On examination.—Pale, dry skin with absent axillary and scanty pubic hair. Atrophic genitalia. Some pigmentation of parts exposed to sun.

Investigations.—Radioiodine studies (Dr. A. W. G. Goolden): Reduced extrarenal disposal rate. T=2·4 (normal 2·8—13). Water clearance test: Delayed water excretion. 17-ketosteroid excretion: 3·2 mg./twenty-four hours. Chest X-ray: Bilateral apical fibrosis.

Progress.—Much improvement with cortisone and thyroid.

Comment.—This patient presents a classical picture of post-partum pituitary necrosis. Subsequent pregnancies in such patients are rare, but usually result in recovery by producing hypertrophy of the remaining pituitary tissue (Sheehan, 1939).

Pulmonary tuberculosis, active or quiescent, is very common in these patients (Simpson, 1883). It is interesting that diagnosis in such a patient can be delayed for eighteen years. Much chronic ill-health must result from post-partum hypopituitarism, though this complication is now less frequent with modern methods of transfusion and the use of ergometrine during delivery.

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Cushing's Syndrome with Pituitary Tumour and Pigmentation.—J. R. REES, M.R.C.P. (for R. I. S. BAYLISS, F.R.C.P.).

Mr. J. L., aged 28.

First admission (November 1953).—Six months' history of increasing obesity, fullness of face and mild depression. Three weeks' history of striae on thighs and upper arms and diminished potency. Typical appearances of Cushing's syndrome. Blood pressure 160/110.

Investigations.—Blood count, serum electrolytes, glucose tolerance, X-ray of skull, chest, spine and presacral air insufflation all normal. Urinary 17-ketosteroid excretion 35 mg./day (mean of 7 estimations). Plasma 17-hydroxycorticosteroids 24 μg./100 ml. After ACTH stimulation (20 units i.v. over eight hours) urinary 17-ketosteroid excretion 74 mg./day and plasma 17-hydroxycorticosteroid level 75 μg./100 ml.

Operation 16.11.53 (Mr. Selwyn Taylor).—Bilateral adrenal hyperplasia. Whole of right adrenal removed (11·5 grams) and three-quarters of left (5·5 grams). Good response to operation with loss of cushingoid features and fall in blood pressure to 145/90. Urinary 17-ketosteroid excretion 7 mg./day and plasma 17-hydroxycorticosteroids 9 μg./100 ml. following operation, with insignificant response to ACTH stimulation. Pigmentation first noted in mouth in January 1954.

Second admission (January 1956).—Recurrence of depression with intermittent bitemporal headache and increasing pigmentation. Found to have recurrence of Cushing's syndrome with mild pigmentation. Blood pressure 180/120.

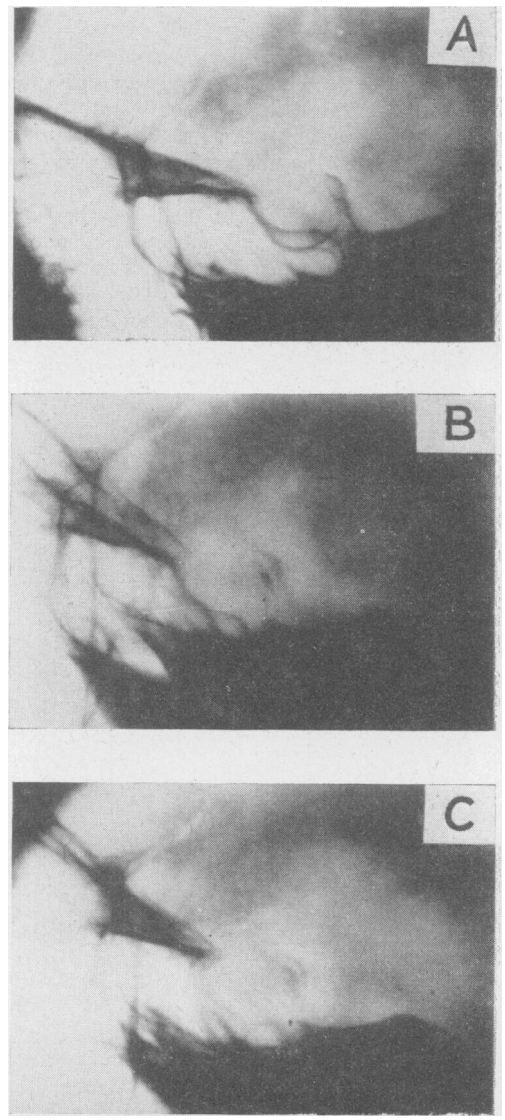

FIG. 1.—Comparative coned views of pituitary fossa. A. (November 1953), normal. B. (June 1957), shows no increase in diameter (14 mm.) but definite decalcification of the dorsum sellæ. C. (June 1958), shows expansion of the pituitary fossa (diameter 22 mm.) and definite evidence of pituitary tumour.

Investigations.—Blood count, serum electrolytes and glucose tolerance normal. Urinary 17-ketosteroid excretion 25 mg./day, urinary 17-hydroxysteroid excretion 50·1 mg./day. After fluorohydrocortisone 8 mg. daily for five days no change occurred in urinary 17-hydroxysteroid excretion but 17-ketosteroid excretion fell to 11·4 mg./day.

Operation 8.3.56 (Sir Stanford Cade).—Left adrenalectomy. The adrenal remnant was found to be hypertrophied (weight 13 grams) and histology showed diffuse hyperplasia. Good response to operation and discharged on oral cortisone 25 mg. b.d. increasing to 25 mg. t.d.s. In August 1956 his depression became severe and he was admitted to a mental hospital following a suicidal attempt.

Third admission (June 1957).—Transferred from mental hospital with complaint of weakness, impotence and mild frontal headache. Receiving supplement of cortisone 75 mg. daily and fluorohydrocortisone 0·5 mg. alternate days. Examination showed no evidence of Cushing's syndrome but deep generalized pigmentation with heavy buccal involvement was seen.

Investigations.—Urinary 17-ketosteroid excretion 7·5 mg./day. Plasma ACTH (Dr. Barbara Clayton) 38 mU./100 ml. Plasma melanophore-expanding hormone 1 i.u./7 ml. plasma. Skull X-ray considered normal, but definite decalcification of dorsum sellæ is seen although the transverse diameter of the pituitary fossa is not increased.

Fourth admission (June 1958).—History of increasing pigmentation and intermittent frontal headache for one year, with diplopia and blurring of vision for two weeks.

On examination.—Blood pressure 130/80. Not cushingoid. Deep cutaneous and buccal pigmentation. Incomplete bitemporal hemianopia. Partial left III and VI nerve paralysis.

Investigations.—Urinary 17-kestoteroid excretion 9 mg./day. Urinary 17-hydroxysteroid excretion 25·8 mg./day (mean of 4 estimations). Urinary F.S.H. excretion less than 6 mouse units/twenty-four hours. Plasma ACTH level less than 7·5 mU./100 ml. B.M.R. −13%. Skull X-ray: enlarged pituitary fossa. Air encephalogram: elevation of anterior end of third ventricle with obliteration of optic and infundibular recesses.

Operation 8.8.58 (Mr. G. Macnab).—Removal of pituitary tumour.

Histology (Dr. A. G. Pearse).—A mucoid cell adenoma (basophil adenoma) without evidence of malignancy. The tumour cells showed excellent preservation of mitochondria and considerable activity of the DPN-linked dehydrogenases. Succinic dehydrogenase activity rather low. Uneventful recovery from operation. Maintained on cortisone 75 mg. daily and thyroxine 0·2 mg. daily. There was little change in the pigmentation until November 1958, three months after removal of the pituitary tumour, when definite depigmentation became apparent.

Comment.—This patient was first reported in 1954 (Bayliss and Hunter, 1954) and shows the liability of young patients with Cushing's syndrome to relapse despite apparently adequate subtotal adrenalectomy. The striking features of this case are the development of pigmentation and the discovery of a pituitary tumour. Pigmentation was not present before partial adrenalectomy and was only slight before the second operation. It became severe after total adrenalectomy when a marked elevation of the plasma melanophore-expanding hormone was demonstrated. This resembles the case of Nelson *et al.* (1958) in whom a chromophobe pituitary tumour was found, and differs from other cases (Edmunds *et al.*, 1958) in whom pigmentation developed with the Cushing's syndrome and subsided after adrenalectomy. The extension of a basophil adenoma outside the pituitary fossa to produce pressure symptoms must be extremely unusual and suggests it had been present longer than most or that its growth had been more rapid. Nelson *et al.* (1958) suggested in their case that the pituitary tumour might have been a sequel of adrenalectomy. We have insufficient evidence to decide this point in our patient. The depigmentation following removal of the tumour suggests that the excess of melanophore-expanding hormone was produced by the basophil adenoma itself. Since pigmentation only became severe after total adrenalectomy it is probable that this operation was a powerful stimulus to pituitary activity, facilitating increased growth of the basophil adenoma, or even its development.

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