other epidemiological characteristics and both lived in an area where hepatitis A is highly endemic. The low prevalence of anti-HAV in patients with thalassaemia is unlikely to be due to a resistance to the infection endowed by the disease, since an increased prevalence of anti-HBs as well as of antibodies to cytomegalovirus and other viruses has been found in such children.¹⁸

Thus regular blood transfusion probably gives sufficient protection against HAV under usual conditions of exposure, postponing infection until later in life. The inverse relationship between the number of blood transfusions and the prevalence of HAV infections further supports this view. Transfusions may produce passive immunity—anti-HAV protects against re-infection by HAV both experimentally in man and animals^{2 3 15} and clinically when given immune globulin.¹⁵ The protection given to patients with thalassaemia should be highly efficient under the usual conditions of exposure, since they are transfused almost every month with blood from donors who are nearly all anti-HAV positive.¹⁹ The prevalence of HBV infections in contrast presumably increases with the number of blood transfusions because only about 20–25% of Greek blood donors have anti-HBs—but also because passively acquired anti-HBs cannot protect adequately against the enormous amount of HBV transmitted in a unit of blood positive for HBsAg.²⁰

The correlation between the prevalence of HAV and HBV infections in controls suggests that certain factors such as poor hygienic conditions increase the risk of exposure to both viruses.²¹ The inverse relationship observed in the patients with thalassaemia underlines the importance of blood transfusion in the transmission of HBV and its ability to protect against HAV infection.

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Requests for reprints should be addressed to Dr Papaevangelou.

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SIDE EFFECTS OF DRUGS

Unusual fetal malformations after antiemetics in early pregnancy

Debendox (dicyclomine hydrochloride 10 mg, doxylamine succinate 10 mg, pyridoxine hydrochloride 10 mg) is widely prescribed for nausea and vomiting in pregnancy and is generally regarded as non-teratogenic, though reduction deformities in infants whose mothers have taken the drug have occasionally been reported.¹ We describe three patients who took Debendox from an unusually early stage of pregnancy and subsequently gave birth to babies with a rare combination of abnormalities, including extrusion of abdominal contents and reduction deformity or total absence of a leg. The women lived in widely separated areas of the north-west of England and the babies were born between July 1975 and May 1977.

Case reports

Case 1—A 24-year-old primigravida with a regular menstrual history (4/28-32) took one Debendox tablet each morning and two at night for nausea, beginning six weeks from the first day of her last menstrual period. She took no other potential teratogens. In July 1975, when 18 weeks pregnant, she was admitted to hospital with lower abdominal pain and vaginal bleeding, and after four days spontaneously aborted. The fetus was macerated and at necropsy was found to have exomphalos and absence of the left leg. A subsequent pregnancy in 1976 was uneventful, no drugs being taken except an iron and folic-acid preparation, and a normal girl was delivered.

Case 2—A 29-year-old primigravida with a regular menstrual history (5/28-30) took one Debendox tablet twice daily and two at night for nausea and vomiting. The drug was begun five and a half weeks from the first day of the last menstrual period. She continued on this regimen until term and there was no history of infection or of exposure to other drugs, except for an iron and folic-acid preparation from 16 weeks' gestation. Spontaneous labour began at term in May 1977 and delivery was by forceps for delay in the second stage. The baby died 15 minutes after birth. It weighed 2600 g. The liver and most of the gastrointestinal tract were contained in a thin-walled sac protruding through a defect in the left lower abdominal wall. The right leg was thickened and bowed, while the left leg and foot were absent. At necropsy a solitary renal mass and a single gonad were found. The pelvis was hypoplastic and the thoracic spine showed gross kyphoscoliosis.

Case 3—A 22-year-old primigravida with a previously regular menstrual cycle (5/30) was prescribed Septrin (trimethoprim 80 mg, sulphamethoxazole 400 mg) twice daily for five days for a urinary tract infection, beginning three weeks from the onset of her last menstrual period. Debendox, one tablet daily and two at night, was prescribed at six weeks' gestation, and treatment continued for six weeks. She had no other infections and took no drugs apart from an iron and folic-acid preparation from 12 weeks' gestation. She was admitted in labour in March 1977 when 38 weeks pregnant, and had a breech delivery of a stillborn girl weighing 3885 g. Postmortem examination showed exomphalos containing small intestine, stomach, liver, and spleen. The left foot was attached to a grossly shortened leg and there was severe thoracic scoliosis giving rise to a reduced left hemithorax.

Comment

Protrusion of abdominal contents and reduction deformity or absence of a leg seems to be an extremely rare combination, though

Werthemann² described a baby with exomphalos and absence of the right leg, hemipelvis, and a single testis. Surveys of infants born to over 3000 women given Debendox in pregnancy^{3,4} showed no increase in the incidence of abnormalities. We do not therefore necessarily associate the abnormalities seen in the three fetuses described here with the effects of this drug combination. Our patients, however, took Debendox unusually early in pregnancy (five and a half to six weeks after the last menstrual period). As pregnancy is being detected earlier due to the increased use of urine pregnancy tests, fetuses may be exposed more often to drugs during the period of intense organogenesis with consequent increased risk of damage, even from apparently safe drugs like Debendox. We hope our report will alert others to this possibility.

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Department of Medical Genetics, St Mary's Hospital, Manchester M13 0JH

DIAN DONNAI, MRCP, DCH, senior registrar

R HARRIS, MD, FRCP, reader in medical genetics and consultant physician

Bilateral central fracture-dislocation of hips after myelography with meglumine iocarmate (Dimer X)

Investigation of suspected lumbar disc protrusions with a contrast medium that mixes with the cerebrospinal fluid outlines the nerve root sheaths (radiculography) and enables a higher proportion of lateral protrusions to be detected than when a non-miscible medium is used. We describe a case of central fracture-dislocation of the hips that occurred after the water-soluble contrast medium meglumine iocarmate (Dimer X) was used.

Case report

A 27-year-old telephonist of previously good health enjoyed a normal pregnancy. Labour was induced at term by surgical rupture of the membranes and delivery effected under epidural anaesthesia using Kielland's rotation forceps. The baby, a boy weighing 3800 g, was normal. After delivery she complained of pain in the lumbar region and left calf. Straight-leg-raising on the left was restricted to 45°. There was no neurological abnormality, and radiographs of the lumbar spine were normal. She was treated with epidural injection, three weeks of bed rest, and a lumbar corset. Her symptoms persisted, and after three months myelography was performed. With the patient lying on her side and the head end of the table raised 15°, 7 ml of meglumine iocarmate mixed with 3 ml of cerebrospinal fluid was introduced into the lumbar canal under television control. Left-sided protrusion of the L4-5 disc was seen (fig 1). After the procedure she was kept sitting up in bed for 12 hours. Her back pain became worse and she developed cramp-like pain in the legs and paraesthesiae, occurring in waves of 10-20 seconds, in the groins and buttocks. Intramuscular diazepam and pentazocine were administered. Twelve hours after myelography she cried out with sudden agonising lower abdominal and groin pain. She was pale, blood pressure was 80/50 mm Hg, there was lower abdominal guarding, and she held her legs rigidly. Right footdrop was noted. Radiography (fig 2) showed bilateral central fracture-dislocation of the hips. She was transfused with 4 units of blood. Under general anaesthesia the hips were manipulated and skeletal traction was applied.

The occurrence of these fractures together with initially low serum calcium (2.2 mmol/l; 8.8 mg/100 ml) and phosphorus (0.58 mmol/l; 1.8 mg/100 ml) concentrations suggested metabolic bone disease. Results of detailed investigations one month later were as follows: serum calcium 2.35-2.70 mmol/l (9.4-10.8 mg/100 ml), phosphorus 1.10-1.42 mmol/l (3.4-4.4 mg/100 ml), alkaline phosphatase 9 KA units/dl, and urea 5.2 mmol/l (31.3 mg/100 ml); no Looser's zones or subperiosteal erosions on skeletal survey; 24-hour

urinary calcium and phosphorus (5.2 mmol and 20.62 mmol (208 mg and 0.6 g) respectively) normal; urine and plasma amino-acid chromatograms normal; iliac bone biopsy normal; and plasma 25-hydroxy vitamin D (20 nmol/l (8 ng/ml)) normal. Serum parathyroid hormone was not measured owing to positivity to hepatitis B antigen.

On mobilisation at 12 weeks she developed recurrence of the left sciatic pain. The disc protrusion was excised and the nucleus pulposus evacuated

FIG 1—Myelogram showing lateral protrusion of L4-5 disc.

FIG 2—Plain x-ray appearances of fracture-dislocation of hips.

using a fenestration approach. Nine months after the fractures she was free of sciatic pain but both hips were painful and very stiff. The right footdrop had resolved.

Comment

Because of the side effects of water-soluble contrast media used for myelography some radiologists prefer iophendylate (Myodil). Clonic spasms, fractures, and death have followed the use of meglumine iothalamate (Conray).¹ Severe bilateral pelvic fractures have also been described.² Meglumine iocarmate, a dimer of meglumine iothalamate, was reported by Danziger and Bloch³ to have few serious side effects.