Discussion

"The treatment of spontaneous pneumothorax is a rather unhappy story. Many methods have been and are still being tried, but none is entirely satisfactory" (*British Medical Journal*, 1965). There is general agreement that a tension pneumothorax must be treated as an emergency by inserting a wide-bore needle or intercostal catheter (Davies, 1969), which can be connected subsequently to an underwater seal or to a valve (Knight, 1967). There is, however, considerable controversy about the treatment of cases not under tension. Some believe that, in the absence of respiratory distress or underlying lung disease, the patient can be followed up as an outpatient while continuing at work in most cases (Stradling and Poole, 1966; Davies, 1969). Stradling and Poole (1966) successfully managed 80% of their patients in this way. Some believe that an intercostal catheter should be inserted in those with a large pneumothorax (Horne, 1966; *British Medical Journal*, 1968; Lennox, 1970), and others that catheter drainage or some other surgical procedure should be carried out in almost all cases (Ruckley and McCormack, 1966; Thompson and Bailey, 1966).

The principal reason put forward for inserting an intercostal catheter in those with a large pneumothorax is to shorten the course of treatment (Lennox, 1970). The average length of hospital stay in several large series treated by intercostal catheter varied from 5 to 30 days, with a mean of 13 days (Klassen and Meckstroth, 1962; Smith and Rothwell, 1962; Killen and Jackson, 1963; Ransdell and McPherson, 1963; Withers *et al.*, 1964; Lynn, 1965; Timmis *et al.*, 1965; Thompson and Bailey, 1966). There was an average failure rate of 19%. In one series of 88 patients nine died (Ransdell and McPherson, 1963).

In the present series oxygen therapy resulted in a fourfold increase in the mean rate of absorption. Further study would be necessary to check whether a similar increase in absorption could be achieved with a lower flow rate of oxygen. The observation that the effect of oxygen was less pronounced in patients with a small pneumothorax may be due to the fact that in these patients the two layers of the pleura tended to come into contact in parts of the pleural space, so that the surface area available for absorption was reduced.

The calculated time for full re-expansion with daily oxygen therapy ranged from three to eight days, with a mean of five days. The patient can presumably be discharged from hospital either at this stage or else before full re-expansion has been obtained. This method of treatment, therefore, compares favourably with the use of an intercostal catheter as a method of shortening hospital stay. There were no failures in the present study, and no serious complications. Though high concentration oxygen at atmospheric pressure can have a toxic effect on the lungs, this seems to be limited to patients receiving it continuously for 24 hours daily, and the effects of intermittent exposure are not cumulative (Pratt, 1965). Administration was intermittent in the present study, and none of the patients developed radiological changes suggestive of oxygen toxicity. The inspired oxygen concentration was not measured, but it is very unlikely to have been as high as 100%, though it was probably higher than the 50 to 60% obtained with the Polymask using a lower flow rate of eight litres per minute (Leigh, 1970).

It is clearly important that treatment with high concentration oxygen should be avoided in patients with respiratory failure and in those with a tension pneumothorax. This method of treatment should probably be limited to the common primary type of spontaneous pneumothorax occurring in the absence of any generalized lung disease.

My thanks are due to the consultant staff of Guy's Hospital for allowing me to study patients admitted under their care.

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MEDICAL MEMORANDA

Emergency Hypophysectomy in Pregnancy After Induction of Ovulation

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British Medical Journal, 1971, 4, 88–90

Since the introduction of human gonadotrophin therapy by Gemzell *et al.* (1958) it has been possible to induce ovulation in patients suffering from hypogonadotrophic states, including those caused by pituitary tumours. This paper reports the sudden increase in size of an unsuspected pituitary tumour during pregnancy after the successful induction of ovulation with human menopausal gonadotrophin (Pergonal).

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Case History

The patient was first seen in April 1967 at the age of 30 years with a history of secondary amenorrhoea for 14 months. The menarche was at 15 years and menstruation was regular until she started nursing at the age of 19. Menstruation then became irregular and there were periods of amenorrhoea lasting up to 12 months. Full physical examination showed nothing abnormal apart from a minor degree of hypo-oestrogenization of the vaginal wall.

Investigations.—Haemoglobin 13·6 g/100 ml; serum cholesterol 302 mg/100 ml; radioactive triiodothyronine red cell uptake 13·8% (normal 11·5 to 19·5%); protein bound iodine 6·4 μg/100 ml; radioactive iodine (^{131}I) neck uptake at 24 hours 13·8% (within the

normal range for this hospital). Total urinary gonadotrophins 0-0·8 mg/24 hours; 17-oxosteroids 12·4 mg/24 hours; total 17-oxogenic steroids 8·8 mg/24 hours. Pregnanetriol 0·22 mg/24 hours; oestrone 6 μg/24 hours; oestriol 17·0 μg/24 hours; oestradiol 3·0 μg/24 hours. Buccal smear was chromatin positive. Vaginal smears taken at weekly intervals over a period of five weeks showed a pronounced hypo-oestrogenic pattern. *X*-ray picture of the skull was reported as normal, but on reviewing the film retrospectively a double floor to the fossa was recognized, though the actual dimensions of the sella were within normal limits (Fig. 1).

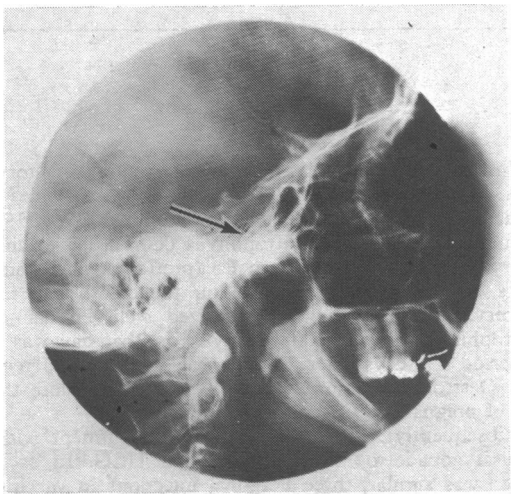

FIG. 1—*X*-ray picture of skull in 1967 showing double floor to pituitary fossa (arrowed).

The patient was admitted to hospital for examination under anaesthesia and for diagnostic curettage. The uterus was small and histological examination of the curettings showed inactive and slightly cystic endometrial glands. The investigations showed low gonadotrophin production and hypo-oestrogenization of the vagina but normal function of the thyroid and adrenal glands. It was thought that the most probable diagnosis was that of secondary amenorrhoea due to corticohypothalamic dysfunction.

She married in August 1967 and 18 months later returned for reinvestigation complaining of infertility. Only two menstrual periods had occurred since April 1967. All the tests except *x*-ray examination of the skull were repeated; the results were unchanged apart from the vaginal smear series, which showed some evidence of cyclical activity with at least a moderate degree of oestrogenic response.

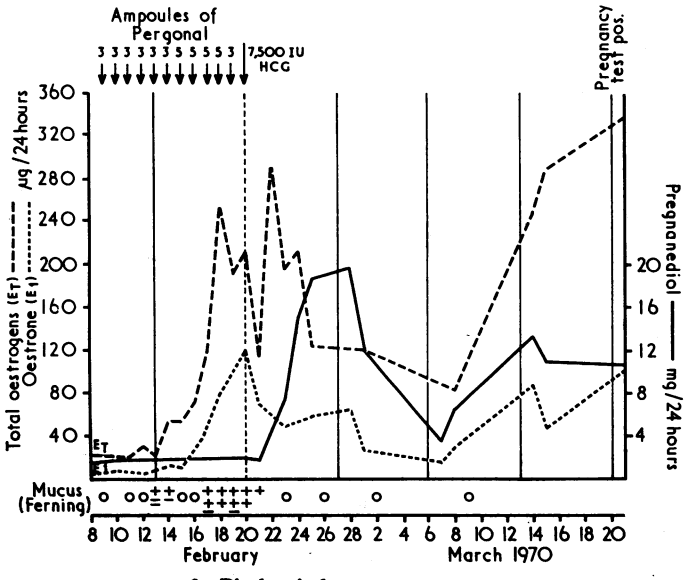

FIG. 2—Biochemical response to treatment.

The patient was treated with two courses of clomiphene citrate (150 mg daily for five days). The vaginal smear series during therapy showed a change from poor to moderate oestrogenic response on both occasions, but menstruation did not occur. On 9 February 1970 Pergonal therapy was started (3 ampoules daily containing a total of 225 IU of FSH). After six days there was no clinical or biochemical response, so the dose was increased to 5 ampoules (375 IU of FSH) daily for a further four days, at which time there was evidence of ferning of the cervical mucus and a change in the vaginal cytology from pronounced hypo-oestrogenic to good oestrogenic response. There was also a satisfactory increase of urinary oestrogens (Fig. 2). Human chorionic gonadotrophin 7,500 units was given on day 12. This was followed by a rise in basal body temperature to 37·0°C. On 23 March pregnancy was confirmed with a positive immunological test. In April frontal headaches occurred. These were not very severe and were similar to headaches which she had suffered from for some years and which had been labelled "migraine." The headaches persisted through the summer, and it was only in September, when she became aware of visual disturbance, that she sought advice. On examination she was found to have bitemporal hemianopia, which was complete on the left side and partial on the right. Both optic discs looked pale. *X*-ray film of the pituitary fossa showed considerable change since 1967, with gross erosion of the posterior clinoids and pronounced thinning of the cortical bone of the dorsum and the floor (Fig. 3).

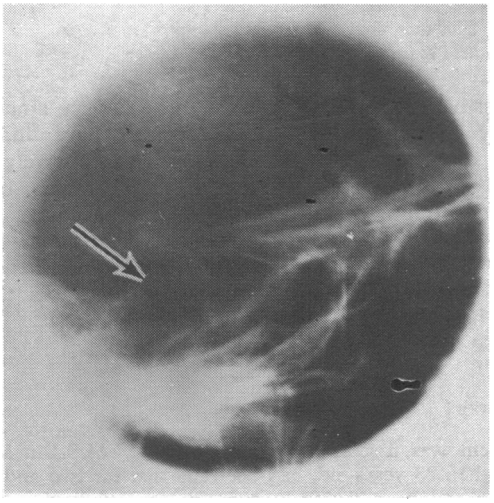

FIG. 3—*X*-ray picture of skull in 1970 showing gross erosion of the posterior clinoids (arrowed).

There was also undercutting of the anterior clinoids. A right carotid angiogram gave further evidence of a large pituitary tumour extending into the right parasellar area.

On 14 October at 35 weeks' gestation, a right frontal osteoplastic craniotomy was performed by Mr. C. A. Gleadhill and a large pituitary tumour was removed. Histologically the tumour was a chromophobe adenoma.

The patient made an excellent recovery on cortisone and thyroxine replacement, and her visual fields returned to normal in both eyes. She went into spontaneous labour on 5 November (at 38 weeks) and was delivered by low forceps of a healthy male infant (2,400 g).

Comment

The sudden increase in size of a pituitary tumour during pregnancy after the induction of ovulation by human gonadotrophin has not been reported previously. Hypothalamic dysfunction is a diagnosis of exclusion, as a small pituitary tumour causing selective gonadotrophic deficiency may remain undetected for many years (Jefferson, 1957). Careful radiography of the pituitary fossa, possibly combined with tomography of the sella, must therefore be carried out at regular intervals in these patients to endeavour to exclude pituitary tumours.

The case reported here was not unusual in being first investigated three years before treatment for infertility was instituted. Many patients who attend initially with secondary amenorrhoea only later request treatment for infertility. It is suggested that if a diagnosis of hypothalamic dysfunction has been made originally repeat *x*-ray films of the pituitary fossa should be taken before gonadotrophic ovarian stimulation is undertaken. Even if there is no evidence of pituitary fossa enlargement at this stage, headache or any other symptom suggestive of an expanding intracranial lesion during pregnancy merits urgent investigation in these patients.

We wish to thank Dr. D. A. D. Montgomery and Dr. J. M. G. Harley for their advice in the preparation of this case report, and Professor J. H. M. Pinkerton for referring the patient and for his criticism of the paper.

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Visual Disturbance in Pregnancy after Induction of Ovulation

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British Medical Journal, 1971, 4, 90–91

It is possible that some women with secondary amenorrhoea, especially if associated with galactorrhoea, have undetectable pituitary or parapituitary lesions. Now that relatively effective methods for inducing ovulation in such women, by means of gonadotrophin therapy, are available account must be taken of the risk that pregnancy may produce adverse changes in these lesions leading to ocular manifestations. We report such an occurrence, though the precise nature of the lesion remains obscure.

Case Report

The patient was first seen by one of us (G.I.M.S.) in May 1969. She was then 23 years old, had been married for two and a quarter years, and had been trying to conceive for one and a half years. She had no siblings and her mother was said to have been hypothyroid since the age of 35. She herself had no relevant medical history apart from that related to menstrual function. Her menarche had occurred at 12 years and she had had regular 28-day menstrual cycles until she was 16. The cycle then decreased to 21 days but reverted to 28 days again by the age of 18. After her marriage the cycle became irregular, with increasing oligomenorrhoea. In 1967 she used an oral contraceptive for three cycles and had regular withdrawal bleedings, the last in August of that year. There had since been no further period. From the time the oligomenorrhoea began some breast secretion had been noted. Various investigations had been made, including chest *x*-ray examination, blood tests, cervical smear, and seminal analysis, and were said to be normal. Examination under anaesthesia had shown a small uterus (cavity 2½ in.; 6·4 cm) and patent tubes but no curettings were obtained. Two five-day courses of treatment with clomiphene, one at 100 mg daily and the other at 200 mg daily, had failed to produce any menstrual bleeding.

Physical examination showed no special features. Galactorrhoea was not present. There was normal female development, no hirsutism, little cervical mucus, a small uterus, and a well-oestrogenized vaginal smear. A skull *x*-ray film showed no abnormalities of the sella turcica. Adequacy of the husband's seminal fluid was confirmed (volumes 3·0 and 4·4 ml; sperm counts 67 and 65 million/ml, with 13% abnormal forms and satisfactory sperm activity).

A gonadotrophin stimulation test (Swyer *et al.*, 1968, 1969) with pregnant mares' serum gonadotrophin 18,000 IU led to an increase in urinary oestrone excretion from 1·5 (pretreatment) to only 4 μg/24 hours on the seventh day, and on the eighth day there was scanty cervical mucus, which crystallized well. Human chorionic gonadotrophin (HCG) 10,000 IU given on that day was followed by a period 11 days later. The basal temperature record was atypical. Oestrone excretion reached a peak of no more than 9 μg and that of pregnanediol 2·2 mg/24 hours.

She subsequently received six courses of treatment with human menopausal gonadotrophin (Pergonal) and HCG. In each course the design was similar, three Pergonal injections in varying dosage being given on alternate days, followed by HCG 10,000 IU on the eighth day, calling the day of the first Pergonal injection day 1. Evidence of a luteal response (and therefore possibly ovulation) was obtained for the second and third of the first five courses, the details of which are omitted for the sake of brevity. The sixth course, which led to conception, was started on 1 June 1970 and is illustrated in Fig. 1. In this course three injections of 900 IU of Pergonal were given.

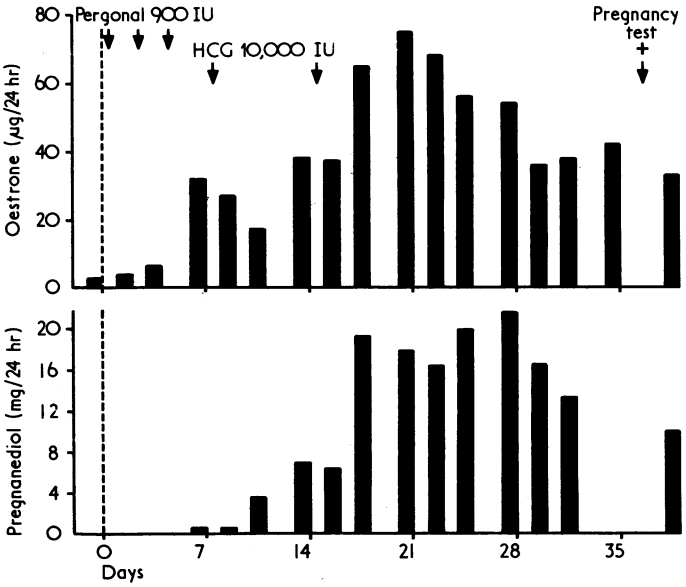

FIG. 1—Urinary oestrone and pregnanediol excretion in the conception course of Pergonal treatment.

The patient was then transferred to the antenatal clinic. The pregnancy progressed normally but she developed a urinary infection (*Escherichia coli*) at the end of November and was treated with nitrofurantoin 100 mg four times a day for three days and then 50 mg four times a day for seven days. At the end of December she noticed clouding of vision in the left eye "like a net curtain"—and on 15 January 1971 the vision in the left eye was

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