

SEXUAL INFANTILISM WITH OPTIC ATROPHY IN CASES OF
TUMOR AFFECTING THE HYPOPHYSIS CEREBRI.*

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A disturbance of menstrual function may be one of the earliest symptoms of a certain class of intracranial tumors. Particular attention has recently been called to this fact by Axenfeld and Yamaguchi, by von Abelsdorf and by Müller. Growths in most diverse situations, or, indeed, an increase of intracranial tension from conditions non-neoplastic, have been known to affect the regularity, or even to completely interrupt for long periods, previously normal catamenia. In the personal records of about sixty cases of brain tumor, the majority of which have come under my care in Dr. Halsted's service during the past five years, a history of menstrual disturbance has been recorded in several instances. The physiological explanation of this symptom can only be conjectured, but it seems quite possible that in some way it is due to an interference with the normal activity of the pituitary gland.

The cases may be divided into two groups: One, those in which amenorrhea accompanies tumors arising from the hypophysis or affecting the gland by direct compression; the other, those in which menstrual disturbance is a symptom of tumors situated elsewhere. In the latter group Müller has suggested that an internal hydrocephalus, through distension of the recessus infundibuli, may interfere with the function of the gland. There is, however, no certain proof of this. In the former group—those with tumors in the hypophyseal region—the relation of sexual development and menstrual activity to the condition of the pituitary gland is more clear. I shall limit myself to the consideration of lesions of this type; and inasmuch as the two patients, whose histories I shall report have been women, I shall not consider the effect of similar lesions on the male, although in

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this sex, as well, instances of hypoplasia of the genital organs associated with hypophyseal tumors have been recorded.¹

Axenfeld,² in 1903, pointed out that basal tumors involving the hypophysis are those which most commonly produce amenorrhea and optic atrophy, and he drew a comparison between this symptom-complex and acromegaly, a disease often associated with an hypophyseal enlargement or tumor and accompanied by amenorrhea. His cases were subsequently reported in full by Yamaguchi.³ One of them, a patient who had never menstruated, was sexually undeveloped, and the optic atrophy, which was present in this as well as in the other patients, was a simple ascending atrophy not consequent upon a choked disc. He suggested that the closure of the nerve sheath prevented the formation of a "papillitis," but as will be seen in the first of my cases, a choked disc may develop in a nerve already partially atrophied as the result of direct pressure.

In the same year Abelsdorff,⁴ in a note concerning Yamaguchi's paper, called attention to a previously recorded case of benign growth of the base, presumably an enchondroma, in which amenorrhea preceded all other symptoms for ten years. Subsequently disturbances on the part of the optic nerves appeared.

Again Müller,⁵ in a recent article, has collected five cases from the Breslau clinic, one of which (Case 4) seems to me to have possibly belonged to this group. A patient, 29 years of age, had been a slowly developing, weak child. She had had some slight, irregular menstruation first at 21 years of age, but after a few months the scanty flow ceased to reappear. Not until she was 22 had her breasts enlarged, and she was otherwise developmentally backward. There had been a gradual loss of vision. In addition to these symptoms, there had been frontal headaches, vomiting, and occasional brief lapses in conscious-

¹Fröhlich: "Ein Fall von Tumor der Hypophysis Cerebri ohne Akromegalie." Wiener klinische Rundschau, 1901, Nr. 47 and 48. Contains a review of the literature.

²"Sehnervenatrophie und Menstruationsstörungen bei basalen Tumoren." Neurolog. Centralblatt, 1903, p. 608, Sitzungsbericht.

³"Ein Beitrag zur Pathologie des Sehnerven bei Hirnerkrankungen." Klin. Monatsbl. f. Augenheilk., 1903, Festschrift für Manz. Beilageheft zum, xli., p. 180. Ref. Jahresbericht des Neurol. u. Psychiat., 1904.

⁴Abelsdorff, G.: "Offene Correspondenz." Klin. Monatsbl. f. Augenheilk., Vol. xli., 1903.

⁵Müller: "Ueber die Beeinflussung der Menstruation durch cerebrale Herderkrankung." Neurolog. Centralbl., 1905, No. 17, p. 790.

ness. It is noteworthy that here there were no so-called localizing symptoms; the writer, however, regarded the case as one of probable tumor.

In consultation with Dr. A. P. Herring, I have seen a patient with symptoms very similar to those thus described by Müller. A young woman, of 21, has suffered for years with headaches. She has been blind since she was 16. There is double optic atrophy with no edema of disc or retina. She has never menstruated. The pelvic organs and breasts are undeveloped. Her intelligence, considering that she has received no education, seems normal. She has become spastic, and her extremities are wasted and contracted.

Some light is shed on the seat and nature of the lesion from which these patients were suffering by the case which I may now report more fully:

CASE I. Mary D., a seamstress, 16 years of age, was admitted to Dr. Osler's wards in the Johns Hopkins Hospital Dec. 12, 1901, complaining of pain in the back, dizziness and headache. Little could be learned of her family history. She has two elder sisters, who are healthy.

She has led an unhygienic life; has worked for some years as a seamstress (shirt maker) for eleven hours a day, walking several miles to and from her place of employment. She has suffered from headaches for years. She has never menstruated; never "developed."

A month before her admission her headaches became worse; she began to have pain in her eyes, and dark spots obscured her vision. She has also suffered with pain "over her kidneys," chilly sensations, fever and sweats. She has been drowsy. There has been anorexia, with nausea and vomiting on taking food. Her bowels have been constipated. She says her legs have been swollen for a week, and she cannot stand or walk.

For two months after her admission the patient was kept under close observation and made the object of special study. She was much undersized, looking like a child of twelve. She seemed well nourished; mucous membranes of a good color. Her skin was smooth, almost waxy in appearance. Her hands and feet were small like a child's; she had short, unusually tapering fingers. Her tongue was heavily coated, her breath foul, her gums soft and spongy.

Examination of her chest and abdomen was negative. Her breasts were undeveloped. There was a scant growth of axillary and pubic hair. There was no certain edema of the extremities, though the smooth, waxy skin over the abundant panniculus

made it seem that "pitting" would be possible, and one observer records "very slight edema of feet and hands." There was no cranial nerve involvement; ophthalmoscopic examination was negative; vision was normal. Beyond a constant slight leucocytosis, elaborate examinations of the blood revealed nothing abnormal; there were no arthritic symptoms; no purpuric spots. The urine, likewise, on repeated examinations, except for an occasional hyaline cast, proved negative.

Reading between the lines of the history, it is evident that until Feb. 12th, when a definite choked disc was found, the diagnosis of the patient's condition had been very obscure, and that renal disease or some unusual form of malnutrition, perhaps associated with scurvy, was suspected.

Though the eye grounds had been examined on several occasions, the first mention (other than that there was "a suspicious blurring of the nasal half of the discs," Dec. 24th) of a definite change occurs under the date of Feb. 12th, when a double optic neuritis ("neuro-retinitis") is noted. It is apparent from the history that this finding only sufficed to further obscure the diagnosis.⁶

From this time on the patient's condition became progressively worse. She had frequent attacks of severe headache with projectile vomiting. She was in a more or less stuporous condition much of the time, but would often sit up in bed suddenly and cry out with pain. She constantly complained of pain in her eyes and of failing vision. The swelling of the discs increased rapidly, especially on the left, where some retinal hemorrhages were found on Feb. 15. The deep reflexes at knee and ankle were active, but there was no clonus. Plantar reflexes were normal. She once had incontinence of urine during a period of bad headache.

On Feb. 16th her vision had so far failed that she was barely able to count fingers. Vision 20-40. Perimetric fields difficult to chart owing to dull mental condition. They show little more than a general shrinkage (Fig. 1). No bitemporal hemianopsia.

On Feb. 17th a lumbar puncture was performed, and 20 cc. of clear fluid under increased tension (maximum 51 cm., minimum 39 cm.) were withdrawn. This only served to increase her headache.

On Feb. 18th the patient was seen by Dr. H. M. Thomas, who considered the headaches more characteristic of intracranial growth than of nephritis. No localizing symptoms could be made out.

⁶It is merely another instance of the difficulty of distinguishing between the so-called albuminuric retinitis and choked disc. I have commented upon this elsewhere (*Surgery, Gynecology and Obstetrics*, October, 1905), and some experimental observations (with Dr. Bordley and Dr. Gilman) have led us to believe that the process is the same in tumor and nephritis.

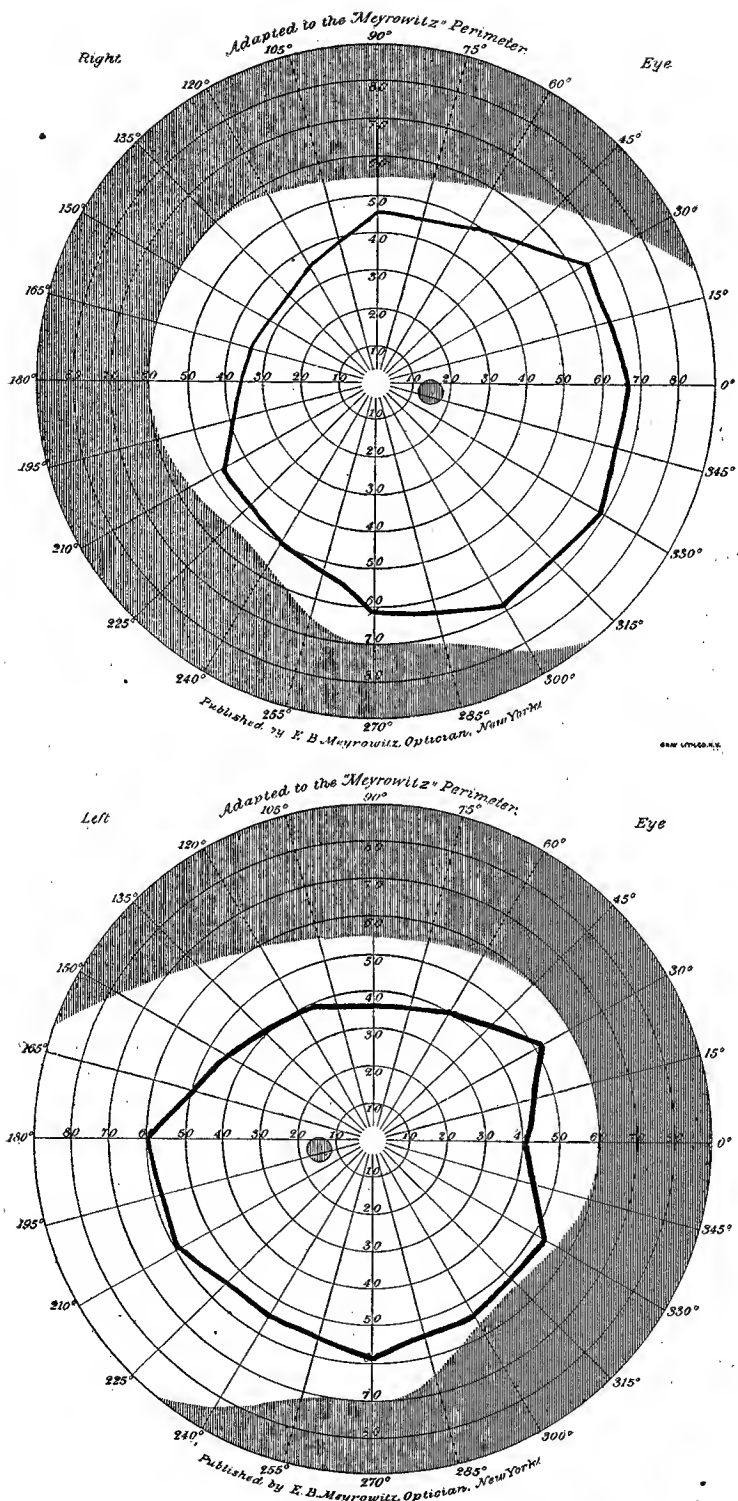


FIG. I. FORM FIELDS OF CASE I, SHOWING MERELY CONCENTRIC SHRINKAGE.

On Dr. Thomas's advice she was transferred to the surgical side for an exploratory operation. Little was understood at this time of palliative operations, and looking back upon the case it is difficult to see what we could have expected to gain by surgical measures.

Operations: On Feb. 21st an exploratory craniotomy was performed. A bone flap was turned back from the left hemisphere; the dura was opened; a tense bulging brain was disclosed, which made subsequent reclosure of the dura impossible;⁷ the layer of bone was removed and the scalp resutured in place. The operation sufficed to completely relieve the patient's headaches, but it left her with some contralateral palsies, which we to-day understand to have been the result of the protrusion of cortex through the dural opening, this having been so made as to include much of the motor cortex. The wound healed without reaction.

On March 8th a second exploration was made over the right hemisphere. The same condition of affairs was found, and again the bony shell of the flap was removed, the dura left open and the scalp wound closed. The ventricle was not aspirated on this or the previous occasion. The wound healed per primam.

Following the operation, the patient improved greatly. The paralysis, which had resulted from the hernia through the opening made at the first operation, disappeared, and by the third day the edema had almost completely faded from the disc and retina of each eye. The hernial protrusions, furthermore, were very slight and gave evidence of little tension. She was free from pain, had no vomiting and was subjectively well and happy.

Not satisfied with this result, we were led, through the development of some ataxic symptoms, into what proved to be a meddlesome and disastrous operation.

On March 17th a third operation was done, and the cerebellum was exposed. The exploration proved negative, and the wound healed perfectly, but the patient soon after grew dull and stuporous, the hernial protrusions again became tense, marked spasticity of all the limbs, with great exaggeration of the reflexes,

⁷I have only recently learned how it may be possible in these cases to resuture the dura when it is desired to do so. I have on three occasions been able, after a lumbar puncture and removal of the ventricular fluid, to close the dura over the hemisphere, which before the puncture bulged to such an extent that closure could not have been effected without injury to the brain, if at all. It would have been a suitable procedure in this case considering the internal hydrocephalus, and had it been done the dura might have been closed and the subsequent hernia avoided. In purely palliative operations, however, it is desirable, indeed essential, that the dura be left open and the overlying bone removed, as has been learned from later experiences (cf., "The Establishment of Cerebral Hernia as a Decompressive Measure for Inaccessible Brain Tumors," *Surgery, Gynecology and Obstetrics*, October, 1905).

set in, and she remained in an unconscious condition until six weeks later, when death occurred from inanition and inhalation pneumonia. It is probable that, as a result of the suboccipital operation, with consequent cerebellar protrusion, some dislocation of the tumor had taken place which led to an obstruction of the

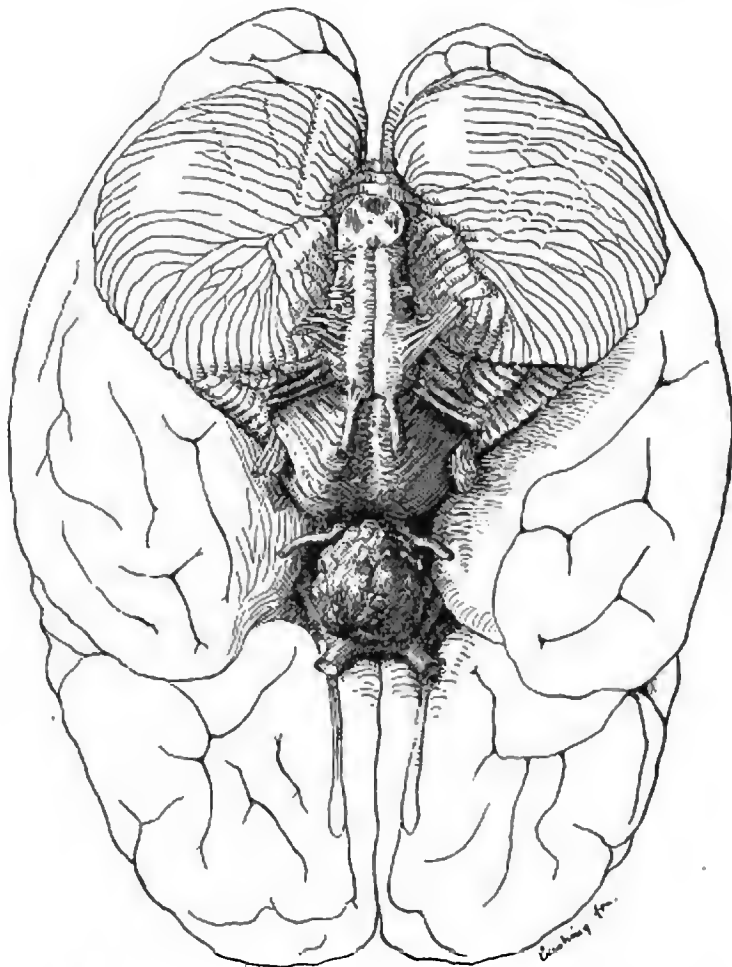


FIG. 2. DRAWING OF BASE OF BRAIN AND TUMOR (CASE I), FROM SKETCH OF THE TISSUES MADE AT THE TIME OF THE AUTOPSY.

third ventricle and an active stasis of fluid in the ventricles of the hemispheres.

Autopsy, May 1st, 1902. An examination was held by Dr. MacCallum, and the immediate cause of death found to be an

extensive broncho-pneumonia. The thoracic and abdominal viscera were otherwise normal. The pelvic organs were well formed, but infantile in appearance.

On removing the brain a hard, nodular tumor mass, the size of a walnut, was found occupying the space between the crura cerebri and the optic commissure (Fig. 2). The tumor was intradural and attached to the leptomeninges, involving and displacing the structures at the base of the brain by compression alone. The growth occupied the position of the tuber cinereum and overlaid the pituitary body, which was small and greatly flattened out. The chiasm was pushed forward and the optic tracts widely separated. The optic tract on the left seemed to be particularly encroached upon, but it retained its normal form. The cranial nerves otherwise were uninvolved.

On separating the hemispheres and dividing the corpus callosum from above, the growth was found projecting under the floor of the third ventricle. The foramina of Monro were both greatly dilated, as were the lateral ventricles. The third and fourth ventricle were of natural size. The substance of the hemispheres seemed somewhat edematous throughout. The ependyma was everywhere smooth.

Sections of the tumor showed it to be a mixed tumor containing cartilage and tissue cells of various other sorts. It was pronounced a teratoma by Dr. Welch. Unfortunately, no histological study was made of the pituitary body.

To summarize and to analyze this case report it would seem that a slow-going, congenital, intracranial tumor, mesially placed and so situated as to compress the hypophysis cerebri, had for years given no symptoms (barring an occasional headache) other than a retardation of sexual development accompanied by some obscure nutritional disturbances. The rather acute onset of intracranial symptoms, with rapid formation of bilateral choked disc, was in all probability due to the final production of an internal hydrocephalus consequent upon the projection of the tumor into the third ventricle. From a tumor in this situation, one might have expected a bitemporal hemianopsia, and had this characteristic symptom been present, a localizing diagnosis would certainly have been made. The only objective evidence of ocular disturbance, before the choking of the discs became apparent, lay in the narrowing of the visual fields and some pallor of the nerve-head.

In the following case the diagnosis cannot be certified, but its clinical similarity to the foregoing one makes it more than probable that a similar lesion is present at the same basal point.

CASE 2. Miss Daisy W., a saleswoman, 26 years of age, was referred to me Dr. Hiram Woods and Dr. H. M. Thomas in March, 1905. She complained of severe headaches and failing vision.

There was nothing in her family history bearing upon her present condition. She was the eldest of a family of four, having three brothers living and well.

As a child she had had whooping cough, diphtheria, measles, typhoid fever and pneumonia. She has always been short of breath on exertion. She has had some bladder trouble with occasional burning on micturition.

She menstruated once when fourteen years of age, but never since then. She gives no history of vicarious menstruation, no nose bleed, etc. She has occasionally noticed some watery discharge from the nipples, and there are periodical shooting pains in her breasts.

She has taken a great deal of morphia for her headaches, and suffers from chronic constipation.

Since she was sixteen years of age she has suffered from headaches, which for the past few years have become more or less constant and at times are very severe. They were at first general in character, but of late have been confined largely to the right side of her head. The pain seems to be extracranial, as well as intracranial, and to extend chiefly into the right trigeminal territory. It is exaggerated by any excitement or physical strain, and may even extend into the neck and shoulder. She sees "balls of fire" at these times.

She has had no nausea or vomiting, though for a year there has been some "distress" after eating. She has lost about ten pounds in weight.

She has been blind in her left eye for four years, the trouble beginning, according to her story, as a temporal blindness. The vision in the right eye has been failing rapidly of late.

She has noticed some dulling of sensation in her right cheek, and has had some tremor in her hands, so that it is at times difficult for her to feed herself. Apart from this, there have been no other manifestations of a motor or sensory nature. For three years she has had occasional "dizzy spells" lasting a few moments, and during which she has to hold on to something. These are followed by a hot flush and by thirst. She has visual hallucinations during these attacks, but has never fallen or lost consciousness during them.

Physical Examination: Before her admission the patient had been examined by Dr. W. W. Russell, who found her sexually infantile. Though rather undersized, she was a healthy looking, well-nourished young woman, with a colorless, waxy look to her face. Her skin was smooth, youthful in appearance, like that of a young girl. There was a certain bogginess of the subcu-

taneous tissue of the extremities (as in Case 1), almost suggesting edema. This was particularly apparent in the hands and feet. The fingers were delicate and tapering. Though there was an abundance of panniculus over the breasts, the glandular structure could not with certainty be palpated, and the nipples were undeveloped.

Eyes. There was a lack of parallelism in the axes of the globes, not apparent, however, at all times. The pupils were considerably dilated and equally so. They reacted promptly to

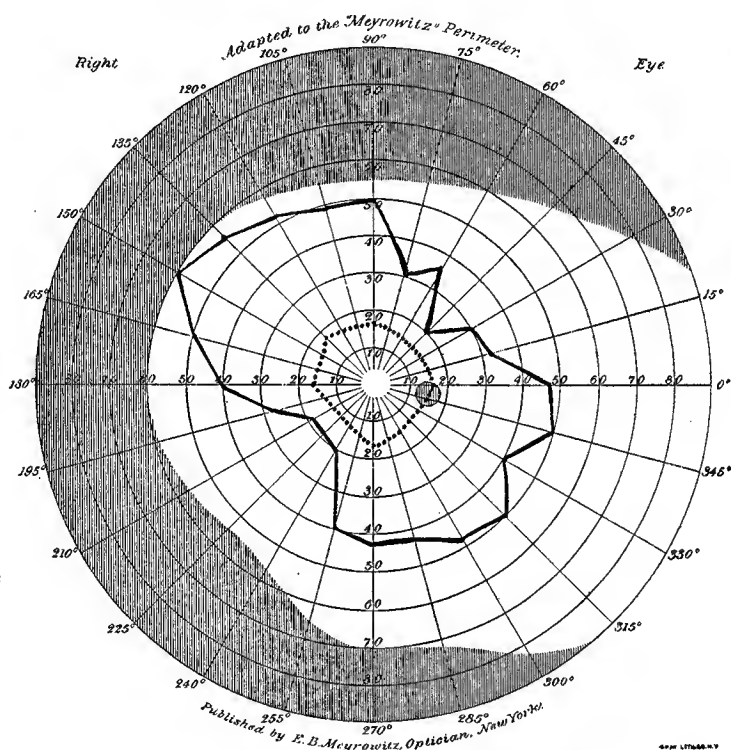


FIG. 3. CASE II. COMPOSITE CHART SEVERAL OBSERVATIONS, MARCH, 1905.

light and accommodation. The left pupil reacted consensually from the right, but there was no left to right reaction. There was no light perception in the left eye. There remained some central vision in the right eye, 20-30, but the field was considerably narrowed (cf. Dr. Wood's chart, Fig. 3). Both nerves showed evidence of white atrophy, more advanced on the left. There was no edema of the disc nor dilatation or tortuosity of the vessels. No nystagmus; no exophthalmos.

The sense of smell was considerably impaired on the right

side; substances recognized promptly on the left were not appreciated on the right.

There was a dulled perception of impulses for pain, touch and temperature over the skin fields of the three trigeminal divisions on the right. The area was also somewhat hyperesthetic to certain forms of stimuli. The other cranial nerves (excepting for the diplopia already mentioned) showed no evidences of involvement.

The patient's intelligence was normal. There was no evidence of motor or sensory disturbance in the spinal fields. The reflexes were normal.

Operation: On March 14th, 1905, a bilateral decompressive craniectomy was performed by the writer's method. Through an intermusculo-temporal approach the thin shell of bone underlying the muscle was rongeué away on each side. The dura was opened on the right side alone. There was but little increase of cerebral tension; the exposed portion of the hemisphere was normal. Both wounds were closed without drainage and healed per primam.

Post Operative Condition: Rather to our surprise, the patient's headaches were greatly relieved, and it is gratifying to state that her vision also slowly improved. The evidence of pressure upon the trigeminus disappeared, and it seems probable that the cranial openings allowed the brain and tumor to lift away from the affected nerves at the base so that they in a measure were able to recover their normal functions.

At the present writing, May, 1906, a year after the operation, the patient has returned for an examination. She is very much better in many respects. Her old intracranial headaches have left her completely. Her vision has greatly improved. An examination of the right eye (the left remains blind), made by both Dr. Woods and Dr. Bordley, shows her vision to be about 20-20. The visual field for form has enlarged considerably, except for the temporal half of the retina, where vision remains contracted as before. It is noteworthy that there is an improvement in the recognition of colors: whereas a year ago there was an uncertain central field for red and no appreciation whatever of blue and green, she now recognizes all colors promptly, though only upon the nasal side (Fig. 4) of the retina. There is a tendency, therefore, not only in the color field, but in that for form, to a nasal hemianopsia.

There has been no return of catamenia during the past year, and certain symptoms have led her physician, Dr. Galloway, to believe that a removal of the ovaries would greatly benefit her. These symptoms are of periodic occurrence, and appear with great regularity every four weeks. She cannot clearly describe her sensations during these "spells," as she calls them. The period of discomfort lasts usually for four or five days, some-

times for as long as an entire week. Several times daily she has a sensation of something rushing up from her body, which gets in her throat and chokes her. She oftentimes has a taste of blood in her mouth, and her nostrils feel raw. During these spells there are visual disturbances, so that she can only distinguish large objects. Consciousness is not lost at any time, but she often has a peculiar sinking sensation. Some time after the

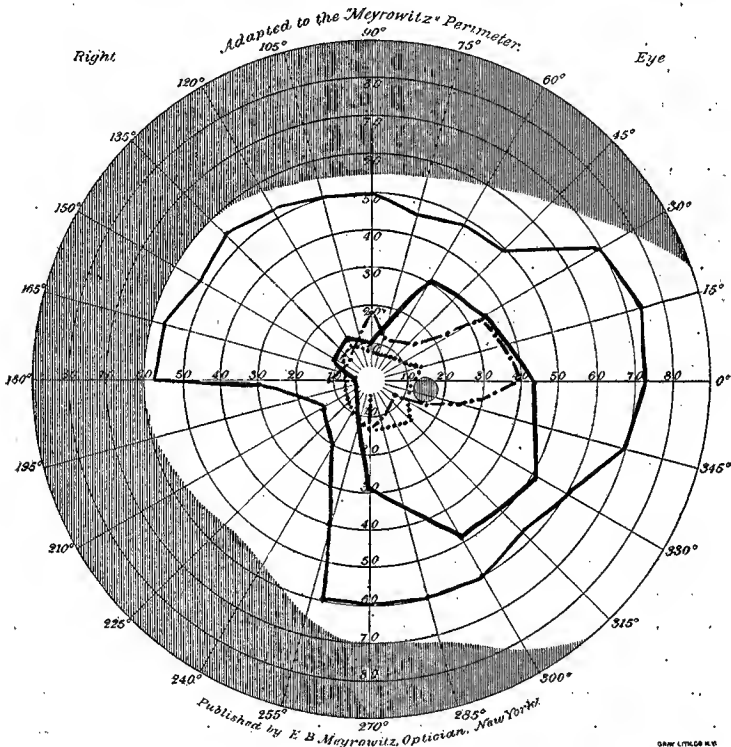


FIG. 4. CASE II. COMPOSITE CHART MAY 23 AND MAY 24, 1906.

spells pass away, her hands do not appear to belong to her. There are bright flashes before her right eye, like tiny specks of fire, and at times millions of scintillating specks. She also at these periods has pain and tenderness on pressure over her left ovarian region.

It is possible that an oöphorectomy may put a stop to this periodic monthly discomfort, which suggests in some respects an attempt at vicarious menstruation. This operation is at present under consideration.

An X-ray taken by Dr. Baetjer has shown that there is a shadow with deformation of the base of the skull in the situation

of the clinoid processes and the sella turcica, which suggests the unmistakable presence of a growth in this situation.

To make a certain localizing diagnosis of brain tumor without autopsy or operation is often difficult enough, but here the bilateral optic atrophy, which we assume to be a primary atrophy, is sufficient to place the lesion in the neighborhood of the chiasm. In a discussion of the effect of hypophyseal or neighboring growths upon the optic tracts, Oppenheim⁸ has shown that the bi-temporal form of blindness is by no means the most commonly produced disturbance, although when it does occur, it is, of course, a most important localizing symptom. There may be simple shrinkage of the visual field in each eye, or unilateral blindness may be present. Ophthalmoscopic examinations may reveal no abnormality in the disc, though in a majority of cases an atrophy sooner or later will be found, and only occasionally a choked disc. As in Case 1, the process has been of such long duration that it may with propriety be considered a benign growth, one probably arising from a congenital *anlage*. The amenorrhea, furthermore, if we are to agree with the opinion of others, shows that the hypophysis has suffered in some way, presumably from compression.

In summarizing these cases one may lay emphasis again on the peculiar association of amenorrhea with hypophyseal tumors and of sexual infantilism in case the process has started early in life. This symptom, together with optic atrophy, may suffice, in the female, to make a diagnosis reasonably certain. In the male sex, as is shown by the cases which Frölich gathered, a corresponding condition may be present. These cases tend to show at the same time certain evidences, hard to describe, of nutritional disturbance, with an abundant development of subcutaneous fat. They do not present any of the appearances characteristic of acromegaly or gigantism.

⁸Oppenheim: "Die Geschwülste des Gehirns." 2 Auflage. Nothnagel's Spec. Pathol. u. Therapie, 1903, Bd. IX., p. 197.