the seizure, but our examination has, so far, revealed neither haemorrhage nor embolus, and there remains the further, but unsolved, problem of paralysis from a long-continued cortical uraemic poisoning, intensified in the latter months of life.

As regards the statement that, prior to the seizure, the patient suffered from neither deafness nor dimness of vision, examination of the corresponding cortical areas hardly supports the statement. The visuo-sensory area is considerably diminished in extent, especially on the left side, and it is significant that after the seizure she com-

plained of dimness of vision in the right eye. The fact that the patient displayed no marked locomotor disability prior to her attack, and showed no signs of wasting or paralysis of her limbs, renders examination of the pre-central convolutions of some interest, especially on the left side. A comparison, in Figs. 1 and 2 on Plate, of the areas on the immediate frontal side of the central sulcus reveals the fact that on the right side the area in question appears fairly normal, whereas on the left side, consequent on the failure of development of the frontal operculum, the pre-central convolution appears as though it had been cut in two and the lower half removed. This clearly could not have been the case. It is therefore more probable that the pre-central convolution on the left side has been well developed, but that its lower half has been bent forward. This deduction from the observed facts is also supported by the clinical evidence of the patient's ability to speak, though her vocabulary was both limited and obscene.

Hints as to Aetiology

An examination of this brain shows that there has been a complete cessation of brain development in one part of the telencephalic wall, and that this cessation occurred at about the sixth week of intrauterine life. The result is that the primitive wall of the telencephalic neural tube has been left upon the surface of the cerebral hemisphere along the line of the adult lateral fissure of Sylvius, and this failure has been more complete on the left side than on the right. At the sixth week of normal development, in about a 10 mm. embryo, the five brain vesicles are present, and the ependymal, mantle, and marginal layers of the walls of the vesicles and neural tube are well represented, while the aortic arches and cardinal veins are completed. The primitive vessels extend into the head and extremities. On the left side cerebral development has, in one part of the telencephalic vesicle, ceased at this time. On the right side the developmental failure has been, as stated, less complete, and has occurred much later.

Notwithstanding the extraordinary amount of research on experimental embryology and artificial teratology, it does not seem yet possible to give any adequate explanation of the causes of these errors and failures of embryological development. In a recent number of the *Journal*¹ Keith stated that lions born and bred in the London Zoo were peculiarly liable to cleft palate, but that with an altered maternal dietary during pregnancy, a plentiful supply of vitamins, and better surroundings, this developmental error practically disappeared from the offspring. Are some, at least, of these developmental failures during pregnancy the result of faulty maternal feeding, of an aberrant blood supply, or of another allied cause? Or have we to look still farther back, to a deficiency of the chromatin substance of the parental chromosomes or to the genes "which determine the course of development of the fertilized egg" for our explanation as to why some embryos manifest these, and many other similar, developmental failures, whilst others proceed along perfectly normal lines. If the chromosomes are responsible, then the hereditary factor once more emerges as a potent cause of amentia. In this case, unfortunately, nothing is known of either the parentage or the hereditary history, but as the patient was a board of guardians case it is probably safe to assume that her ancestry was of that inferior stock from which so many mental defectives seem to spring.

DESCRIPTION OF FIGURES

Fig. 2 shows the left cerebral hemisphere after removal of the meninges. The embryonic walls of the lateral ventricle are clearly visible upon the surface, that of the occipital end being devoid of all covering of embryonic tissue, whilst the larger and more frontal one is partially covered by such tissue, which is the remains of the mantle and marginal layers of the telencephalic vesicular wall. The superior temporal convolutions appear well developed. A comparison of this figure with Fig. 1, which represents the corresponding

surface of the right cerebral hemisphere, shows the striking difference between the two hemispheres.

Fig. 3 shows the inferior surface of the cerebellum with a large non-cortical area on the right cerebellar hemisphere roughly coincident with Bolk's "leg" area, and an oblique, depressed, non-cortical area on the left cerebellar hemisphere. As the chief developmental failure affects the left cerebral hemisphere (heterolateral) and the right cerebellar hemisphere (homolateral), it is difficult to believe that, prior to her seizure, this patient displayed no weakness of her limbs. The cause of this patient's failure of cerebellar development has not yet been determined, but it appears to have been of different origin from that affecting the cerebral.

Fig. 4 shows the internal or medial surface of the left cerebral hemisphere, upon which are to be noticed the diminution in thickness of the corpus callosum, especially in its occipital half; the detachment of the fornix from the corpus callosum; the absence of the interventricular foramen of Monro; the wide opening of the left lateral ventricle, here filled with cotton-wool; the imperfection of the visual area within, and about, the calcarine sulcus; and the imperfect fissuring of the cortex. The whole of the cortex and white matter of this left cerebral hemisphere is, as a matter of fact, little more than a thin shell spread out over the wall of the lateral ventricle.

Fig. 5 is a diagrammatic cross-section of the telencephalic vesicle of a 10 mm. embryo (six weeks old), the original walls

FIG. 5.—Diagram of normal and arrested brain development.

of which are bounded by dotted lines. On the right side there is indicated normal cortical development, with a formation of the opercula, insula, and lateral fissure of Sylvius; whilst on the left side there is diagrammatically indicated the developmental failure which has resulted in the rather remarkable and instructive brain of this imbecile woman.

CONCLUSIONS

Wigglesworth described in 1897 two cases of porencephaly,² and pointed out that "it is incorrect to use the term 'porencephaly' as connoting a separate pathological entity, since different cases undoubtedly have their origin in different pathological processes." His first case Wigglesworth regards as "a true developmental defect." His second case is, he thinks, not one of "developmental defect, but has been caused by a definite destructive process of some sort." He inclines to the view that the "definite destructive process" was an encephalitis, "the result of injury inflicted during the process of birth, not improbably by means of the forceps." He also furnishes a brief list of references to previously published cases. In 1904 Turnbull³ described a case similar to the present one. He states: "The cysts, seen in the post-mortem examination, formed the walls of the posterior portion of the right and left ventricles, and represented enormously attenuated portions of cortex." He concludes that "the abnormalities consist in a distension of the ventricles and destruction of a large area of the cortex."

Read in the light of modern embryological knowledge, some thirty years later, it seems much more probable that all three cases, as well as the present one, are not due to destruction of previously existing cerebral cortex, but to the fact that, developmentally, it was never there. Certainly, in the present case, the porencephalic condition is the result of an arrest of cortical development in the telencephalic neural wall occurring at, or about, the sixth week of intrauterine life.

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- ¹ *British Medical Journal*, 1932, i, 388.
- ² *Brain*, 1897, xx, 88.
- ³ *Ibid.*, 1904, xxvii, 209.

R. J. A. BERRY AND R. M. BATES: PORENCEPHALIC IMBECILITY

FIG. 1.—External surface, right cerebral hemisphere.

FIG. 3.—Cerebellum: inferior surface.

FIG. 2.—External surface, left cerebral hemisphere.

FIG. 4.—Internal surface, left cerebral hemisphere.

ALBERT RAMSBOTTOM AND CYRIL G. EASTWOOD: SPONTANEOUS HYPOGLYCAEMIA

Gall-bladder and appendix from a case of spontaneous hypoglycaemia.