and a marked fall in circulating ketone bodies (Table 1). Caffeine may have increased adipose tissue cyclic 3',5'-AMP concentrations by inhibition of phosphodiesterase, thus stimulating lipolysis; there may also have been an increase in catecholamine release.

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## Pituitary Tumour Treated by Pituitary Implantation of Yttrium 90 During or Before Pregnancy [Two Cases]

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### Case 1

A woman aged 37 presented with 17 years secondary amenorrhœa but no other overt signs or symptoms of hypopituitarism. She had been told her prospects for fertility were hopeless after investigation in fertility clinics, but attended Hammersmith Hospital (Professor J C McClure Browne) after newspaper publicity of gonadotrophin therapy. Left-sided headaches, with lacrimation of the left eye, had been present for 14 years. X-rays of the pituitary fossa showed obvious enlargement with a double contour, and lateral tomography confirmed substantial extension of a pituitary tumour downwards into the left side of the sphenoid sinus.

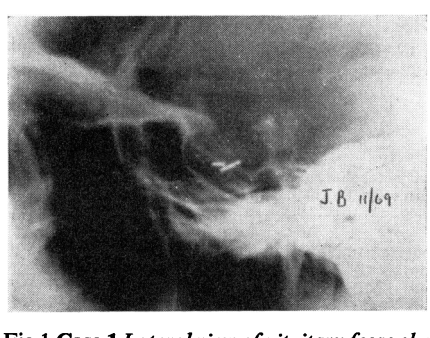


Fig 1 **Case 1** *Lateral view of pituitary fossa shortly after implantation of* $^{90}Y$. *Note the enlargement, and second contour of floor within sphenoid sinus*

*Investigations:* (1) Normal urinary gonadotrophin excretion (bioassay); (2) normal pituitary-adrenal function (metyrapone and lysine-vasopressin tests) and normal growth hormone response (25 ng/ml) to insulin hypoglycæmia (0·1 u/kg); (3) normal ECG and cholesterol but low-borderline $^{131}I$ test; (4) normal visual fields and acuity.

*Treatment:* Pituitary implantation of $^{90}Y$ (Fig 1), using a low radiation dose (20,000 rads calculated to diaphragma sellæ from two seeds), with the object of relieving local effects of the tumour and restoring menstruation. This was successful in that the headaches disappeared, and regular menses returned 14 months later. There was no certain evidence of ovulation, however, and clomiphene was given. Ovulation resulted from the second clomiphene course, and pregnancy from the third (100 mg/day for 5 days).

*The pregnancy* (triplets) was uncomplicated except for: (1) minor recrudescence of headache at 20 weeks, which subsided after delivery; (2) serum-free thyroxine factor (Goolden *et al.* 1967) became subnormal at 26 weeks (although the PBI remained in the expected range for pregnancy), and so thyroxine was started. Urinary free cortisol at 27 weeks was 96 μg/day, a normal value for singleton pregnancy. Spontaneous labour occurred at 35 weeks and delivery was by Cæsarean section under steroid cover. Lactation was suppressed. One triplet had a small meningomyelocele, but has progressed satisfactorily following surgical closure.

*Present status:* Her original headaches have not recurred; there are no visual complications and no replacement therapy is being given. PBI is 4·4 μg/100 ml. Amenorrhœa, however, persists (aged 42).

### Case 2

A woman aged 24 presented with infertility and secondary amenorrhœa for one year. There were no overt signs of pituitary disease, except for some galactorrhœa on breast expression.

*Investigations:* (1) Low urinary gonadotrophins (bioassay); (2) normal cortisol (29 μg/100 ml) and growth hormone (>40 ng/ml) responses to insulin hypoglycæmia; (3) thyroid function normal; (4) X-ray of pituitary fossa showed double floor appearance (Fig 2), confirmed by tomography, but the fossa was of normal size and not definitely abnormal.

*Treatment* with Pergonal resulted in a singleton pregnancy. The successful course was 4 ampoules

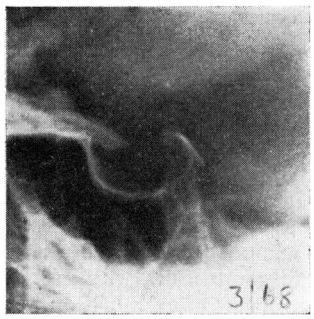

Fig 2 **Case 2** *Lateral view of pituitary fossa. Minor double floor appearance only*

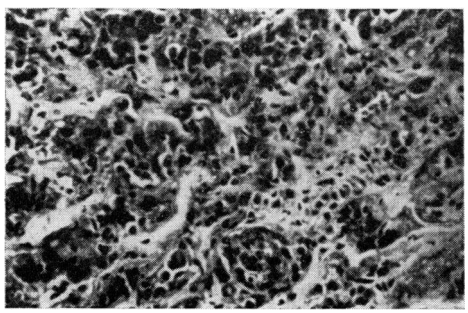

Fig 3 **Case 2** *Pituitary biopsy taken at implant. Tripas stain.* × *200*

on Days 1, 3 and 5, followed by 5,000 units of HCG on Day 8 and 2,000 on Day 10. During her last 3 courses of Pergonal she developed left-sided headaches, with lacrimation of the left eye.

*The pregnancy* was complicated by similar but more severe headaches during the first 8 weeks. X-ray of pituitary fossa still showed no enlargement but a minor change of contour had occurred (slight 'undercutting' of tuberculum). At 14 weeks she complained of blurring of vision in the left eye, and over the next two weeks a bitemporal visual field defect rapidly developed. This was treated by a high dose pituitary implant of $^{90}Y$ (150,000 rads calculated to diaphragma sellæ from two seeds). Dosimetry measurements showed negligible radiation dose to fœtus either from screening X-rays during the procedure or Bremsstrahlung radiation. Pituitary biopsy showed an active adenoma, with strongly acidophilic granularity of cytoplasm and much nuclear pleomorphism (Fig 3) (Dr Paul Lewis). The visual field defect regressed rapidly after the implant (Fig 4). Precautionary steroid replacement (prednisone 5 mg/day) was continued throughout the remainder of the pregnancy, which was later complicated by severe pre-eclamptic toxæmia and terminated by Cæsarean section at 33 weeks. Serum-free thyroxine factor remained normal throughout.

*Present status:* Mother and baby have done well and the mother has produced up to 900 ml milk daily. Milk production is now declining (6 months *post partum*). No replacement hormones are being given; cortisol and growth hormone responses to insulin hypoglycæmia are still normal; PBI 6·3 μg/100 ml; visual fields and acuity remain normal; blood pressure 130/80; no proteinuria.

*Comment*

Both cases illustrate the value of pituitary radiography in women with amenorrhœa, even in the absence of overt clinical signs of pituitary disease. The second case points to the desirability of maintaining a suspicion of pituitary tumour as the primary diagnosis in an amenorrhœic woman even when radiological abnormalities of the pituitary fossa are slight.

This second case shows, too, that a pituitary tumour within a fossa of normal size may rapidly produce an upward extension large enough to cause optic nerve compression of sudden onset in pregnancy. Presumably in this second case the tumour expanded so rapidly that there was no time for expansion of the bony confines of the fossa to develop. We are aware of two other cases of pituitary tumours which enlarged rapidly in pregnancy, with potentially serious results. Some enlargement of the normal pituitary is thought to be associated with pregnancy (Erdheim & Stumme 1909); the mechanism of this change is not known with any certainty.

The first patient may have been protected from this problem of tumour expansion by implantation of $^{90}Y$ before embarking on pregnancy. Pituitary implantation of $^{90}Y$ may be an effective way of dealing with tumour expansion during pregnancy, and appears safe, both from the radia-

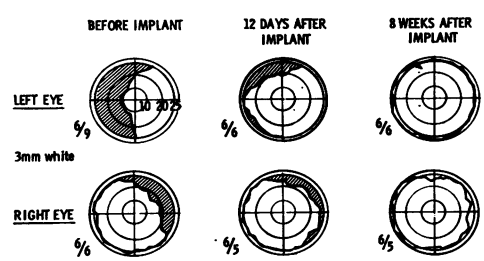


Fig 4 **Case 2** *Visual field chart showing rapid improvement after pituitary implant*

tion and the obstetric viewpoints; but it would appear preferable that a low-dose pituitary implant should precede fertility drug treatment in the management of infertility when a pituitary tumour is thought to be present.

Hypopituitarism itself in pregnancy is only likely to be important if it results in thyroxine or cortisol deficiency. Measurement of total concentrations of thyroxine and cortisol in blood are vitiated in pregnancy by increases in the concentrations of their specific plasma binding proteins. The problem of assessment of these functions during pregnancy can be overcome by tests reflecting non-protein-bound hormone levels, e.g. free thyroxine factor (Goolden *et al.* 1967) and urinary free cortisol (Burke & Roulet 1970) estimations, as illustrated in our cases.

*Acknowledgment:* We are grateful to Professor J C McClure Browne for permission to report these cases.

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## Multi-endocrine Autoimmune Disorder in Mother and Son

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### Case 1

Mrs R T, aged 40. Housewife

*History:* When aged 7 years, developed psoriasis affecting body and knees, which is still active on and off. At age 11 hair began to go grey; this progressed to alopecia which is now almost total. Menarche occurred normally at 13 and periods are still regular. Since age 14 has had diabetes mellitus, now controlled with 52 units insulin daily. At about that time she began to have vitiligo and from 18 onwards has had iron deficiency anæmia on and off. During first and only pregnancy at age 24 had severe hyperemesis gravidarum lasting 8 months and also suffered a nervous breakdown with depression and confusion necessitating admission to mental hospital for six weeks. Three months after delivery she developed a polyarthritis affecting mainly small joints in hands and feet, which lasted for nine months and has not recurred since. When aged 32 she developed signs of primary myxoedema and also cataract of the right eye.

In 1966 a serum vitamin $B_{12}$ level of 59 ng/ml was noted but apparently no treatment was given. Further investigations were carried out in 1970 when she was in good health with insulin and thyroxine replacement. On examination her thyroid gland was impalpable and she had no evidence of glossitis. There was extensive vitiligo of the body alternating with patches of excessive pigmentation and diffuse small psoriatic lesions. Blood pressure 130/80, with no symptoms of adrenal deficiency. The patient was adopted at birth and no information is available about her family history.

*Investigations:* Hæmatological: Hb 9·7 g/100 ml; RBC 3·4 million; MCV 84 $\mu m^3$; WBC 4,400/$m^3$; PN 66% with moderate right shift. Blood film showed hypochromasia, anisocytosis and poikilocytosis. Serum iron 50 µg/100 ml (normal 80–180) with an iron-binding capacity of 500 µg/100 ml. Serum folate 9·4 ng/ml. Vitamin $B_{12}$ 69 ng/ml. $B_{12}$ absorption, whole body count at 7 days 14·1% (normal 30–50). With added hog intrinsic factor the 7 days' absorption value increased to 23·3%. Gastric juice after stimulation with pentagastrin: volume 12 ml, pH 8·0; intrinsic factor could not be detected and gastric juice contained 4 units intrinsic factor antibody per ml, IgA class.

Endocrine: Serum thyroxine 117 ng/ml (on replacement); urine ketosteroid excretion 6 mg/24 h (normal 15–25); serum calcium 9·9 mg/100 ml; phosphates 2·9 mg/100 ml; alkaline phosphatase 8 K-A units.

Immunological: Serum immunoglobulins: IgG 1,720 mg/100 ml, IgA 56%, IgM 320% of normal serum pool. Serum autoantibodies: antithyroglobulin titre tanned red cells 1:640; antimicrosomal CFT 1:64; colloid and cytoplasmic immunofluorescence strongly positive. Gastric parietal cell fluorescence positive to 1:10 (low titre), intrinsic factor antibodies 150 u/ml (moderate titre). Adrenal cytoplasmic fluorescence positive on several occasions; the antibody did not cross-react with human ovary or rat testis. Antibodies to striated and smooth muscle were not detected.

*Conclusion:* In addition to all the conditions already diagnosed, this patient has latent pernicious anæmia and a possible partial atrophy of the adrenal glands which might be revealed with more detailed adrenal function tests.