ADRENAL FAILURE OF PITUITARY ORIGIN

Plasma Protein Studies (Tiselius)

Report of Four Cases

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In cases of pituitary deficiency in which lack of somatic and skeletal growth is outstanding, it has been customary to speak of pituitary dwarfism or pituitary infantilism despite the obvious coexistence of gonadal deficiency. In the same sense we speak of pituitary myxedema.

By speaking of adrenal failure of pituitary origin we purposely call attention to the fact that many of the serious symptoms of pituitary disease are of adrenal origin and that a great deal can be accomplished by treating the adrenal failure as it is treated in Addison's disease. For some years, we have used adrenal extract in such cases. More recently, the chief therapeutic agents have been desoxycorticosterone acetate the NaCl; adrenal extract, testosterone propionate or methyl testosterone have been added in some cases, and occasionally small doses of thyroid.

The 4 cases reported here are instances of rather severe pituitary failure. We purposely are not calling these cases Simmond's disease because the term suggests the type of acute pituitary damage which was the basis of the condition in Simmond's original cases and emphasizes the feature of emaciation which was not present here. Williams and Wittenberger[1] reported similar cases which they classified as Simmond's disease and treated in much the same way as we have treated ours. Our cases are similar to the type which Albright[2] designated panhypopituitarism, in which he emphasized the pecularities of the glucose and insulin tolerance tests.

The selected cases demonstrate some of the interesting diagnostic features and present methods of treatment. In one case there were peculiar crises characterized by stupor, fever, weakness, vomiting, and hypoglycemia. These episodes were very similar to those present in a case described recently by Dynes,[3] which he believed were the result of hypothalamic pressure. In ours there was little to suggest that hypothalamic pressure existed, and we believe that the attacks were similar to those which occur in the crises of Addison's disease. In the cases presented here studies were made of the protein chemistry which has not previously been described.

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CASE REPORTS

Case 1—A 44 year old white clerk complained of an illness which probably began about 5 years ago when he had noticed that he was "below par" generally. He had complained to his physician of frequent colds and weakness and had been given liver injections and iron capsules for "anemia."

During the previous 8 months the patient had experienced increasing weakness and fatigue, both mental and physical. He tended to be excessively sleepy much of the time. During the previous month dizziness had bothered him to the extent that he had found it difficult to walk at times, and 2 weeks before admission he had fainted on the street and had fallen, striking his head and left arm on the pavement. Several times since then he had had to use a support to keep from falling.

His appetite and digestion were moderately good. He was intolerant to cold. The appearance of his skin had not changed. There was no numbness of the extremities, no brittleness of the nails, no falling of hair, nor edema.

Sexual maturity had been incomplete. There had never been any axillary or pubic hair; facial hair was very sparse. Shaving was not necessary more than once or twice a week. Sexual libido and potence had been slight or nil.

Examination showed a rather pale man with a very placid expression with a suggestion of edema (Fig. 1). His height was 65 inches; weight 163 pounds. Temperature and pulse were normal. Blood pressure was 90 systolic and 70 diastolic. He stood with an attitude indicating little energy and showing dorsal kyphosis. The evidence of gonadal failure was obvious. The head hair was profuse; the temporal hairline was not retracted. The supraorbital ridges were small; facies rather immature; the larynx small; and the chest relatively narrow. The genitalia were developed to what might be normal for the age of 16 or 17 years. The testes were small but solid. The prostate gland was about ½ normal size; its borders could scarcely be made out. The hands had a peculiar thickness of the tissues, and the facies suggested the possibility of a previously existing or "fugitive" acromegaly. Neurologic examination showed no evidence of central nervous system disease. The cardiac examination revealed distant heart sounds.

The results of some of the more important laboratory tests and special examinations are indicated in the following table.

TABLE 1

X-ray sella—depression of sellar floor and erosion of posterior clinoids
Visual fields—normal; fundi—normal
Kepler index[4]—12.8 (normal above 25.0)

Glucose tolerance[5]
(mg. glucose per 100 cc. blood)

Hours	F.	½	1	2	3	4
	96	116	99	79	74	74

Insulin tolerance[6]*
(mg. glucose per 100 cc. blood)

Minutes	F.	** 20	30	45	60	90	120	*** 45	60
	76	58	45	40	34	52	56	110	100

* High carbohydrate diet for 3 days preceding test
** 6.8 units insulin intravenously
*** 0.68 cc. adrenalin 1:1000 intramuscularly

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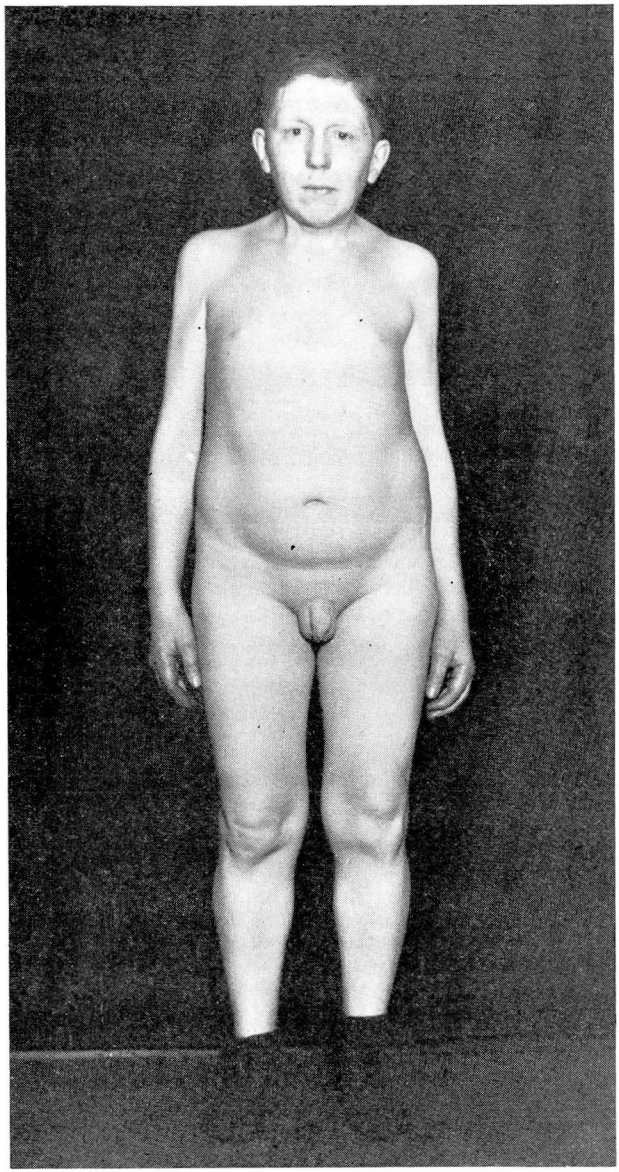

Figure 1. Note immature appearance and genital hypoplasia.

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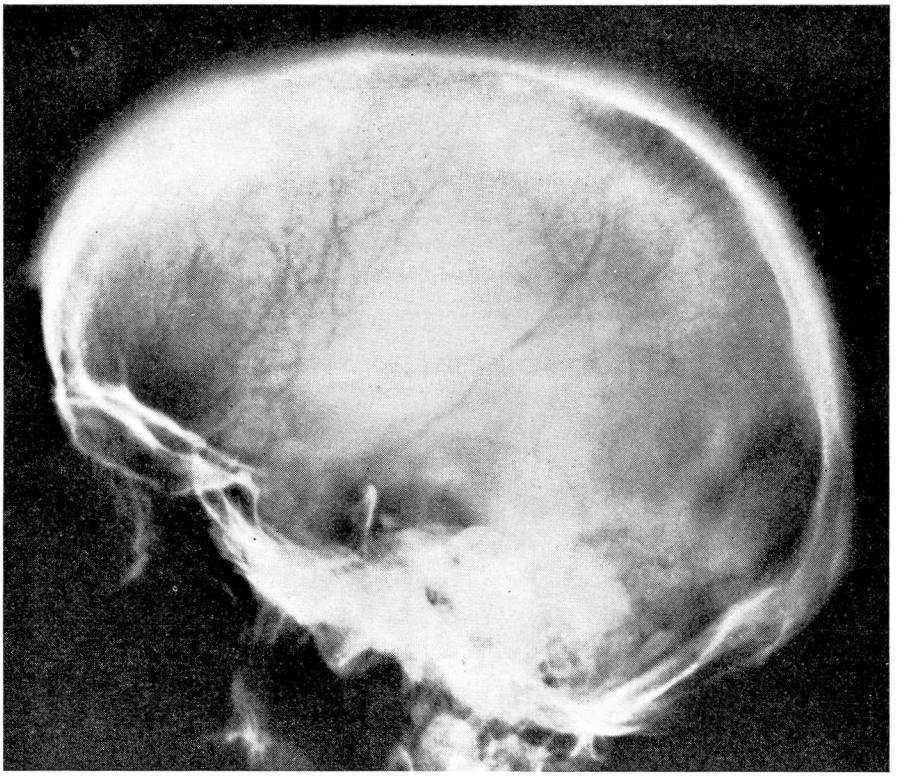

FIGURE 2. Case 1—Depression of sellar floor and erosion of posterior clinoids.

Amino-acid tolerance[7]*
(mg. amino N/100 cc. blood)

Minutes.....	F.	17	23	30	45	60
	6.1	8.8	7.0	6.6	5.8	4.8

* 50 cc. 10 per cent amigen intravenously (Amigen—Mead Johnson & Co.) Amigen is a dried enzymic digest of purified casein and pork pancreas containing amino-acids and polypeptides. The total nitrogen content is 12.0 percent, amino nitrogen 7.4 percent. The above composition is quoted from the manufacturer's claim.

Plasma proteins (Tiselius)[8]
(Gm. per 100 cc. plasma)

	Total plasma proteins	Alb.	α Glob.	βGlob.	γ Glob.	Fib.
4-10-43.....	6.85	3.83	0.27	1.34	0.95	0.46

Gonadotropic hormone assays[9] (3)—none measurable
Urinary androgens[10] 2.0 mg./24 hrs. (normal—7.0 to 15.0 mg.)
0.7 mg./24 hrs.
Basal metabolic rate[11]—minus 7 per cent

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The serum calcium[12], phosphorus[13], and cholesterol[14]; the red blood cell count and hemoglobin, and urinalysis were within normal limits. The blood Wassermann was negative.

The diagnosis was a calcified tumor within the sella turcica. The pituitary activity was of a very low grade and obviously had been producing very little gonadotrophic hormone since before puberty, causing the prepuberal type of eunuchoidism. There was little evidence of hypothyroidism. The most striking explanation of symptoms lay in the very low blood pressure. Urinary keto-steroids[15] too low to be accounted for by testis failure alone and a positive Kepler test supported the diagnosis of decreased activity of the adrenal cortices. The dramatic response to therapy also favored the diagnosis.

Treatment was begun on April 9, 1943 with 5 mg. injections of desoxycorticosterone acetate* in oil intramuscularly daily. Six Gm. of salt as enteric coated 1 Gm. tablets each day and a relatively high carbohydrate diet with intermediate feedings were also prescribed.

After 3 injections the patient felt very much stronger and had no dizziness. His blood pressure had risen to 126 systolic and 80 diastolic. The dosage of sodium chloride was then increased to 10 Gm. daily. The desoxycorticosterone acetate dose was reduced to 3.5 mg. 3 times weekly by injection. In addition he was given testosterone propionate 25 mg. 3 times weekly to encourage protein retention and muscle development and to promote genital growth and sexual maturity. On May 3 his weight had increased 4 pounds; his blood pressure was 126 systolic and 82 diastolic. Four pellets of 75 mg. each of desoxycorticosterone acetate were implanted subcutaneously. The dose of salt was reduced to 5.0 Gm. daily, and methyl testosterone 30 mg. per day was substituted for the injections of testosterone propionate. The patient was symptom free.

Case 2—A white woman, aged 56, was first seen in July, 1942 with the complaint of severe weakness which confined her to her room and much of the time to her bed. The debility had been troublesome for several years, but more so since an acute illness in May, 1941. That attack, as well as others later, was characterized by fever, stupor, vomiting, weakness, and on several occasions severe hypoglycemia. The fever has always been difficult to explain on a basis of inflammation although a mild upper respiratory tract infection has been thought to be the precipitating factor on two occasions.

The patient was healthy until her marriage at the age of 26. She had 3 pregnancies terminated by therapeutic abortions because of uncontrollable hyperemesis gravidarum. Her fourth pregnancy in 1923, when she was 36 years of age, was allowed to come to term in spite of vomiting throughout the period of gestation. After this last pregnancy she had an acute illness diagnosed influenza, following which she was thought to have developed meningitis. She was stuporous and was said to have been blind for 3 days. The spinal fluid was normal. From an x-ray of the skull a pituitary cyst was diagnosed. Following the spinal puncture her sensorium cleared. After recovery from the acute illness, she did not menstruate again. She lost both axillary and pubic hair which has not returned. Since then she has complained of headaches of an indefinite type; her vision has been less acute than formerly; and she is said by her friends to have been disinterested in any activity which requires physical exertion.

* Cortate—Schering Corp.

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In May, 1941 she had an acute illness which was similar to that observed in 1923 and to other attacks since then. For several days she complained of lack of appetite and vague gastrointestinal distress. On May 1 she had an attack of diarrhea. Projectile vomiting developed, and after 4 days of the illness she became very stuporous, her blood pressure was low, and she was extremely weak with a subnormal temperature as low as 95.6 F.

After the second hospital day her temperature rose to 105 F. She was treated with intravenous saline and glucose and blood transfusion. After 2 days the temperature returned to normal. During the acute phase of that illness the white blood count was in the neighborhood of 5000. Albumin was found in the urine on one or two occasions. The agglutination tests for typhoid and paratyphoid were negative. Stool examinations were negative. Spinal fluid was normal. Sedimentation rate was 69 the first hour and 98 the second hour (normal 15 to 20). The blood chloride level was as low as 350 mg. per cent, and the blood sugar was as low as 31 mg. per cent. A few days after the attack her

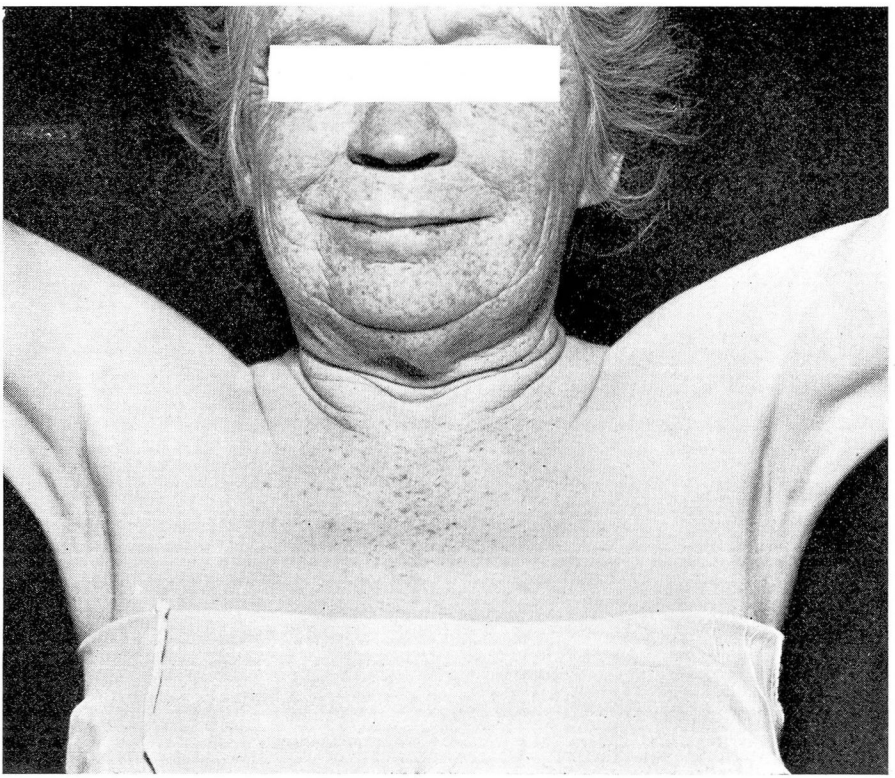

Figure 3. Case 2—Note puffiness of the face, marked freckling of the skin, and hairlessness of the axillae.

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basal metabolic rate was minus 36 per cent. Since that time she has taken desiccated thyroid 1 Gm. daily with little relief.

When first seen by one of us (E. P. McC.) in July, 1942 she presented the appearance of a pale, tired-looking woman (Fig. 3). Her skin had a yellowish tint, and her face showed many freckles. Her voice was low. She moved with little energy. Her face had a puffy appearance, decidedly suggestive of myxedema. Her height was 66 inches; her weight 117 pounds; temperature 96.8 F.; pulse 96; blood pressure 115 systolic and 60 diastolic. The thyroid gland was not palpable. The breasts were flat and atrophic with very little palpable breast tissue. The nipples and areolae appeared completely without pigment. There was virtually no axillary nor pubic hair. The skin of the body was slightly dry, fine in texture, and was not so thick as is usually seen in myxedema. The heart sounds were rather distant. The external genitalia were atrophic; the vagina small; the vaginal mucous membranes smooth and atrophied. The uterus and cervix were very small, and the vaginal smears were typical of a castrate type. The muscles generally lacked tone. No abnormalities were found on neurologic examination.

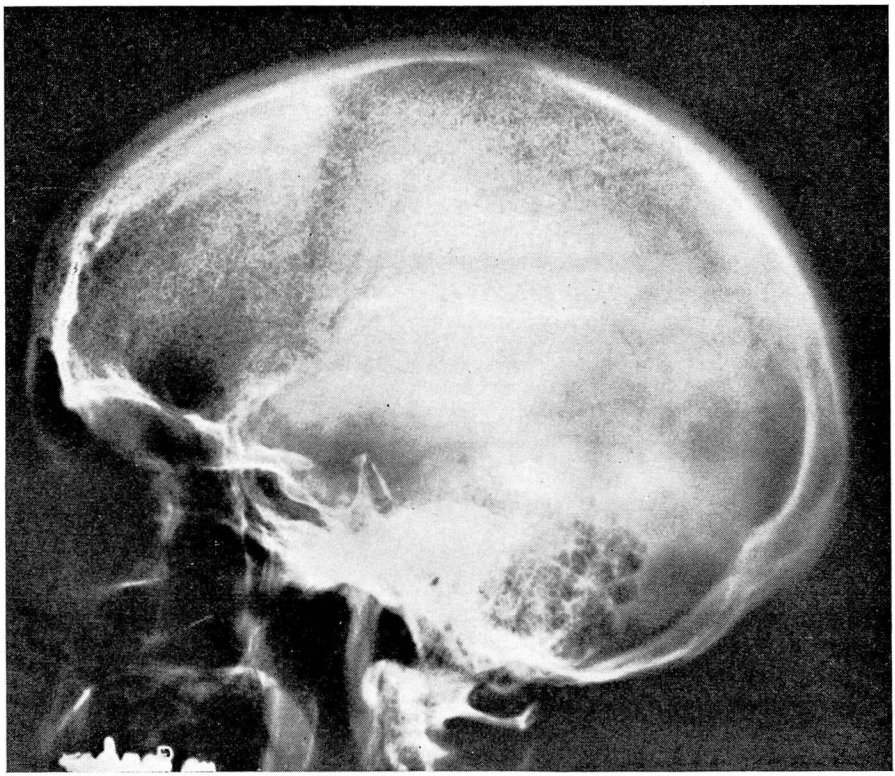

Figure 4. Case 2—Intrasellar calcification.

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The results of the more pertinent special examinations were as follows:

TABLE 2

X-ray sella—rather marked intrasellar calcification (Fig. 4)
Visual fields—normal; fundi—normal
Kepler index—11.4 to 6.9 (normal above 25)

Glucose tolerance
(mg. glucose per 100 cc. blood)

Hours	F.	1	2	3
	60	147	124	78

Insulin tolerance*
(mg. glucose per 100 cc. blood)

Minutes	F.**	20	30	60	120***	45	60
	84	40	37	37	39	64	64

* High carbohydrate diet for 3 days preceding test
** 6.8 units insulin intravenously
*** 0.68 cc. adrenalin 1:1000 intramuscularly

Plasma protein (Tiselius)
(Gm. per 100 cc. plasma)

Total plasma proteins	Alb.	α Glob.	βGlob.	γ Glob.	Fib.
5-28-43..... 5.97	3.12	0.36	1.04	1.12	0.33

Urinary androgens—none measurable
Basal metabolic rate—minus 36 per cent
Serum cholesterol—145 mg. per cent
Red blood count—3,700,000 per cu. mm.
Hemoglobin—9 Gm. per 100 cc.
The serum calcium and phosphorus were within normal limits; urinalysis was also normal. The blood Wassermann was negative.

The diagnosis was intrasellar lesion producing rather severe pituitary gland failure. Myxedema of the pituitary type was suspected, although her lack of improvement on thyroid mediciation made it very doubtful. However, she obviously had a very severe ovarian deficiency and a relatively severe adrenocortical hypofunction. Adrenal cortical deficiency was indicated by the low Kepler index, abnormal insulin tolerance, and the absence of urinary androgens. There was also a rather marked hypochromic anemia. Her improvement and progress have been excellent on the treatment outlined until recently when she experienced another acute episode or crisis similar to those which she had in 1923, May, 1941 and in November, 1942. This recent attack was as follows:

She had increasing stupor for 3 days, complained of mild headache, and vomited repeatedly. It was thought at first that she had a very slight cold, but none could be demonstrated on hospital admission. Her temperature was 103.1 F.; pulse 110; blood pressure 110 systolic and 40 diastolic; respirations were normal. Her white blood count was 6250 per cu. mm.; red count 4,300,000; and hemoglobin 71 per cent, or 11 Gm. per 100 cc. Her blood urea was 39 mg. per cent; the chlorides were somewhat below normal, being 490 mg. per cent; blood sodium was consistent with that found in Addison's disease, being 308 mg. per cent. The blood potassium was within normal limits at 17.7 mg. per cent. Urinalysis was normal. There was no evidence of an inflammatory lesion

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sufficient to cause this reaction. She was treated with adrenal extract* in doses of 10 to 20 cc. per day.

Intravenous glucose in saline was given, and she was fed with an intranasal tube supplying approximately 2100 calories per day. The 53 Gm. protein which was given daily by this method was supplemented with amino-acids by mouth in the amount of about 30 Gm. daily. The temperature steadily decreased for 3 days and on the fourth day was as low as 95.6 F. It was subnormal most of the time during the next 2 weeks.

Treatment was started in August, 1942. A diet was prescribed which contained 300 Gm. of carbohydrate per day. Extra feedings were given between meals and at bed time. Sodium chloride was given in enteric coated tablets 4 Gm. daily, and desoxycorticosterone acetate in injections of 2 mg. per day. In addition she continued with the use of desiccated thyroid 1 gr. per day and ferrous sulfate. In September, 1942 her blood pressure had risen to 130 systolic and 88 diastolic; her weight had increased about 6 pounds. The puffiness of the face suggesting myxedema did not disappear with the use of thyroid. In September, 1942 four 75 mg. desoxycorticosterone pellets, the shape of cylinders, were implanted subcutaneously. Her improvement was striking. From October to December, 1942 extra adrenal extract† was administered by mouth, one tablet 3 times daily, but produced no noticeable clinical change.

Her weight increased to 123 pounds, and the blood pressure rose to 140 systolic and 100 diastolic when the extra sodium chloride was discontinued. Her weight and blood pressure were maintained at normal. Her blood count rose to 4,620,000 red cells per cu. mm. and 11 Gm. per 100 cc. (71 per cent) of hemoglobin. Her strength was good, and she was free of symptoms and able and anxious to undertake more activity than she had for years, until her progress was interrupted by the recent crisis which has been described. Because of the extremely low assay for androgens, she was given methyl testosterone 10 mg. per day orally for several weeks, but this made little if any change in her symptoms and was discontinued. Her present treatment includes desoxycorticosterone pellet implants, thyroid and extra sodium chloride daily as before, and 4 cc. of adrenal extract†† per day.

Case 3—A 39 year old steam engineer claimed good health until one month before admission, when he noted weakness and anorexia. His own physician had diagnosed streptococcus throat infection, but no cultures had been taken. His symptoms had been characterized by slight fever and sore throat for one week. Weakness, marked fatigue, anorexia together with mild abdominal distress persisted. He had lost 11 pounds in weight during the month previous to admission and was unable to work.

The past history and systemic review revealed that puberty had been somewhat later than average; libido and potence were minimal but unchanged recently.

Examination showed a pale, slightly obese, rather stooped man who showed little evidence of normal energy. His height was 65.5 inches, weight 179 pounds. His span was 69 inches. He was somewhat bald, had very little chest and axillary hair, and the pubic hair was in feminine distribution (Fig. 5). The penis was less than average size, and the testes were small but perhaps within the range of normal. The prostate was less than average in size. The important special examinations and laboratory tests are summarized in Table 3.

* Eschatin (50 d.u./cc)—Parke Davis & Co.

† Cortalex—Upjohn Co.

†† Adrenal extract(50 d.u./cc)—Upjohn.

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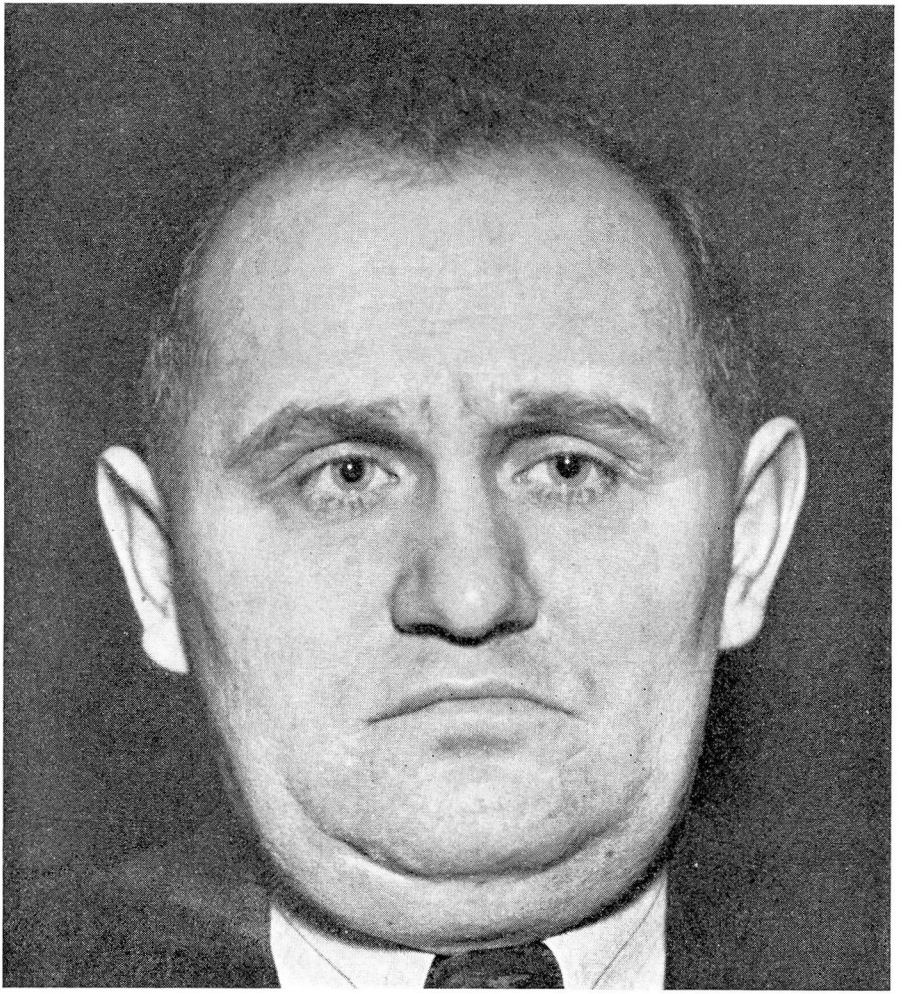

Figure 5. Case 3—The appearance is placid, the color sallow, and the eyes show slight evidence of residual ocular muscle weakness.

TABLE 3

X-ray sella—enlargement with elevation and erosion of posterior clinoids (Fig. 6)
Visual fields—bitemporal hemianopsia for form and color; fundi—temporal pallor of discs
Kepler index—1.4 (normal above 25.0)

Glucose tolerance
(mg. glucose per 100 cc. blood)

Hours.....	F.	½	1	2	3	4
	113	193	176	150	133	85

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Plasma protein (Tiselius)
(Gm. per 100 cc. plasma)

Total plasma proteins	Alb.	α Glob.	βGlob.	γ Glob.	Fib.
3–18–43..... 6.57	3.02	0.39	1.58	0.99	0.59

Gonadotrophic assay—none measurable
Urinary androgens—2.6 mg./24 hrs. Dec. 1940 (normal 7 to 15)
12 international units (capon test) (normal 18 to 80)
6.0 mg./24 hrs. April, 1943
1.5 mg. (Ketonic fraction)

Basal metabolic rate—minus 15 per cent
Red blood count—4,200,000 per cu. mm.
Hemoglobin—12.5 Gm. per 100 cc.
Serum calcium and urinalysis were normal.

Clinically, this patient was suspected of having a pituitary tumor. This was corroborated by x-ray and perimetric examinations. Complete absence of measurable gonadotropic hormone by the rat test is unusual in men. This plus the clinical evidence of

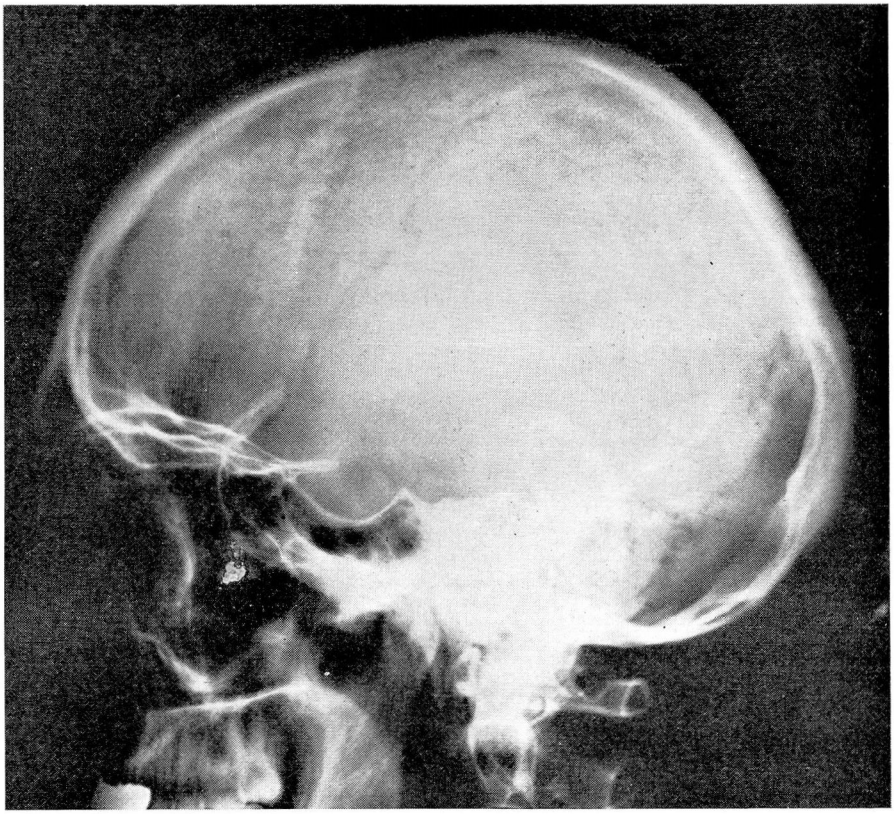

Figure 6. Case 3—Enlargement of the sella turcica with elevation and erosion of posterior clinoids.

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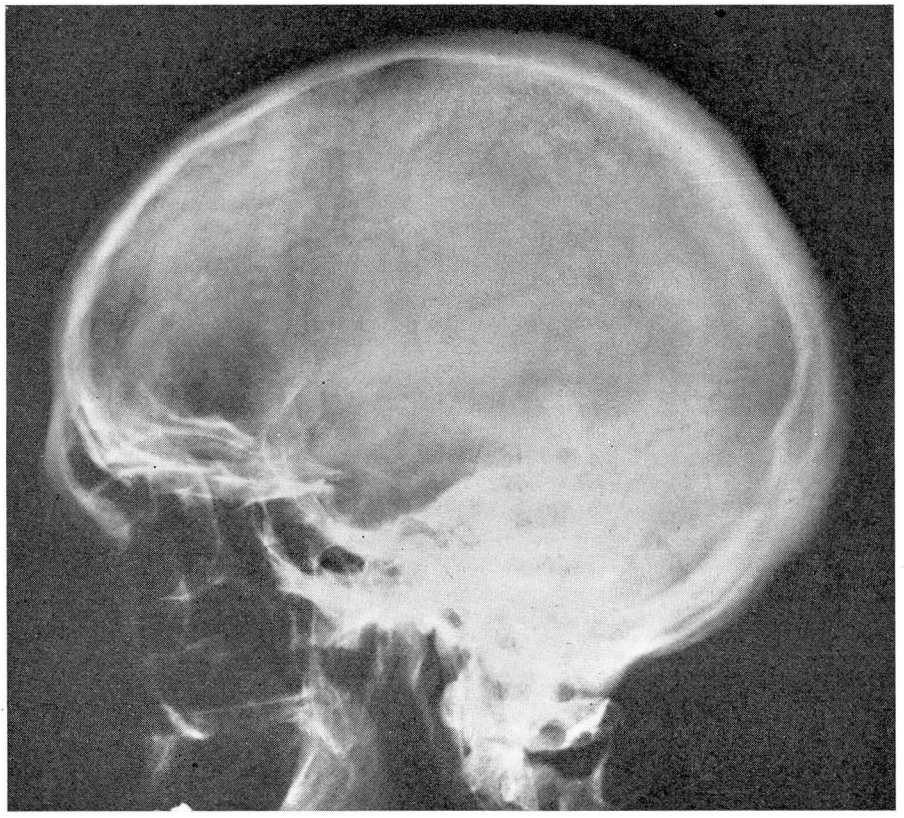

FIGURE 7. Case 4—Erosion of the sellar floor and posterior clinoids.

hypogonadism and very low assays for androgens both by bio-assay and by colorimetric test indicated testicular failure of pituitary origin. The androgen levels were lower here than are seen in gonadal failure alone and indicated the second source of androgens, namely the adrenals, were also deficient. The presence of adrenal deficiency was corroborated by the positive Kepler test. The abnormal plasma proteins simulated those seen in Addison's disease and appeared consistent with this view.

Treatment. X-ray therapy to the pituitary gland was administered daily for 2 weeks. Each treatment consisted of 200 r to three portals. In addition, he received thyroid gr. 1 daily, testosterone propionate 25 mg. 3 times weekly by injection, and 6 to 9 Gm. enteric coated salt tablets daily. He improved moderately on the above treatment. Libido increased, and strength was somewhat better. Desoxycorticosterone acetate in 5 mg. doses 3 times weekly was added, and his general vigor and strength were much improved. Later, a second course of x-ray therapy was given. The visual fields became normal. Testosterone propionate was changed to methyl testosterone 30 mg. daily by mouth. Improvement continued, and when last seen in April, 1943 he was able to carry on his regular occupation and was feeling better than he had in years.

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Case 4—A 45 year old man complained of "weakness and anemia." The present illness began 9 years before admission at which time he complained of loss of energy and endurance. For 5 months preceding admission the weakness and exhaustion were extreme. He found himself exhausted after walking 6 city blocks. The referring physician diagnosed anemia and questioned the possibility of Addison's disease.

The past history and systemic review were noncontributory.

Physical examination disclosed a well developed and well nourished, but extremely pale, individual. Height was 69 inches and weight 151 pounds. Temperature was 98.2 F.; pulse 72; and blood pressure 120 systolic and 85 diastolic. Aside from the marked pallor of the skin and mucous membranes, the physical examination was within normal limits. There were no significant pigmentary changes of the skin. The genitalia appeared normal.

The diagnosis of cryptic anemia, possibly resulting from carcinoma of the gastrointestinal tract, kidney, or from multiple myeloma was seriously considered. The pertinent laboratory studies are indicated in the following table.

TABLE 4

X-ray sella—marked erosion of floor and posterior clinoids (Fig. 7)
Visual field—left superior quadrant defect, discs hazy

Glucose tolerance
(mg. glucose per 100 cc. blood)

Hours.....	F.	½	1	2	3	4
	94	124	101	89	86	65

Insulin tolerance
(mg. glucose per 100 cc. blood)

Minutes.....	F.*	20	30	40	60	120 **	45	50
	83	48	37	37	42	61	125	125

*6.8 units insulin intravenously
**0.68 cc. adrenalin 1:1000 intramuscularly

Amino-acid tolerance*
(mg. amino N/100 cc. blood)

Minutes.....	F.	15	20	30	45	60
	6.1	9.6	8.5	6.0	5.2	5.2

* 50 cc. 10 per cent amigen intravenously

Plasma Protein (Tiselius)
(Gm. per 100 cc. plasma)

Total plasma proteins	Alb.	α Glob.	βGlob.	γ Glob.	Fib.
3–5–43..... 6.49	3.88	0.36	1.25	0.56	0.45
4–6–43..... 6.64	3.67	0.46	0.98	1.04	0.49
5–26–43..... 6.35	3.72	0.49	0.95	0.82	0.36

Urinary androgens—3 mg./24 hrs.
1.9 mg. 24 hrs. (Ketonic fraction)
Basal metabolic rate—minus 20 per cent
Red blood count 4,330,000 per cu. mm.
Hemoglobin—11.5 Gm. per 100 cc.
Serum calcium, x-ray of chest and gastrointestinal tract, and urinalysis were normal.

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The final diagnosis was pituitary neoplasm with anterior lobe failure and adrenal and gonadal deficiency. In spite of lack of clinical evidence to support the diagnosis of adrenal cortical failure, the positive Kepler test and response to treatment left little doubt that this was present. The urinary androgen was so low as to indicate both adrenal and testis failure, although this was not clinically evident.

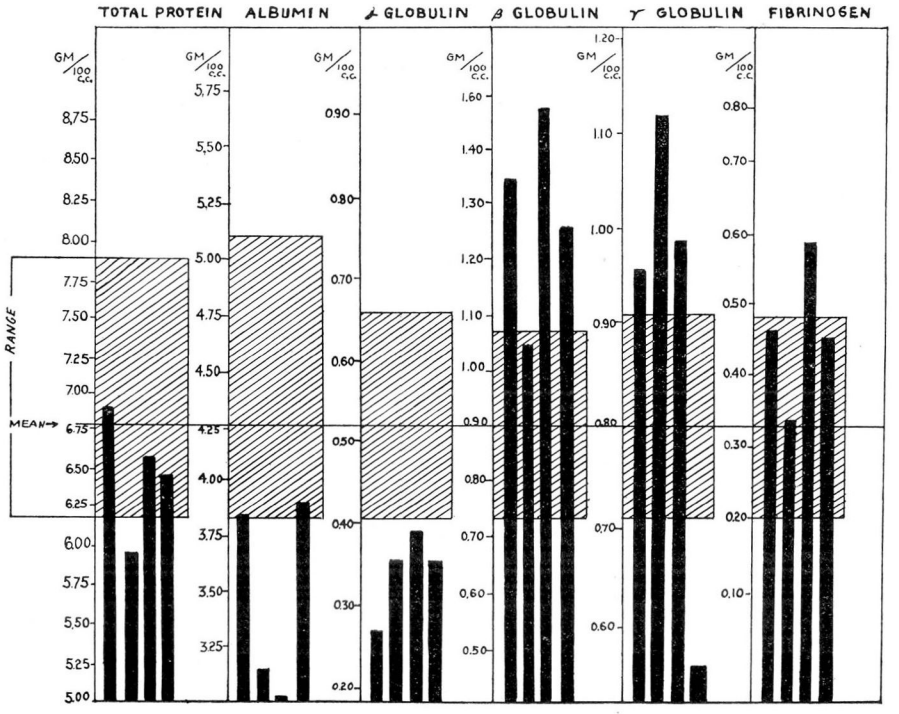
Treatment consisted of a 3 weeks' course of deep x-ray therapy to the pituitary gland, ferrous sulfate gr. 15 daily, 6 to 9 Gm. enteric coated NaCl tablets daily, desoxycorticosterone acetate 1 mg. daily, and testosterone propionate 25 mg. 3 times weekly. On April 7, 1943 300 mg. of desoxycorticosterone acetate was implanted as 75 mg. pellets. At this time the blood pressure went as high as 150 systolic and 90 diastolic, and he experienced episodes of hypoglycemia. Since then he has used only enteric coated salt tablets, ferrous sulfate, and methyl testosterone 30 mg. daily. Under this treatment improvement has been gradual, definite, and progressive. He is able to carry on his regular employment but has less than normal energy and endurance, due chiefly we believe to recurrent hypoglycemia.

COMMENT

All 4 cases had evidence of an organic pituitary lesion. In addition the outstanding symptom in each case was weakness, and in case 1

PLASMA PROTEIN FRACTIONS

Adrenal Failure Secondary to Hypopituitarism



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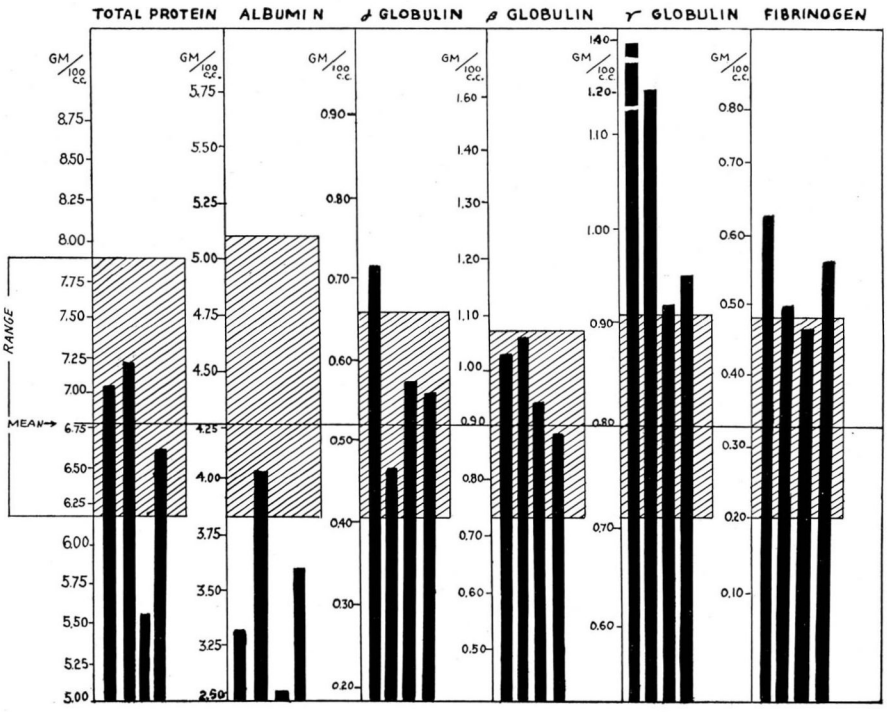
PLASMA PROTEIN FRACTIONS

Addison's Disease



weakness and faintness. In case 2 crises occurred which simulated those sometimes seen in Addison's disease.

The evidence of adrenal failure included the very low urinary androgens and the positive water excretion test in all 4 cases. The Kepler test yielded figures of 1.4 to 12.8, while the normal is 25 or over. This result was produced because of the marked delay in water excretion, no striking abnormality being shown in blood or urinary urea or chlorides in any of the cases. Serum sodium and potassium levels were normal on repeated occasions in cases 1 and 4. In case 2 the blood sodium level was 308 mg. per cent on one occasion during a crisis. Hematocrit levels were not remarkable in any of the cases.

The glucose tolerance was not abnormal in any case. In such cases at times an abnormality in this phase of metabolism can be best demonstrated by the intravenous tolerance test and by carrying the test on for a 3 or 4 hour period which may indicate any lack of gluconeogenesis. Insulin tolerance was estimated in 3 cases, and in all the blood sugar

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level failed to rise to normal fasting levels in 2 hours. In cases 1 and 2 the test was preceded, as it should be, by a high carbohydrate diet for 3 days. In case 4 this was not possible.

Response to therapy in each case supported the contention that adrenal failure did exist. In case 1 it was dramatic. In case 2 it was excellent but was not capable of preventing the recurrence of crises. In cases 3 and 4 the results were very good and controlled the symptoms well enough so that the patient could work regularly.

Plasma protein studies were made in these 4 cases using the Tiselius electorphoretic technic as modified by Longworth[16]. In 3 of the 4 cases the total protein was in the lower limits of the normal range, in case 2 it was abnormally low. The albumin and α globulin were decreased while the other globulin fractions β and γ and fibrinogen were within normal limits or increased. These results are in contrast with those obtained in Addison's disease showing adrenal insufficiency. In the latter the albumin is decreased, but the α globulin is within normal limits or slightly increased. The normal plasma protein values obtained in this laboratory are in close agreement with those reported by Longsworth[16] et al and Swensson.[17] These results will be published in detail later.

In all normals the amino N level had fallen to the fasting level, or below, 30 minutes after the beginning of the injection. In the 2 patients

Normal Amino-acid Tolerance
(mg. amino N/100 cc. blood)

Minutes.....	F.	15	20	30	45	60
	5.6	8.8	6.8	5.4	5.4	5.6

in this series in whom amino-acid tolerance tests were done, there was no significant deviation from the normal.

SUMMARY

Four cases are presented showing evidence of organic pituitary lesions. In each there are symptoms and laboratory evidence to indicate the presence of adrenal cortical deficiency.

Amino-acid tolerance and plasma protein levels (Tiselius) are similar to those observed in cases of Addison's disease, but differ somewhat in the height of the α globulin fraction.

Response to treatment with desoxycorticosterone was good in each case. Adrenal extract, testis hormone, and thyroid were used as adjuncts to therapy. The results of treatment were better than we have been able to secure with other forms of therapy in similar cases.

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