

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.

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## Visual Disturbance in Pregnancy after Induction of Ovulation

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It is possible that some women with secondary amenorrhoea, especially if associated with galactorrhoea, have undetectable pituitary or parhypophysial 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.

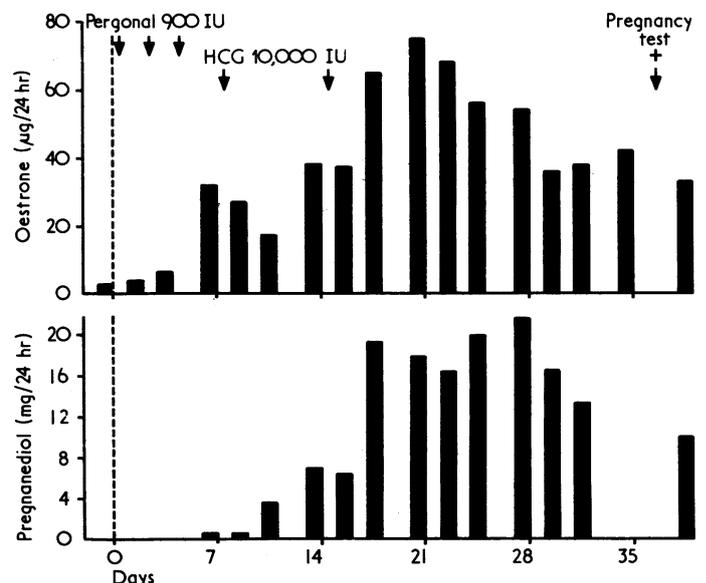


FIG. 1—Urinary oestrone and pregnanediol excretion in the conception course of Pergonal treatment.

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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found to be 6/18, with bilateral pallor of the discs. The visual field was normal in the right eye but in the left eye there was a defect of the inferior outer quadrant. Skull x-ray film (Fig. 2) now showed erosion of the posterior clinoid processes, with loss of the lamina dura of the dorsum sellae. The sella itself was not enlarged and there was no parasellar calcification. A suprasellar tumour compressing the optic chiasm was suspected. The defect in the left visual field increased and she became almost blind in the left eye. On 20 February labour was induced and a normal live female

infant weighing 5 lb 5 oz (2,400 g) was delivered by forceps. Lactation ceased spontaneously. On the day after delivery her eyesight gradually returned and was virtually normal by the time she was transferred on 2 March to the care of B.J.H. for further investigation.

By this time the visual fields were full to confrontation; the discs were pale, the left more than the right; and there was fine nystagmus in both eyes on deviation to the right. All the other findings on general and neurological examination and the cerebrospinal fluid were normal. A brain scan and carotid arteriogram were normal, and so probably was a lumbar air encephalogram though the recesses of the third ventricle were not completely visualized. The findings gave no indication of a parapituitary lesion.

### Comment

Though the combination of amenorrhoea and galactorrhoea arouses the suspicion of a pituitary or parapituitary lesion objective evidence of these lesions is often lacking or sometimes emerges only after long-term follow-up. Spontaneous ovulation rarely occurs in such patients, and so the hazards which pregnancy may produce have received little recognition. In the present case galactorrhoea was stated by the patient to have been present before she was seen by us but was not actually observed either before and during treatment or during pregnancy. Moreover, the rapid return of vision after delivery scarcely seemed consonant with a space-occupying lesion, especially as the angiogram and encephalogram showed nothing abnormal. The erosion of the posterior clinoids remains unexplained. The possibility of a demyelinating disease, such as multiple sclerosis, to account for the symptoms was considered but thought to be unlikely by Dr. G. Stern, who examined her on 9 March 1971. He agreed that there was pallor of the discs, more so on the left than on the right, and found a residual haemorrhage at 6 o'clock on the right. There was no residual scotoma and no nystagmus. He raised the question of whether a vascular lesion had been responsible for the visual symptoms before the pregnancy ended.

At follow-up examination on 3 June the patient was well, the visual acuity was 6/4 right 6/6 left, the visual fields on the Bjerrum screen were normal, and the blind spots were not enlarged. On the other hand, the baby had recently been admitted to another hospital with viral meningitis. It seems doubtful if this can be other than coincidental.

We thank Mr. J. M. Holmes, who administered the antenatal care, and Mr. J. H. Kelsey, who gave the ophthalmological examination.

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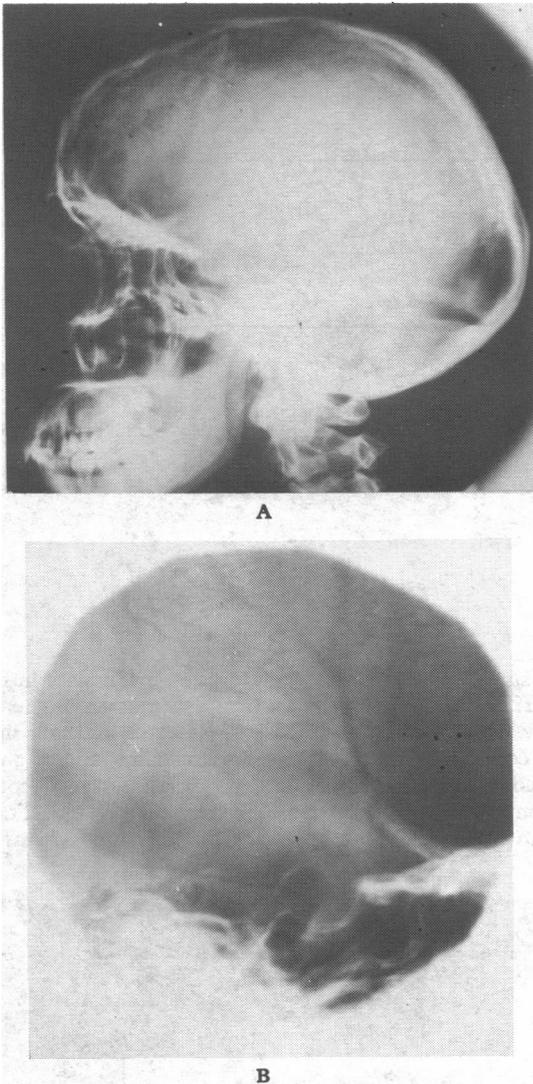


FIG. 2—A, Skull x-ray picture showing erosion of posterior clinoid processes with loss of lamina dura of dorsum sellae (21 January 1971). B, Coned film of sella turcica (3 June 1971).