

PITUITARY HEADACHES AND THEIR CURE *

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Headache as a symptom is well known to all. The patient who complains of it is too often given a cathartic and aspirin and dismissed without adequate study to determine its true etiology. He may then go elsewhere and return after he has developed more definite signs. I remember one patient who returned four days later with the complete picture of a tuberculous meningitis.

Headache commonly presents itself to us as the symptom of some systemic disease, such as circulatory disturbance, especially hypertension, nephritis, anemia, an acute febrile disease, or poisoning by various toxic substances. These may be exogenous or endogenous; for example, lead, carbon monoxid, alcohol, or the toxins resulting from acidosis, diabetes, uremia, or from the gastro-intestinal tract. Syphilis is a frequent cause of headache. There are likewise local causes in disturbances of the cerebral circulation, a myositis of the occipitofrontalis muscle, periostitis or gumma of the cranium, inflammation of the accessory sinuses, increased intracranial tension resulting from abscess, meningitis, tumors, etc., errors of refraction and eye-strain, or migrain which may prove to be an intermittent claudication of the cerebral arteries. Certain headaches are of reflex origin, as those which come from menstrual irregularities or pelvic disease. Headache may be a symptom of hysteria and the various neuroses and psychoses. So much for the multitudinous causes to which we often ascribe this distressing symptom.

The part which the pituitary gland may play in the production of headache is frequently overlooked. The clinical picture of severe frontal headache, somnolence, mental dulness, polyuria, increased sugar tolerance or glycosuria, oculomotor palsies, bitemporal hemianopsia, and evidence of disturbed bony metabolism or adiposity, sexual regression, etc., is a well known syndrome caused by pituitary tumors. But it is the early and less easily recognized pituitary disturbances on which interest must center, for that is the stage in which therapy will help; and one of the first symptoms of a pituitary gland which is functioning improperly is a frontal headache which does not yield to the usual remedies.

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It is this type of headache which I wish to present in all its phases, hoping that it may aid a little toward the knowledge of the therapeutic value of pituitary. Several case reports added at the end will show the clinical value of these observations.

ETIOLOGY

The cause of pituitary headaches is, briefly, an enlargement of the hypophysis following on a stimulus or demand made on it, or a pathologic condition of the gland. It is more common in women than in men, and may occur at any age, though it is most frequently seen in adolescence and early adult life.

PATHOLOGY

Among glandular structures the anatomy of the pituitary gland is unique, in that it is situated at the base of the brain, connected to it by a narrow stalk, the infundibular process, and lying within the confines of the sella turcica, a bony crib to whose physical limitations it is subject. The size of the hypophysis is quoted by various authors,¹ averaging in the sagittal plane from 6 to 10 mm., vertical from 10 to 14.5 mm., transverse from 5 to 9.75 mm., the weight 0.6 gm., comparing favorably in size to the hazel nut. The gland, made up of three parts, is surrounded by a thin capsule—a continuation of the dura mater; anterior to it lie the olivary eminence and the anterior clinoid processes; below, the dorsum sellae; behind, the posterior clinoid processes; and above, overhanging the entrance to the sella in the form of a diaphragm, is a firm prolongation of the dura which is perforated by the infundibular process. The nerve supply is derived from sympathetic plexuses along the carotid artery. Tilney,² in an admirable article, has contributed largely to the phylogenesis and anatomy of the hypophysis. To Cushing³ and Falta⁴ we owe important contributions to its physiology and clinical significance.

From the foregoing it can be seen that the pituitary gland is entirely surrounded by a firm framework, on three sides by bone, above by dura and only on the lateral aspect is there any opportunity for expansion. If the gland were situated in masses of loose areola tissue such as the thyroid or the adrenals, a considerable enlargement would be possible before pressure symptoms were felt or could even be detected; but, let the hypophysis enlarge just 2 or 3 mm., and there will develop

1. Zander: Quoted by Munson and Shaw, *Archives Int. Med.* **14**:493, 1894. Hitchcock: *Med. Rec.*, New York, Sept. 10, 1911.

2. Tilney: *Pituitary gland*. Mem. Wistar Inst., 1911.

3. Cushing, H.: *Pituitary Gland and Its Disorders*, 1912.

4. Falta: *Ductless Glandular Diseases*.

a train of symptoms dependent on this mechanical discrepancy. We see, then, that there are two factors which enter into the production of these headaches, the size of the sella turcica and the size and pathologic condition of the pituitary gland.

In a series of twelve cases showing no dyspituitary signs or symptoms, normal sella turcica measurements are shown in Table 1.

TABLE 1.—NORMAL SELLA MEASUREMENTS AS DETERMINED BY THE AUTHOR

Name	Antero-posterior	Depth	Name	Antero-posterior	Depth
A	11	10	F	10	8
D	11	10	S	11	7
B	12	10	M	11	9
M	10	8	E	11	10
P	10	8	H	11	8
A	9	8	M	11	10
Average	9-12	7-10			

Average measurements quoted by other writers are as shown in Table 2.

TABLE 2.—MEASUREMENTS OF SELLA NOTED BY VARIOUS OBSERVERS

Name	Anteroposterior	Depth
Keith ⁵	10-12	8
Potts ⁶	8-13	6-10
Fearsides ⁷	10-12	8

To compare with the foregoing a series of fifteen cases which showed distinct dyspituitary signs, Table 3 reveals either an enlargement of the sella or else a definite contraction:

TABLE 3.—COMPARISON OF CASES SHOWING DYSPITUITARY SIGNS

Name	Antero-posterior	Depth	Name	Antero-posterior	Depth
D. S.	12	9	R. W.	17	13
E. H.	11	11	S. F.	9	8
J. T.*	15	11	E. M.†	30	30
E. F.	14	12	D. S.*	12	8
S. J.	11	8	W. G.*	9	7
E. W.*	12	12	N. C.*	15	13
S. W.	12	10	N. F.*	15	8
J. L.	13	12	M. B.*	5	5

* Cases marked with * are measurements of sellae of case reports.

† E. M. is a case of pituitary tumor with acromegaly.

Another table will serve to show the comparative measurements of the normal hypophysis and the sella turcica (Table 4):

TABLE 4.—COMPARATIVE MEASUREMENTS OF NORMAL HYPHYPHYSIS AND SELLA

	Sella-Turcica	Hypophysis
Anteroposterior	9-12	6-10
Vertical	10-14	7-10

5. Keith: Lancet, London, 1911, **1**, 993.

6. Potts: Jour. Am. Med. Assn., 1913, **61**, 1188.

7. Fearsides: Lancet, London, 1914, **2**, 16.

From these figures and facts we determine that normal pituitary glands usually have normal sella conformation, but should the glandular function be disturbed there will result certain signs and symptoms and the roentgenogram will show an abnormal sella turcica.

Roentgenograms of this type of case having "pituitary" headaches and dyspituitary signs reveal a wide variety of sellae turcicae and I should like to note here the importance of a careful study of each plate by the clinician with a standard normal plate as reference. There may be a very small contracted fossa with clinoids in apposition, or there may be a large fossa with a similar formation of clinoid processes; the former of these would be expected to show hypopituitary and the

Figure 1.

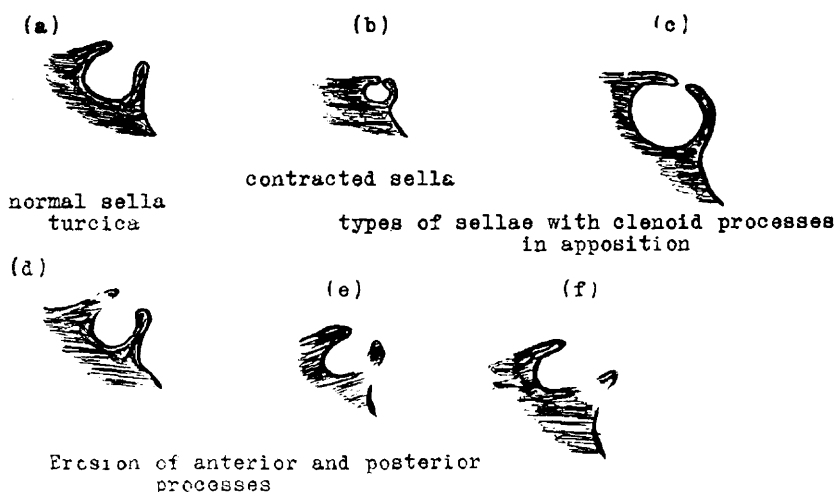


Fig. 1.—Various types of sella turcica.

latter hyperpituitary signs. Then again, there might be evidence of erosion of the posterior clinoid processes with, perhaps, pyramidal tract signs, or of the anterior processes with bitemporal hemianopsia or contraction of the visual fields, indicating in the former, enlargement of the gland posteriorly and in the latter anteriorly. There is also the generally enlarged sella turcica, the sella whose posterior process is tilted backward; and last of all, the complete destruction of the fossa and dorsum sellae, such as occurs in neoplastic overgrowth of that region. If a careful study of the physical signs and symptoms of the patient is made prior to the roentgen ray picture, the conformation of the fossa can frequently be prognosticated with considerable accuracy. Drawings of various types of sellae are shown in the accompanying diagram (Fig. 1).

Why the pituitary gland should enlarge is the next question that comes to mind. It is well known that during menstruation and pregnancy there is a physiologic enlargement of the gland, Falta noting an increase in weight from 0.6 to 1.0 gm. This enlargement may be cyclical and account for the periodical occurrence of the menses, or else we can ascribe it to stimulation from the gonadal secretion. Other glandular disturbances are also liable to influence the pituitary, etc., such as pineal or thymic subinvolution, adrenal or thyroid disease, which is most probably in the nature of a compensatory phenomenon.⁸ A mental shock or traumatism to the skull may be the exciting cause to an altered hypophyseal function. These occasionally result in a hyperplasia of the glandular elements, but the gland may be also the seat of colloid degeneration, cysts, abscess, hematoma, adenoma, adenocarcinoma, sarcoma, endothelioma and teratoma.

In many ways, therefore, we see there can occur a disproportion between the pituitary body and the sella with the production of pressure on the sensory nerves to the dura; and by its encroachment on the cavernous sinuses it may cause interference with the cerebral circulation, the whole setting up the train of pituitary symptoms, including the headache.

SYMPTOMS AND SIGNS

The pituitary headache has three characteristics: its location; its duration and persistence; and its relief under specific medication. A patient will come to the physician complaining of a frontal headache. On questioning further he will say that it is situated "deep in the forehead behind the eyes," often feeling as though it were pressing on them, giving a "dazed" sensation. Not infrequently, without asking, and always on asking, the patient, placing the finger on either temple, pointing directly inward at the hypophysis in the attitude of the accompanying picture will say, "Doctor, it is between here" (Fig. 2). Depending on its severity, it is described as a tightness between the temples, a feeling of pressure or distention, or an intense, bursting ache. Rarely they complain that there is a sensation of "something in there" and on moving the head, they may feel as though "a marble-like object were rolling about." Deep pressure on the temples may elicit some tenderness.

This headache is very persistent, usually lasting from one-half hour to forty-eight hours, and it may be continuous, frequently coming on in the female at the time of the menses. It often leaves very suddenly, returning again with exacerbations; it is accentuated by excitement, stooping over, and by the ingestion of sugar. At the climax of the headache we may see nausea and vomiting, with which there will come

8. Timme, W.: New York M. J., Oct. 16, 1915.

relief. Marked fatigue accompanies the headache, the patient hardly being able to drag himself about, and there is present to stroking a broad white skin line as evidence of suprarenal deficiency caused by the drain on the adrenal function by the exhausted pituitary. The patients feel slowed down in their activity, yawn excessively, are sluggish and willing at any moment to seek an opportunity for sleep. These patients are particularly prone to attacks of depression, which come on without any cause, and have as their basis some very insignificant fact. In children there is apt to be evidence of mental retardation, with dulness, sluggishness of the mind and lack of the higher reasoning powers, this usually occurring in hypopituitary conditions, while in adults we sometimes see a loss of moral control resulting in frequent visits to the police courts. The menstruation has certain characteristics in these pituitary individuals. It may begin very early, at the age of



Fig. 2.—Location of pituitary headache (Case 7). Note the coarseness of features and the nasal eyebrow.

10 or 12, or else very late, at 16 or 18. The periods are irregular, often coming every two or three weeks, and the flow excessive. Sexual development may be very precocious in the hyperpituitaries. Polyuria is occasionally present and constipation frequently accompanies the height of the headache with diarrhea at its termination.

Knowing that the pituitary, together with the adrenals, controls the mobilization of sugar in the body, it is not strange that these patients should have anomaly of sugar metabolism, as is seen in the periodic development of an intense craving for sweets, a sort of dipsomania, as it were, for sugar. The satisfaction of this desire being completed by eating candy, it is almost invariably followed by a typical pituitary headache. We can readily see that owing to the increased demand on it, there is an enlargement of the pituitary gland, and following on this the adrenals are called on to assist in mobilizing the sugar, the excessive drain on them causing great fatigue and the formation of a vicious circle.

How, then, are we to recognize these cases and tally their physical signs with the symptoms enumerated? Do we expect to see finished acromegalics or giants, or adiposis with sex regression? No! but there are certain dyspituitary signs which are of aid in diagnosis.

The growth of hair has certain peculiarities; it is more apt to be dark and coarse in texture. The amount is abundant, the arms, legs and body being covered with a quantity of hair; the pubic hair not infrequently is of masculine type in the female, growing up to the umbilicus in a triangular fashion and in the male it may be of the female type, straight across over the mons veneris. The eyebrows are heavy and long and they often meet in the midline over the nose forming a nasal eyebrow. The female may show a tendency to a mustache. The bony framework is altered, there being either excessive length or breadth of bone, depending on whether or not the epiphysis had united when the metabolism was disturbed. The appearance of the face might show one or all of the following: eyes too close together or too far apart, a large nose, prominent superior maxillae, a prognathism of the lower jaw, a general coarseness of the features with thickening of the lips. The teeth, especially those of the upper jaw, either widely spaced or else unusually broad. These persons are sometimes very tall, with large hands and feet, and there is a broadening of the hands, with clubbed fingers. Deposition of adipose tissue may be excessive. Pulse and blood pressure are both apt to be low, especially during the headache, this being more an expression of adrenal exhaustion than pituitary. Blood sugar determination and sugar tolerance will in most of these cases reveal either too high or too low a figure. A contraction of the temporal fields of vision is occasionally found and, rarely, a primary optic atrophy.

TREATMENT

Specific remedies for the cure of disease constitute the treatment *par excellence* and modern medicine has given to us a number of such agents; for example, arsphenamin for syphilis, the employment of serums in pneumonia and epidemic meningitis, thyroid in myxedema and cretinism, etc. Such a specific is the administration of pituitary to cure pituitary headaches.

There are a number of good pituitary preparations on the market, the most satisfactory being Armour & Company's and Burroughs Wellcome's tablets of the whole gland. If the latter are used they should be prescribed in doses four times as large as any others. We commonly use Armour's tablets in doses varying from $\frac{1}{4}$ grain to 2 grains three times a day; an average for an adult is 1 grain, preferably given one hour after meals. Much larger doses are recommended by some authors, Cushing giving as much as 15 grains in some

of his cases. For a more rapid action it is claimed that hypodermic injection of pituitary extract, 0.5 to 1 c.c., is valuable, but I have seen better results with preparations of the whole gland.

Continuous medication with pituitary will result within a few days in a decrease in the intensity of the headaches; there will be a longer period between their occurrence, the head will feel less "tight," and fatigue, nausea, and vomiting will also disappear. An examination of the case reports given later will show very gratifying results. A number of these cases cure themselves, and it is the belief of Timme⁹ that the person who has a small sella turcica with dyspituitary signs and symptoms will remain so indefinitely, even though pituitary administration helps toward relief; but if the sella is large and there is room for expansion, there will occur the foregoing type of symptoms and the patients will eventually cure themselves, even though they become acromegalic in the process. We can therefore regard symptomless acromegalics as a finished product, according to this investigator.

But there are also those cases which, having symptoms of pituitary disease, do not improve on treatment, and it is then that we must begin to consider the possibility of a neoplasm and careful observation becomes essential. Just a word of caution against too long continued pituitary therapy. After the symptoms show improvement, diminish the dose and give it only three or five days out of the week; this gives the gland a chance to readjust itself.

Case reports follow, and as they are all from clinic patients, it has, unfortunately, been impossible to have blood sugar and sugar tolerance tests made.

CONCLUSIONS

1. Pituitary disturbances constitute a fairly common cause of headache.
2. Pituitary headache is located between the temples, deep in behind the eyes and is accompanied by dyspituitary signs.
3. Abnormality of the sella turcica is demonstrable in almost every case of pituitary disease.
4. Administration of the whole gland cures these headaches and the accompanying symptoms in a large percentage of cases, provided there is not a progressive neoplastic growth.

REPORT OF CASES

CASE 1.—J. T., a woman, aged 40, married, had severe frontal headaches beginning at the age of 15, with the onset of the menses. The headaches were infrequent, occurring usually once a month at the menstrual periods until six years prior to observation, since which time they have increased in severity and frequency so that they now come on several times a week. The head-

9. Timme: A New "Polyglandular Syndrome," "Endocrinology," 2:209, 1918.

ache lies between the temples and moving the head accentuates it. Vomiting has occurred about once in two weeks lately. The patient is fatigued at times and has polyuria, and the menses are always irregular. There has been no loss of appetite or craving for sweets. At the age of 30 she suddenly became very obese and increased in weight to 185 pounds. An aunt has goiter.

Physical examination shows a well developed woman, short, obese, with small hands and feet. The head is large, eyes set close together, jaw prognathous. The eyebrows are heavy, with nasal eyebrow marked. The teeth are small and not crowded, and fingers are broad, short and clubbed. The roentgen ray shows a general enlargement of the pituitary fossa, with slight erosion of the posterior clinoid processes (see Table 3, J. T.).

Pituitary, $\frac{1}{4}$ grain twice a day, was given. In one month the headaches and other symptoms had greatly improved. At the end of four months, during which time the dosage was increased to 1 grain daily, she said that she had only had two very slight headaches in the previous two months, and had had no nausea or vomiting for three months. Discontinuance of the drug caused a return of the old symptoms. This is evidently a case which originally began as hypopituitary and is now endeavoring to compensate and enlarge.

CASE 2.—D. S., aged 16, schoolboy, was brought to the hospital with a history of several blows on the head, complaining of momentary "staring" spells, followed by a very severe headache, with which he would go to bed. This headache is made worse by playing or excitement and is in the pituitary location. He has stood very low in school, is sleepy, dull and stupid. When younger he had enuresis and has always been fond of candy. Mental examination showed him to be a high grade imbecile, measuring 7 years on the Terman score, not being oriented as to time, and lacking in reasoning ability and judgment.

Physical examination showed a small boy who appears about 10 years of age; structural and sexual growth are backward, there being no secondary sex signs as yet. He has rather a square jaw, teeth are broad but not spaced, the eyebrows are normal in size and the hair growth is scanty. A roentgenogram of the skull shows a slightly enlarged sella turcica with heavy clinoid processes which completely roof over the fossa. (Table 3, D. S.)

On the evidence of the headaches, the roentgenogram, and a hyperpituitary type of father, the boy was given pituitary, $\frac{1}{2}$ grain three times a day. He returned in two weeks without headaches. At the end of a month the headache seemed gone for good, and there was as well a cessation of the "staring" spells. The father noted joyfully that he was less mischievous and more active. The dose was increased to 1 grain three times a day. After three months the boy says that he feels as though a "weight had been lifted off his mind," an observation he could not have made at the onset of his treatment. He is brighter, more interested, and is anxious to learn. He can tell date, year and season, and is standing much higher in his studies. Another mental test showed an advance of one year in three months' time. This is evidently a hypopituitary case which without treatment would never have come out of the imbecile class.

CASE 3.—E. W., woman, aged 24, single, came into the clinic suffering with severe frontal headache, slunk into a chair holding her head, yawned frequently, extremely fatigued, dull, drowsy, nauseated, trying to vomit. She had been this way for three days. As long as she can remember she has off and on had these terrible headaches. Since coming to America four years ago they have increased in frequency and severity; she is very irritable, is constipated, and has lost 42 pounds in weight. Her headaches are paroxysmal in type, lasting for a period of from a few hours to three days; are situated between the temples, and bore in like a knife, causing an aching of the eyes at times; and with the onset of vomiting they are often relieved. There has been no menstrual irregularity. The patient has at times an intense craving for candy. Her father's sister had similar headaches.

The patient is of medium height, large frame, skull is also large, eyes are far apart, jaw slightly prognathous, teeth broad and spaced, eyebrows heavy, with a marked nasal eyebrow; the feet are small. There is a slight but definite contraction of the temporal fields of vision. The fundi show the veins engorged. The roentgenogram shows a rather large sella with clinoid processes in apposition and beginning erosion anteriorly. (Table 3, E. W.)

Pituitary, 1 grain three times a day, was given; increased after three weeks to 2 grains three times a day. In a week there was an improvement in the intensity of the symptoms and in a month the headache had diminished so that the patient has only had a slight ache once in two weeks. There has been no nausea or vomiting, fatigue is very much less, and she is anxious to return to work. She seems much brighter and more active mentally; there is less visual field contraction, and she has gained 5 pounds in weight. Improvement is continuing.

CASE 4.—N. C., a nurse, aged 29, single, when a little girl had headaches all the time, which were made light of by her family because of her robust physique. She was given glasses, which have been frequently renewed, all with no relief. Headaches are severe, coming on in exacerbations in the "pituitary" location, bursting in type and accompanied until one year prior to observation by nausea and vomiting and confining her to bed. Although a large, strongly built woman, she is always fatigued and sleepy and when the headache is most intense she is dull, drowsy and wants to sleep. Several years ago she noticed that on satisfying her craving for sugar the headache became worse, so she does not eat it now. She is constipated at times and has polyuria; also has mild periods of depression. The menses began at 12 years and have been irregular ever since.

The patient has always been big, coming from a tall family. The hands and feet are large and the maxillae are prominent. The eyebrows are bushy and continuous across the nose. The hair growth is plentiful and there is a slight tendency to the masculine pubic hair. The roentgenogram shows a generally enlarged sella turcica, wide open and very deep. (Table 3, N. C.)

Pituitary, 1 grain twice a day, was given, followed by a cessation of the headaches and a diminution of the fatigue within twenty-four hours. The patient since has had only one slight recurrence of the headache, and fatigue and dullness are much improved.

CASE 5.—N. F., a nurse, aged 27, single, had her first headache at 16, which was very severe, and at intervals ever since they have recurred. Coal tar drugs were often taken, with only slight relief. The menses began at 14, then skipped six months, and became regularly established at 16, since when they have been irregular. The headache usually comes a week before the catamenia and continues until the onset; then relief comes. It is typically pituitary in location, between the temples and on top of the head, described as a feeling of tightness, pressure and distention, accompanied by fatigue and occasionally depression. The patient faints easily, has excessive perspiration of the hands and cyanosis of the extremities, and has also a desire for sweets, satisfaction of which causes headache.

The patient is small, thin, square built; skull round, jaw broad, prognathous; hands and feet small, short, stubby; eyebrows heavy, with marked nasal eyebrow; tendency to moustache. Hair growth is excessive on hands and legs; pubic hair masculine in type. A roentgenogram shows that the sella is enlarged anteroposteriorly and there is slight erosion of the posterior clinoid process. (Table 3, N. F.)

Pituitary, $\frac{1}{2}$ grain three times a day. In three days the patient noticed that the head did not feel quite so "tight" between the temples. The next period was preceded by a headache, which was not so severe, and the second was accompanied by only a slight dazed feeling. The headache is now gone.

CASE 6.—M. B., a cook, aged 31, married, five years prior to observation had very severe headaches previous to the birth of her first child; since then

she has suffered with them off and on, becoming worse during the previous six months, lasting a whole day, forcing her to bed, and obtaining relief only by vomiting. She had glasses fitted and teeth extracted without relief. The headaches are described as severe, situated between the temples, behind the eyes, accompanied by fatigue, dizziness and sleepiness. She feels "dopy," sluggish and has no ambition, becomes depressed and unhappy and does not wish to be bothered. The menstruation began at 14 and comes every three weeks. She has no desire for sweets.

The patient is a large, obese woman, weighing 164 pounds, with scanty growth of hair. The teeth are broad, eyebrows heavy, with only a few hairs over the nose; the jaw is broad and slightly prognathous. This woman is hypopituitary in most features and the roentgenogram was no surprise when it revealed an extremely small, contracted sella turcica, with heavy clinoid processes meeting in the midline. (Table 3, M. B.)

This patient has been under treatment only a few months, but in that time has had no suspicion of a headache and says voluntarily that she feels less tired and dopy and is brighter and more ambitious. Medication has been 3 grains daily of the whole gland.

CASE 7.—W. G., a sailorboy, aged 23, single, has had severe frontal headache for five years. The tonsils were removed and glasses procured without relief. The headache is boring, bursting in type, deep in the midline between the temples, as in his picture (Fig. 2). It is accompanied by extreme fatigue and at times the patient has a craving for candy. He is depressed frequently, feels mentally sluggish, his grasp is slow and his memory not so acute as formerly. He says that his hands and feet are larger and his face broader.

The patient is of medium height, has coarse, heavy eyebrows, with nasal accentuation, his nose and lips are large, features coarse, jaw prognathous, lower teeth spaced, the upper broad, hair growth is abundant, masculine type, and the hands and feet are large and square. The roentgenogram shows a small, flat sella with beginning erosion of the anterior clinoid processes. This is a hyperpituitary case which approaches more the acromegalic than any of the others.

Pituitary, 1 grain three times a day, was given. In one week the head felt clearer than in a number of years and the ache was less marked. The patient now has only a very slight headache at times, but notices particularly that his mind is more active, more attentive, and that he has a better grasp.

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