

10% of maternal deaths, and the reported mortality is as high as 80% in some series.<sup>2</sup> Amniotic fluid embolism may occur after diagnostic amniocentesis, but this is uncommon. It is more likely to occur after hypertonic saline or dextrose is injected into the amniotic fluid.<sup>1</sup> In our patient exchange transfusion allowed rapid removal of red cell debris and haemoglobin from the circulation and provided red cells and clotting factors in fresh plasma.

ABO incompatibility between fetal and maternal blood groups appears to have contributed to the severity of our patient's condition; this was similar to the reaction that would be expected after transfusion of ABO incompatible blood. The complete disappearance of a high titre of anti-B immediately after the suspected embolism gives indirect evidence that the rapid deterioration was due to amniotic fluid embolism. Amniotic fluid is known to contain fetal blood group substances,<sup>4</sup> and the findings above may be relevant to experiments in which amniotic fluid was injected into animals in an attempt to define the pathogenesis.<sup>5</sup>

We believe that exchange transfusion helped to change the course of events and contributed to a successful outcome in this patient.

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## Danazol and benign intracranial hypertension

Danazol is used in the treatment of endometriosis, menorrhagia, benign breast disease, and hereditary angio-oedema.<sup>1</sup> We report three cases of benign intracranial hypertension in patients treated with danazol.

### Case reports

**Case 1**—A healthy 23 year old woman was prescribed danazol 600 mg daily for endometriosis. Twelve weeks later she presented with a month's history of severe frontal headache and diplopia on lateral gaze. She had taken no other medication. She weighed 67 kg, and her blood pressure was 132/72 mm Hg. She had bilateral haemorrhagic papilloedema with constricted visual fields and enlarged blind spots. Visual acuities were 6/9 bilaterally. No other abnormal signs were detected. The results of routine haematological and biochemical investigations, skull radiography, electroencephalography, and computed brain tomography were normal. The lumbar cerebrospinal fluid pressure was 300 mm H<sub>2</sub>O, microscopy normal, protein concentration 0.1 g/l, glucose 3 mmol/l.

Danazol was discontinued, but 10 days after admission she developed a left abducens nerve palsy. This resolved within two days, and papilloedema had resolved three weeks later. She remained well three months later.

**Case 2**—A 36 year old woman received danazol 400 mg daily in May 1984 for irregular periods and menorrhagia. She became amenorrhoeic and gained weight. In January 1985 she presented with a fortnight's history of bifrontal headache. She had stopped taking danazol a few days previously because of the headache. Her blood pressure was 130/70 mm Hg and she weighed 82 kg. The only abnormal physical finding was bilateral papilloedema. The results of baseline investigations, including electroencephalography and computed brain tomography, were normal. The cerebrospinal fluid findings were: pressure >300 mm H<sub>2</sub>O, protein 0.38 g/l, glucose 3.5 mmol/l, microscopy normal. Full recovery was attained with weight reduction and diuretic treatment. She remained well two years later.

**Case 3**—A 24 year old woman was prescribed danazol 400 mg daily for endometriosis. Six months later she was admitted with a two month history of headache and diplopia. She had discontinued danazol five weeks before admission because of the headache. She weighed 62 kg and her blood pressure was 120/80 mm Hg. There was bilateral papilloedema with constricted

visual fields. The results of examination were otherwise normal, as were those of routine investigations including electroencephalography and computed brain tomography. The cerebrospinal fluid was not examined. Benign intracranial hypertension was diagnosed and treatment started with chlorthalidone. Her papilloedema resolved within six weeks. Inadvertent treatment with danazol two years later was associated with headache and diplopia, which cleared when she stopped taking the drug. She remained well eight years later.

### Comment

Benign intracranial hypertension is a diagnosis of exclusion, typically occurring in obese young women, often with recent considerable weight gain. Although it is not life threatening, it may result in visual failure. In our patients treatment with danazol was temporally related to the onset and resolution of this syndrome. The patients in cases 1 and 3 were atypical for idiopathic benign intracranial hypertension, being non-obese. In case 3 inadvertent rechallenge resulted in recurrence of symptoms. Danazol suppresses the pituitary-ovarian axis by inhibiting gonadotrophin secretion. It has weak androgenic activity and may cause fluid retention and weight gain.<sup>1</sup> The pathophysiological mechanisms proposed in benign intracranial hypertension include cerebrospinal fluid hypersecretion,<sup>2</sup> impaired absorption,<sup>3</sup> and abnormalities of microvasculature.<sup>4</sup> Danazol induced fluid retention may aggravate these abnormalities. Raised intracranial pressure may also result from cerebral venous sinus thrombosis. Other associations include pregnancy, menarche, hypervitaminosis A, steroid withdrawal, and tetracycline treatment.<sup>5</sup>

There are no published reports of benign intracranial hypertension associated with danazol. The Committee on Safety of Medicines has no other reports of this condition with danazol, although headaches and visual disturbances are frequently reported (personal communication). The manufacturers are aware of two other cases of raised intracranial pressure in patients treated with danazol (Winthrop, personal communication). Intracranial hypertension should be considered in any woman with headache or visual symptoms during treatment with danazol.

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## Clinical evaluation of lysuride in the management of hyperprolactinaemia

Bromocriptine is a semisynthetic ergot alkaloid that acts as a dopamine agonist and is highly effective in achieving normoprolactinaemia in most patients with raised serum prolactin concentrations. Some patients, however, may have unacceptable side effects. Lysuride hydrogen maleate (lisuride; Revanil, Schering UK) is an 8- $\alpha$ -ergolene which has potent dopamine agonist activity both in vitro and in vivo; currently there are few data available about the incidence of side effects with lysuride in relation to its clinical efficacy. We have therefore assessed the efficacy of lysuride in 24 consecutive women presenting with hyperprolactinaemia.

### Patients, methods, and results

All 24 patients (age range 19-42) presented with a serum prolactin concentration (mean of three estimations) above 360 mU/l, which is the upper limit of normal in