

A CASE OF UNILATERAL CEREBRAL HYPERPLASIA,
WITH CO-EXISTENT "ACROMEGALY" OF THE
FEET, AND A SLIGHT DEGREE OF UNILATERAL
GIGANTISM.¹

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(PLATES XXXV.—XXXVII.)

BRIEFLY, the case is that of a 2-year-old female child, unable to speak or walk, who showed some undue prominence of the left frontal tuberosity, and a slight enlargement of the left cheek, left lower limb, and right foot.

A clinical diagnosis having been made, the child was being treated for rickets and myxœdema, when she developed enteritis and died.

The *sectio cadaveris* showed a hyperplasia of the left cerebral hemisphere, acromegaly of the feet, broncho-pneumonia, and enteritis. Nothing was seen pointing to rickets or myxœdema.

The central nervous system and the pituitary and suprarenal glands were removed and preserved. For the opportunity to examine this material and report the case, and for kind direction of the course of my work, it is a pleasure to me to express my thanks to Professor Chiari. For permission to publish the following abstract of the clinical history I am indebted to Professor Ganghofner.

CASE.—The child, Anna Z., æt. 2 years, was entered as a patient into the Kaiser Franz-Joseph Hospital (Clinic of Professor Ganghofner) on the 1st of September 1905, with a history that during the year and a half previous the left side of the cheek had grown in size, and the feet had become large and swollen. The patient could neither walk nor talk. Birth had been normal, and the breast had been taken for three-quarters of a year. (No family history is given.)

The whole left side of the child's head was somewhat enlarged, and the left parietal tuberosity was prominent. The anterior fontanelle was 2·2 cms. The circumference of the head was 49 cms. The pupils were equal, and of normal size; eyes on the same horizontal plane. Nose normal. A small hæmangioma on the upper lip. The left half of the upper lip was somewhat prominent and overhanging as compared with the right. The left cheek stood out more than the right, apparently through a deposit of fat. The thyroid was not palpable.

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No difference noticeable between the right and left arms; their motor functions were not deranged; the epiphyseal junctions of the long arm-bones were slightly enlarged.

Chest circumference, 45 cms. Osteo-chondral junctions of the ribs somewhat expanded. Ribs on the right side somewhat drawn in.

Abdomen enlarged (50 cms.). Superficial veins clearly visible. External genitals normal.

Left lower extremity better developed than the right, though the musculature was feeble in both. Right thigh (max.), 20 cms.; left thigh, 21 cms. Right calf (max.), 16 cms.; left calf, 17½ cms. Lying on the back, both legs showed free active and passive movement. Several colourless patches on the skin of the right lower extremity. Feet still in foetal attitude, especially so with the left foot. Backs of the feet soft and doughy on palpation.

Both sides of the body showed marked vasomotor instability. Percussion and auscultation of heart and lungs showed nothing abnormal. Liver and spleen not enlarged. Stools normal.

September 11, 1905.—“The child was sitting up in bed and playing.” Appetite good. Thyreoidin given; one-third of a tablet daily = 0.1 grm. Weight, 9700 grms.

October 6.—No change this day, when diarrhoea set in, and the thyreoidin was stopped.

The diarrhoea persisted, with occasional vomiting, and much loss of strength and weight (to 8500 grms.)—though no special nervous symptoms showed themselves—till the child died, on the 14th October.

During the period in which the child was under observation the temperature was normal till about twelve days before death, when slight irregular rises (maximum, 100°·8 F.) took place.

The *clinical diagnosis* was myxœdema, enteritis, rachitis.

The report of the *post-mortem* examination (conducted by Professor Chiari) thirty hours after death is as follows:—

The body was 79 cms. long. Bony skeleton moderately developed; muscular system weak; little superficial fat. The latter was only somewhat more developed in the left cheek, both forearms, and in the lower extremities. The dorsi of the feet showed, in addition, some œdema.

The whole skin anæmic, with a little hypostasis dorsally. Rigor mortis not well marked. Hair blonde; the region of the left frontal eminence prominent. The left cheek and left upper lip were clearly, but not much, thicker than the right. Neck thin; thorax somewhat broad; in the right axillary line the ribs were more marked than on the left side. Abdomen sunk and flaccid. Both feet markedly increased in size, with pes varus of a high degree.

NERVOUS SYSTEM.

Outer coverings of the cranial vault anæmic; circumference, 49 cms. On opening, the two sides were quite asymmetrical, as the left frontal tuberosity stood forward, and the capacity of the whole left side was relatively increased. The left half of the frontal bone and the left parietal bone were larger than on the right side. The cranial bones of normal density and thickness. Large fontanelle, 4 sq. cms. In the dural sinuses freshly coagulated and fluid blood. The hypophysis cerebri of relatively normal size, and its lobes proportionate. Internal meninges not thickened, and neither congested nor anæmic (“mittelblutig”). The arteries at the base of normal arrangement and consistence.

Right hemisphere, 565 grms.; left hemisphere, 770 grms.; each half of cerebellum, 67 grms.; pons and medulla oblongata, 20 grms.; total weight of encephalon, 1489 grms.

The right hemisphere was practically normal in arrangement and size of the gyri; in the left, on the convexity of the frontal and parietal lobes, the convolutions were irregular, more numerous, and there was a very considerable

amount of microgyria. Microgyria was also present on the convexity of the temporal lobe, and at the base of the left frontal lobe, but slightly marked. The left occipital and the mesial convolutions were practically normal in appearance. Corpus callosum, fornix, and commissures of the brain normal. Cerebellum, pons and medulla oblongata normal in appearance. The ventricles were not dilated. Ependyma normal; the consistence of the brain generally was normal.

At the *sectio* the brain was not dissected, but was set aside to be hardened in 10 per cent. formol. (Museum specimen, 853.)

The pituitary and suprarenals were also preserved.

The meninges of the spinal cord were normal, but pale; the cord also anæmic, but normal macroscopically on section, except for a slight hydro-myelia in the lumbar region.

The arch of the *diaphragm* rose to the third rib on the right side, and fourth rib on the left.

Thyroid rather small, of normal appearance. Thymus normal.

In the *trachea* was slight mucus. The general mucosa of the trachea, œsophagus, and pharynx was anæmic. *Right lung* free; the upper and middle lobes, and the anterior part of the lower lobe, normal; posterior part of lower lobe hepatised in lobular areas, with subpleural emphysema. *Left lung* free; lower lobe showed many areas of lobular hepatisation; upper lobe more anæmic than that of the right side, and several areas (about 2 cms.) of subpleural emphysema at the anterior margin.

In the *pericardium* were a few drops of clear serum. Heart and great vessels normal. Peribronchial glands not enlarged.

Liver, spleen, pancreas, kidney, and suprarenals anæmic.

In the *stomach* watery gall-stained fluid; mucosa pale.

Small intestine filled with pale chymous material; large, with pale yellow thin fæculent masses. Mucosa of small intestine pale; *large intestine* showed, at the cæcum and sigmoid flexure, acute catarrhal changes.

Bladder with clear urine in it; mucosa anæmic. *Genitalia* normal.

No rachitis present in the skeleton.

PATHOLOGICAL-ANATOMICAL DIAGNOSIS.

Hyperplasia cerebri hemisphærii sin., cranii dimidii sin., genæ sin. et labii sup. dim. sin.; microgyria cerebri hemisphærii sin.; hydromyelia lumbalis; acromegalia pedum; pes varus bilateralis; enteritis catarrh. Intestini crassi; pneumonia lobularis bilateralis; œdema pedum.

After three months' hardening of the nervous system in 10 per cent. formalin a Flechsig's horizontal section was made, showing exquisitely the great difference between the two hemispheres (*vide* p. 310).

The further investigation of the case commenced five months after the post-mortem.

MACROSCOPICAL DESCRIPTION.

I. CENTRAL NERVOUS SYSTEM.

(a) The brain was re-weighed, measured, and photographed. The results of weighing, in comparison with the weights at the post-mortem, were as follow:—

Cerebrum—Right hemisphere, 580; left hemisphere, 780.

Cerebellum—Right lobe, 70; left lobe, 73.

Pons and medulla oblongata, 22. Total weights, 1525.

Difference between hemispheres, 200.

Increase of weight during hardening process, $34 = 2.2$ per cent. (On this point see references in Anton.)

Volumetric readings were—Right hemisphere, 586 cms. ; left hemisphere, 760—1346 ; difference, 174.

The cerebellum, pons, and medulla, it will be seen, are of normal weight ; the right hemisphere is distinctly heavy ; the left hemisphere is over one-third as heavy again as the right ; while the brain as a whole is heavier than the brain of an average adult *male*, and 500 gms. heavier than the brain of an average *female* child of 2 years of age (see Marchand). The cerebellum is 11·8 per cent. ($\frac{1}{3\cdot4}$) of 2 (the right hemisphere), and 8·7 per cent. ($\frac{1}{11\cdot4}$) of 2 (the left hemisphere). (Normal variations being from 7·6 per cent. ($\frac{1}{13}$) in females of one month to 12·8 per cent. ($\frac{1}{8}$) in adult females.—Vierordt.)

(b) MEASUREMENTS—

<i>Greater diameters—</i>		Left.	Right.
Maximum length	.	15·8	14·8
Do. breadth at splenium corporis callosi	.	7·0	6·3
Do. height mid-coronal	.	10·8	10·8
Temporal to occipital pole	.	12·6	11·2
<i>Horizontal sections measurements</i> (left somewhat higher than the right, as seen by the cut splenium).			
<i>Nucleus caudatus—</i>		Left.	Right.
Length	.	2·2	2·0
Breadth	.	1·1	0·8
<i>Nucleus lenticularis—</i>			
Length	.	3·4	3·6
Breadth	.	1·8	1·8
<i>Thalamus opticus—</i>			
Length	.	2·9	2·8
Breadth	.	1·9	1·6
<i>Clastrum to Mesial line—</i>			
Anteriorly	.	3·5	3·0
Posteriorly	.	3·0	2·8
<i>Clastrum to outer surface—</i>			
Anteriorly	.	3·8	3·6
Posteriorly	.	2·4	2·3
Breadth of posterior horn of lateral ventricle	.	1·1	0·5
Cortical measurements from 3·6—2·2, down to 1 mm. in the microgyric areas.			

(c) PHOTOGRAPHS AND DRAWINGS.—These are (1) a photograph of the cerebral hemispheres from above, and the cerebellum from behind (Plate XXXV. Fig. 1) ; (2) four photographs (not absolutely proportional) of the external (Plate XXXVI. Figs. 3 and 4) and mesial (Plate XXXVII. Figs 5 and 6) aspects of the hemispheres ; (3) a drawing of the surfaces of the Flechsig horizontal sections (p. 310) ; (4) a microphotograph from a section through the hypophysis (Plate XXXV. Fig. 2).

(d) Comparing the two hemispheres, the left is seen to be increased in bulk, from whatever aspect it is viewed ; while from the side the temporal lobes, and from below the tentorial surfaces, are quite distinct in character. On the mesial surface a slight convexity of the right hemisphere is to be seen, corresponding to the certain degree of concavity which the bulging marginal convolutions produce on the mesial face of the left hemisphere.

There is no distinct sign of flattening of the convolutions, except on the most prominent part of the left temporal lobe, and this may be an artefact. True microgyria is not present on the right side, though there is a richness of gyri, especially in and behind the posterior third of the gyrus fornicatus. On the left side microgyria is present, well marked over the whole of the external

surfaces of the frontal and parietal lobes, distinct on the orbital surface of the frontal lobe, noticeable on the occipital and temporal lobes.

Sulci.—In the arrangement of sulci and gyri much complexity is to be seen on both sides. No developmental defects are to be seen. The genua of both Rolandic fissures (Cunningham) are poorly developed. The central fissures reach the middle line at a normal point on the arc of the great longitudinal fissure. The right Sylvian fissure is rather highly inclined, and the supra-marginal area is small. The anterior rami of the left Sylvian fissure are difficult to define, as the hypertrophic gyri occulti, as will be later described, border its stem anteriorly. On the internal surfaces the callosal-marginal sulci are not regular in arrangement at their extremities. The calcarine, parieto-occipital, and other chief sulci, so far as can be seen without opening them out, are normally developed.



FIG. 7.—Drawing of Flechsig horizontal section (K. Jedlička). Shows increased vascularity, microgyria, and the claustrum turning outwards anteriorly in the left hemisphere.

Gyri.—The gyri on the right side, though their complexity gives the surface an adult appearance, present no features of pathological interest. The convolutions on the left side, except on the internal surface, show microgyria, and as a whole, bulging as they do from deeply marked fissures, present a great contrast to the convolutions of the right hemisphere. The frontal lobe has a very large \angle -shaped superior central convolution, with three lobules of equal breadth passing forwards from it. The inferior frontal gyrus is recognised in opercular, triangular, and orbital parts; below the opercular part, bordering the stem of the Sylvian fissure, lies the before-mentioned extra tri-lobed area, which, on examination of the horizontal section, is seen to be an enormously hypertrophied and protruding anterior portion of the gyri breves of the insula. Further characteristics of the left hemisphere are that the supra-marginal area is large; that the angular area, and area just below it, is small, with very small gyri; in this presenting a contrast to the temporal convolutions, which are large and bulging, with the horizontal fissures obliterated, and what are apparently the chief fissures lying highly inclined.

On the internal surfaces the hooks of the uncinate gyri are to be noted as differing in size, the *right* being the larger. The other mesial gyri of the left hemisphere (as before mentioned) are prominent, and are distinctly larger than the corresponding convolutions of the right side.

Owing to the comparative projection of the right thalamic region the whole of the third ventricle has been left on the left side in cutting through the corpus callosum.

In the Flechsig horizontal sections the microgyria is seen, slightly in the frontal region, well marked in the island of Reil. The island is larger on the left side, and the section passes through practically no fronto-parietal operculum. The anterior part of the gyri breves is enormously hyperplastic, so that it reaches to the outer surface, and spreads out there; and the drawing shows well how both cortex and medullary mass are involved in this change, the claustrum being turned outwards also.

The left optic thalamus and corpora striata are larger; the caudate nucleus being increased both in length and breadth, the optic thalamus chiefly in breadth. The splenium is broader. The posterior horn of the left lateral ventricle is double the breadth of the right one, and the lining wall is somewhat darker in appearance and firmer to the touch. The choroid plexus is also larger, and darker in colour.

The cerebellum, but for a deformation which has flattened and broadened out the left hemisphere to some extent, is normal outwardly and on section.

The pedunculi cerebri are similar in size. Cross sections of the pons and medulla oblongata show nothing abnormal.

The spinal cord on section seems to be quite normal, except for the slight hydromyelia from the twelfth dorsal to the fourth sacral segments inclusive.

II. HYPOPHYSIS CEREBRI.

Of the hardened specimen (covered by dura mater) the length is 0.8 cm. and the breadth 1.4 c.m. Cross and antero-posterior sections show nothing abnormal.

III. SUPRARENAL GLANDS.

The right suprarenal body is somewhat more than usually better developed than the left, measurements (maximal) being—

	Left.	Right.
Height	1.9 cm.	2.2 cms.
Base	0.9 „	1.6 „
Length	3.0 „	3.6 „

HISTOLOGY.

The cerebrum was examined in the following manner:—

A thin lamella was cut below and parallel to the plane of each horizontal Flechsig section; from these lamellæ portions from corresponding areas of frontal, temporal, occipital, and insular cortex were selected for microscopical examination. The areas of the corpora striata and optic thalami in the lamellæ, and a small segment from the upper part of the middle third of each anterior central gyrus were also examined.

One complete series of sections was stained by Weigert's iron-hæmatoxylin-van Gieson method, and by v. Lenhossék's modification of Nissl's method (with toluidin-blue—as given in Schmorl (1904)). Another complete series of sections in which Weigert's neuroglia method was tried was, to my great regret, probably owing to post-mortem changes, without result. (A similarly treated section of the spinal cord showed the neuroglia fibres moderately well). Certain sections were treated with Sudan III. and by the Weigert-Pal process.

The selected areas were embedded in celloidin, and sections were cut with a Jung-Thoma microtome from 7 to 12 μ in thickness—the Nissl sections being all as far as possible 10 μ . In these sections as a whole in both hemispheres the layers of cortical cells were present in normal relations and proportions (as in Kölliker). The cells showed no changes but those of early post-mortem alteration (such as the general absence of tigroid substance, and the occasional appearance of chromatophilia and vacuolations, swollen clear nuclei, and broken-off dendrites).

The fibres in tangential and projection systems appeared to be normally developed. In the third frontal section the large pyramidal cells seemed to be somewhat more numerous on the left side as compared with the right. (It is difficult to say what value to give to this finding, as the method of selecting portions for examination did not ensure that sections were all at right angles to the long axes of the convolutions). In the Rolandic and the occipital areas no difference could be made out between the two sides. In the anterior protruding part of the left insula there were practically no medullated fibres to be seen, and the whole field showed only numerous neuroglia cells, with an occasional pyramidal cell. In the left gyri occulti, though one could distinguish the typical cell layers of the cortex, there was a certain disarrangement of these cells in the microgyric windings. This also was seen in the temporal cortex to the outside, where in addition septa, richly supplied with small pia-like vessels, with cells and a ground substance like that of the stratum zonale, broke up the continuity of the cell layers.

The left side as a whole was more richly vascularised than the right. The peri-cellular spaces varied widely in different areas. There was nowhere to be seen any inflammatory change of the cells, vessels, or pia mater, nor any fatty degeneration; nor was there any peri-vascular neuroglia proliferation.

The choroid plexus and lining wall of the posterior horn of the lateral ventricle of both sides were examined. No inflammatory change was seen; the left plexus and ependyma were simply hyperplastic, and more deeply pigmented. In the basal ganglia and optic thalami, in addition to the greater total area, the left side showed a richer vascularity and an increased number of ganglion and glial cells. (The Nissl bodies were partially preserved in the large cells of the anterior thalamic nuclei.) In sections of the pons about the upper third the right and left pyramidal bundles were practically equal in area—if anything the left was the larger. In the medulla oblongata, in sections above the middle of the olivary body, no real difference could be seen between the two sides in the white matter or cell groups.

The spinal cord (treated in six segments with the iron-hæmatoxylin—van Gieson method, and with Weigert-Pal and Nissl) showed, but for the hydro-myelia, no variations from the normal when compared with controls of cords of

the same age. Slight post-mortem alteration in the fibres generally was seen. The hydromyelia was beautifully shown by the iron-hæmatoxylin,—van Gieson method, which stains all the structures of the cord,—the cells with their Nissl bodies, the fibres, the glia (golden), and the connective tissue (bright red).

Celloidin sections of the hypophysis cerebri stained with hæmatoxylin (Delafield) or iron-hæmatoxylin, and counter-stained with eosin or orange G, and paraffin sections stained by Scaffidi's method (acid-hæmatoxylin, fuchsin, and orange G) showed a very rich (but not unusual) vascularity of the anterior lobe, and (for a child) an increase in the number of chromophile cells. The colloid substance (in the centre of most of the acini cut transversely) was not very evident. The fine-walled vessels were quite filled with blood. There was little connective tissue to be seen, especially towards the central parts of the lobe, where the granular eosinophile cells equalled the chromophobe cells in number. A few finely granular "cyanophile" cells were seen. In deeply stained sections it seemed that the number of cells to be classed as "eosinophile" or "cyanophile" were increased. But for this comparative increase of chromophile cells the hypophysis showed no difference from normal control preparations.

The suprarenal glands, in sections stained with hæmatoxylin and eosin, appeared to be quite normal.

DISCUSSION.

There are three factors in the case which require to be considered : the cerebral hyperplasia, the unilateral hypertrophy of the body, and the acromegalic condition of the feet. It is to the pathological bearings of the two latter that I wish as far as possible to restrict myself ; the first and more outstanding feature of the case, however, must be more fully dealt with.

(4) Hyperplasia of one cerebral hemisphere has, I believe, been recorded three times.

1. Of these three instances the first, by Sims (1835), in his study of "Hypertrophy and Atrophy of the Brain," is merely a note of the occurrence of the condition.

Case 13, a woman, æt. 40, who died comatose, and in whom "the left hemisphere occupied about two-thirds of the space allotted to the cerebrum. The left corpus striatum was enlarged to twice its usual size ; the right corpus striatum was diminished in size. There were two apoplectic cysts in the left hemisphere, and one in the right, of different dates."

2. The second instance is the brief report by Martin (1844), under the title, "Hypertrophy of the right hemisphere of the cerebrum, with serous effusion in the cerebellum and in the cerebral ventricles."

An able seaman (æt. 24) died in the Royal Naval Hospital, Malta, after an illness of a month's duration. His symptoms were giddiness, severe and paroxysmal occipital headache, and—towards the close—periods of insensibility with muscular rigidity in the lower limbs. At the post-mortem the dura and arachnoid were found to be healthy. "There was considerable hypertrophy and hardening of the right cerebral hemisphere ; it appeared much larger than the left, the mesial line being much to the left side of the foramen magnum. There was a large collection of limpid serum in the lateral and third ventricles, and the right hemisphere of the cerebellum was distended by serum. The medullary substance of the cerebellum was healthy ;

the passage from the third to the fourth ventricles much dilated. No morbid appearances were observed in the thoracic viscera, and the only mark of abdominal disease was excessive vascular congestion of both kidneys."

3. The third case is that reported by J. Batty Tuke (1873), under the title, "A case of hypertrophy of the right cerebral hemisphere, with coexistent atrophy of the left side of the body."

A male epileptic idiot, æt. 37, died from phthisis. A near relative had died of hydrocephalus. Birth was normal. The mother gave a history of trauma on the tenth day, when fits began and continued for nine months, the head rapidly increasing in size. About the tenth year the boy became epileptic again, and continued so till he died. The left side of the body, which was hemiplegic, had always been smaller than the right. At the post-mortem the skull-cap was found to be of unequal thinness, very dense, with practically no diploe. The brain weighed 60 oz. (1800 grms.), and was of tough consistence. The left hemisphere weighed $23\frac{1}{2}$ oz. (705 grms.), the right $30\frac{1}{4}$ oz. (907 grms.), the difference between the hemispheres being $6\frac{3}{4}$ oz. (202 grms.). The left occipital lobe was larger than the right one. The right fissure of Rolando met the great longitudinal fissure farther back than usual. The left hemisphere was markedly darker in its grey matter than the right. The cerebellum was asymmetrical; the left lobe being one-third less than the right. The corpora striata, optic thalami, and pons varolii were symmetrical. The medulla oblongata was markedly larger on the right side above the decussation. The right vertebral artery was almost twice as large as the left one.

Microscopical examination of certain sections showed in the right frontal lobe a proliferation of the neuroglia; in the right third frontal convolution there was an increase of connective tissue, and there were but few fibres seen in the white matter. The right parietal region showed few nerve cells, and increased neuroglia, general and perivascular. In the right occipital lobe were very few cells, and these were atrophied and irregular; there was a very evident increase of neuroglia between the nerve elements.

In the discussion of the case a cause for the condition is suggested in an acute external hydrocephalus. "The disease having been arrested after the skull had become ossified, and the fluid being gradually absorbed, a compensatory substance was demanded, which was supplied by an increase of the neuroglia of the right hemisphere *pari passu* with the absorption. This sclerosis of the packing substance of the right hemisphere impairing its trophesial influence, resulted in arrestment of development of the opposite side of the body."

The condition has also received *clinical* diagnosis in a child by Reissmann, who has reported the case twice (1902 and 1904); it is one of unilateral gigantism, in which the right side of the body is enlarged, together with the left side of the head, especially in the parietal region. The cranial asymmetry seems to him sufficient to justify the diagnosis of hypertrophy of the left cerebral hemisphere. The child (male) was 2 years old in 1904, quite healthy, and able to speak.

Other clinical cases also must exist. Thus recently I have come across a photograph from Lockhart Mummery, in a book by Purves Stewart, of a case similar to Reissmann's, except that the body was enlarged on the left side, and "the right side of the cranium, and probably also the right side of the brain, was larger than the left."

Not too much stress should be laid on these clinical cases, however, as in a case reported by Friedreich, where the cranium was asymmetrical, the brain was found to be normal at the post-mortem examination.

Little is known as to the morbid anatomy of hypertrophy of the brain. Indeed, the term, applied as it is to general, unilateral, and localised states, may include several distinct conditions.

In some of the older writers, as Sachs says of Barthez and Rilliet and Gehhardt, there is a confounding of "obvious interstitial encephalitis with true hypertrophy of the brain." Tuke's case seemed to be chiefly a hyperplasia of the neuroglia—especially in the occipital region. The fibres and cells were poor in number on the affected side, while the ground substance was increased, and the vessels showed proliferative changes. In the case of general hypertrophy reported by Anton, little pathological change was found. In the frontal cortex there were areas which contained very few ganglion cells, and the fibre systems, noticeably the tangential fibres, were lessened. In Schick's interesting cases with acute symptoms in children (with persistent thymi), unfortunately no histological examination has been recorded.

The etiology of these conditions naturally is very obscure. Heredity, hydrocephalus, hyperæmia, trauma, lead-poisoning, enteric fever, rickets, and internal secretion disturbances have all been instanced in a causal connection.

An hereditary influence is suggested in van Walsem's case (21-year old epileptic idiot), where two brothers had died in childhood macrocephalic.

Anton discusses at length the relationship of the suprarenals to cerebral malformations. Lomer, Weigert, Zander, Ilberg, and others have written on the subject. Weigert has also noticed an often associated defective development of the superior cervical sympathetic ganglion. In the suprarenal cases the abdominal sympathetic must be concerned, through its intimate relationship with the chromaffin cells of the suprarenal medulla. The "chromaffin" system generally seems to be of importance in anomalous vasomotor and trophic conditions. (Wiesel, and Biedl and Wiesel.)

That the suprarenals of my case were normal shows that a chemical disturbance of suprarenal origin, such as Anton supposes for his case, cannot be at work in all cerebral errors of development. Nor was rickets here in question (*vide* Baginsky).

Hydrocephalus as an associated condition may have an etiological bearing. Tuke suggests the possibility of an acute hydrocephalus being the cause of the hypertrophy in his case. Edinger mentions hydrocephalus as a cause of hypertrophy of the brain, instancing the fact (also noted by Cunningham in his Anthropological Lectures) that the shape of the crania of many distinguished persons suggests that in early youth they had had slight hydrocephalus. (This was so of Cuvier and Helmholtz.) With reference to microgyria also, Liebscher has remarked how an early hydrocephalus may influence the proportionate development of cortex and medulla.

In my case, however, the left lateral ventricle was so slightly enlarged, the wall and choroid plexus also showing none but the simplest hyperplastic changes, that it is impossible to assert that hydrocephalus had any etiological bearing.

The microgyria shown is of the type described by Liebscher as true developmental microgyria, in contradistinction to that associated with inflammatory or sclerotic changes (or arrested growth, as described by Otto). In this respect the second case of Kotschetkova is similar.

(B) On the subject of unilateral gigantism, into which I believe this case must be considered finally to resolve itself (notwithstanding the fact that in the other cases in which cranial and bodily hypertrophy coexist, the conditions are opposite-sided), we find, with a wealth of clinical observations, very few pathological data which help us towards an understanding of its exact nature.

In the interesting clinical cases of Brüning, and of Machenhauer, the pathology of previous cases (degrees of structures involved and associated conditions) and the etiological theories are dealt with.

[Clinically, it is of interest that in my case the condition was noticed soon after birth, and that it is that of a female, and of enlargement of the *left* side (as in Lewin's table the proportions of male to female are 15 : 4, and Trélat and Monod, 7 : 4, and Brüning, 8 : 2, and of right side to left as 13 : 6 in Lewin, and 8 : 3 in Brüning).]

The chief theories as to the causation of unilateral giant-growth are those of Trélat and Monod, and Wagner (embryological-vasomotor), of Fischer (lymph-circulation disturbances), and of Widenmann and Tillmanns (tropho-neurosis).

Machenhauer writes of intra-uterine trauma as a possible cause, and gives instances where extra-uterine trauma has excited hypertrophic processes. The condition usually appears to be associated with hyperæmia. *Active* hyperæmia in many cases (*e.g.* in Finlayson's case, where the difference in temperature between the two sides was well marked), which would accord with Wagner's theory of over-nutrition of the parts affected. To this category belong the hypertrophic changes noticed after chronic congestions and inflammations, *e.g.* in the nose or tonsils; or in bones, after osteomyelitis, or after necrosis (Helferich). The hypertrophy of the ears of *young* animals which Bidder and Stirling observed after excision of part of the cervical sympathetic is to be noticed in this connection, though I am unaware of any more recent work on this point. (See Jensen's negative finding referred to later.)

Passive hyperæmia also possibly could produce hypertrophic changes, as is suggested by the stimulation of bone formation in cases where Bier's passive congestion method has been used in the treatment of ununited fractures: this would more accord with the Trélat-Monod theory of "stasis." Atrophy, however, appears to be the more probable result.

Unilateral vasomotor disturbance has been noted by Kaiser (in a 69-year old senile dement). The patient, for some months before death, showed a right-sided hyperæmia and œdema. Old softening of the left supramarginal gyrus was found, and a small (1 cm.) recently softened area in the left caudate nucleus, and a fresh cyst in the left lenticular nucleus.

Kaiser refers to the literature on cortical vasomotor centres (Eulenberg and Landois and Otto). In his opinion the caudate nucleus is a vasomotor centre for the opposite side of the body. Reissmann holds a theory of the cortical origin of the condition in his case. In my case the right supramarginal area, it will be remembered, was small.

Vasomotor and trophic conditions (of cortical? or medullary or sympathetic origin), even though present in slight degree, may well be of great potency when long-continued in the embryo; though they may both be but evidence of irregular development of the embryonic layers, as shown in the laborious work of Zingerle for the neuro-epithelium.

(C) Thirdly, the acromegalic state of the feet must be considered. True acromegaly has, according to Reissmann, been recorded as existing in children three or four times. I am not aware of any case in which such a condition appeared earlier than the earliest of Arnold's list of thirty-six cases, namely, in the seventh year. Schmidt's earliest reference is 13 years (a case of Thomas), and it is so extremely unlikely that a disease such as acromegaly (a disease typical of the post-epiphyseal-union period of life) should commence to appear at the age of 2 years, that I consider that we should require fuller grounds than we have in this case for considering it with certainty to be incipient acromegaly.

Acromegaly has close associations with gigantisms and hypertrophies in general. In it, as in them, great vascularity has been noticed (as by Klebs), and obscure nervous and trophic disorders often coexist (as tabulated by v. Recklinghausen). The sympathetic nerves and ganglia may show hypertrophy (Cagnetto, 1907).

With acromegaly in the early stage, when active progress is being made in

the bony overgrowth, there are so commonly to be found associated over-activity and hyperplasia in the glandular part of the hypophysis, that many writers (Tamburini, Benda, and Lewis) advocate the simple view which regards this hyperplasia as the essential cause of acromegaly. Cagnetto's second case shows beautifully how the anterior lobe can be seen enlarging with all transitions into an angio-sarcomatous-like tumour-growth. [The infundibular body is of no known importance in acromegaly, though it is the only part of the normal hypophysis extracts of which produce physiological results. (Schäfer and Vincent, and Howell).] Erdheim has noticed signs of parathyroid activity in a case; and Ballet and Laignel-Lavastine think, from consideration of a case in which widespread glandular hyperplasia was found, that some not yet understood chemical change in the body generally must be the final cause of acromegaly.

On the histology of the hypophysis proper, Lothringer, Zimmermann, Thom, Erdheim, and others have worked. Though Saint-Remy and Benda find all transitions between the two types of cells, while Scaffidi finds only sharply differentiated fuchsinophile and orange G cells, an increase of the granular cells is generally agreed to indicate increased activity of the gland. Erdheim mentions the end of the first decennium as the time when the two types of cells begin to be about equal in number. In the few hypophyses of young children which I have had the opportunity to examine, the chromophile cells were considerably less numerous than were shown by the present case.

Thus if further research confirm theory (1) that a chromophile hyperplasia is the essential cause of acromegaly, we may consider the condition of the feet really to have been commencing acromegaly in a child, which would be a point of additional interest in this already unique case.

On the other hand, if theory (2) be accepted (and Cagnetto has brought forward strong evidence in its favour), that acromegaly and hypophysis tumour are independent results of an underlying metabolic disturbance, we might consider the slight hypophysis change to be possibly compensatory to the smallness of the thyroid, and the enlargement of the feet to be merely another sign of the general trophoneurotic disturbance, as shown also by the vasomotor instability and the patches of leucoderma.

To conclude, I regard the case as essentially a unilateral gigantism, a developmental growth anomaly, with specially marked localisation in the cerebrum.

I have referred above to hydrocephalus as a possible, though very unlikely, cause for the cerebral condition.

For this and the other coexisting states a more probable cause suggests itself in a vasomotor derangement of the left side of the body, and in particular of the left internal carotid artery and its branches.

For this cause to be the efficient one we need to assume, as I think we may, the existence of pial vasomotor nerves. (Literature in Hill and MacLeod, and in Jensen. The latter has shown the presence of vaso-constrictors on stimulation of the sympathetic, though section of the sympathetic produces no definite results on *adult* rabbits.)

Assuming, then, the presence of cerebral vasomotor nerves, we note that the enlargement of the left cerebral hemisphere is confined strictly to the areas supplied by the anterior and middle cerebral arteries; and the right hemisphere is only enlarged (and that to a much slighter degree) in those regions supplied by its communicating

branches with the left side. And as a bundle of post-ganglionic fibres from the superior cervical ganglion accompanies the internal carotid artery, thus probably conveying vasomotor fibres to the vessels of the brain (Langley), and the glandular part of the hypophysis as well (Berkley), it seems not unjustifiable to conjecture that in some such way there may be a real coherency in the diverse features of the case.

Whatever the cause or causes may have been which were at work in this truly unilateral case, they must at any rate have been different, in kind or in mode of action, from those concerned in the production of the conditions coexisting in the other cases above-mentioned of opposite-sided hypertrophies or opposite-sided hypertrophy and atrophy.

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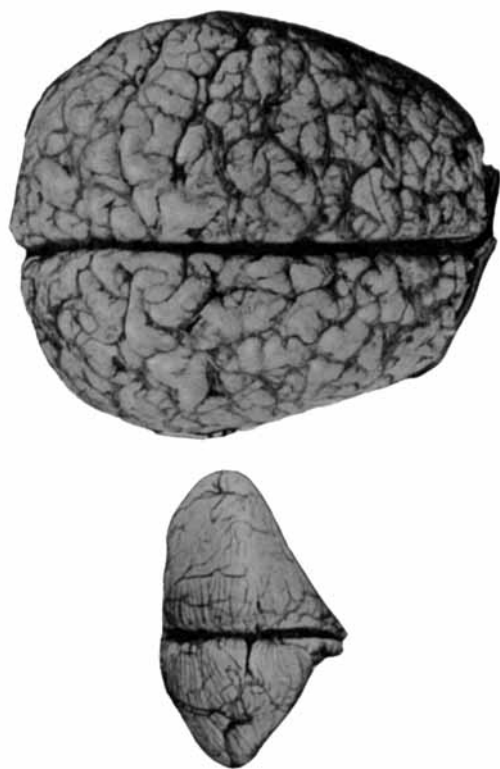


Fig. 1.

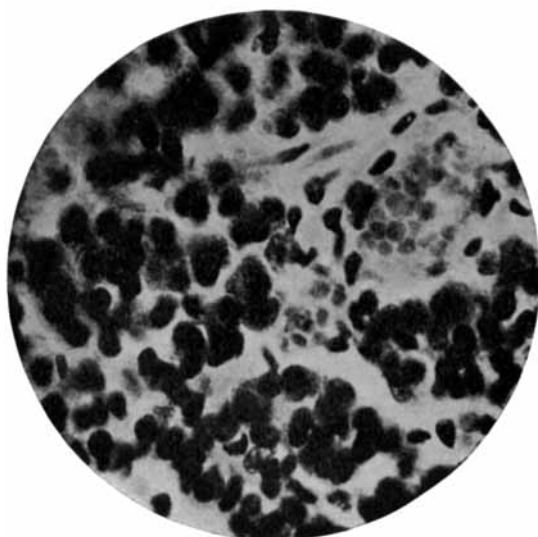


Fig. 2.



Fig. 3.

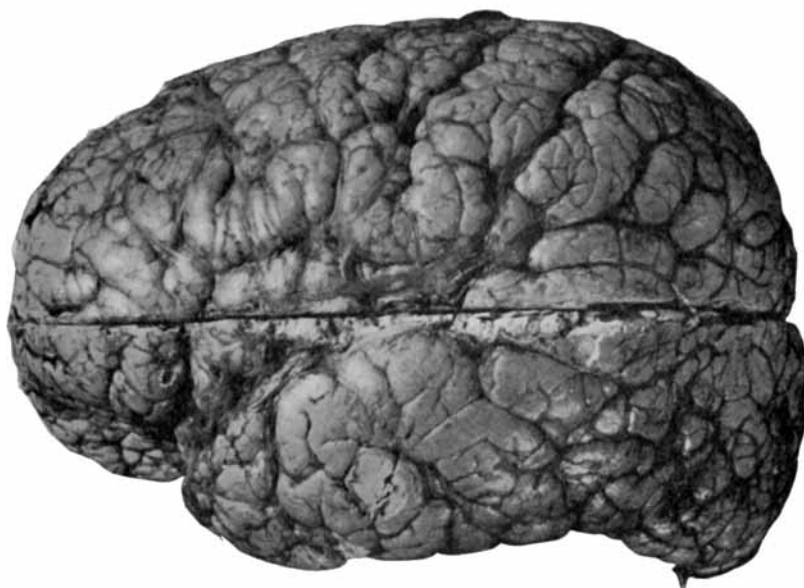


Fig. 4.



Fig. 5.



Fig. 6.

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DESCRIPTION OF PLATES XXXV.-XXXVII.

PLATE XXXV.

- FIG. 1.—Photographs of superior surfaces of the cerebral hemisphere, and of the cerebellum from behind. (Photo, F. Nývák.)
- FIG. 2.—Microphotograph hypophysis cerebri. $\times 700$ (hæmatoxylin and eosin). Showing a large capillary blood-vessel, and a large percentage of coarsely granular eosinophile cells. (Photo, Rd. Muir.)

PLATE XXXVI.

- FIG. 3.—External surface of right cerebral hemisphere.
- FIG. 4.—External surface of left cerebral hemisphere.

PLATE XXXVII.

- FIG. 5.—Mesial surface of right cerebral hemisphere.
- FIG. 6.—Mesial surface of left cerebral hemisphere. (Photos [by Fr. Nývák] not absolutely proportional).