volume, and total lung capacity.⁵ Any reduction in pulmonary mechanical efficiency must be avoided in respiratory failure, and controlled use of carbimazole may permit a fall in basal metabolic oxygen requirement but with thyroid function remaining within the normal range.

Carbimazole would seem suitable for a double-blind controlled trial of treatment in chronic irreversible respiratory failure, and the drug may have a role in otherwise intractable cases while the results of such a study are awaited.

We are grateful to Dr D Davies for help with this paper.

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Neonatal small-bowel obstruction associated with amniocentesis

Mid-trimester amniocentesis is a well established and relatively safe diagnostic procedure.¹ Nevertheless, there are inevitable hazards associated with the technique and if it is to be used in comprehensive antenatal screening programmes² potential complications should be recognised. Injuries to the fetus occur infrequently but they may be serious.

Case report

A boy was born at term (weighing 3270 g) by normal vertex delivery after surgical induction of labour. This was the mother's third pregnancy and because of her age (39 years) she had requested amniocentesis, which had been performed after ultrasound placental localisation at 16 weeks' gestation. Amniocentesis had been straightforward with removal of 20 ml of clear fluid through a 20 G spinal needle with trochar.

At birth a pink fleshy mass 2 cm long with a necrotic tip was noted to protrude through a small epigastric abdominal wall defect just left of the midline (see figure). Meconium had not been passed 20 hours after birth, at which time the baby had a single copious vomit. Abdominal radiograph confirmed intestinal obstruction.

Abdominal wall of the infant showing the protruding, necrotic knuckle of small bowel.

At laparotomy the small bowel was obstructed at about its midpoint by an atretic segment, the bowel being represented by a fibrous cord spanning a defect in the mesentery (Bland Sutton type II atresia). The distal bowel was totally collapsed. Proximally it was distended to about 3 cm diameter, and a portion of its wall passed through the abdominal wall defect to form the fleshy mass seen externally. Peritoneal adhesions around this portion, anchoring it to the edges of the defect, suggested that it had prolapsed some considerable time before birth. The intestinal tract was otherwise normal. Forty centimetres of small bowel were resected and an anastomosis fashioned.

The postoperative period was complicated by a wound infection and a slow return to normal bowel function. After 10 days of intravenous parenteral nutrition the baby improved and was discharged on the 34th day. At the time of writing the infant was thriving.

Comment

The abdominal wall defect described in this case does not have a satisfactory embryological explanation. Similar atretic lesions of the bowel have been experimentally produced in animals by intrauterine perforation of the fetal ileum or by ligation of mesenteric vessels.³ The combination at the same site of a defect in the abdominal wall without embryological explanation and an ileal defect which can be produced experimentally by perforation or devascularisation makes trauma a likely cause. Both might have been induced by needle puncture at the time of amniocentesis. An alternative but unlikely explanation is that the needle puncture allowed an already dilated proximal portion of obstructed ileum to push through the abdominal wall.

When attempts are made to puncture the fetal abdominal wall during intrauterine transfusions for rhesus incompatibility important fetal trauma occurs in at least 10% of cases. Many types of visceral injury have been reported, including traumatic and functional intestinal obstruction. Similarly, amniocentesis for assessment of rhesus disease causes fetal puncture in many hydropic infants.⁴ These procedures, however, are usually performed in the third trimester of pregnancy, when a larger fetus is surrounded by relatively less liquor.

Second-trimester amniocentesis appears to be safer, but fetal injuries have been reported with important consequences such as limb deformity, fetal haemorrhage, and puncture wounds of the eye and other vital organs. Rickwood has also recorded a similar case of ileal atresia with an abdominal wall fistula after amniocentesis at 18 weeks' gestation.⁵

The amniocentesis needle may therefore be responsible for serious fetal trauma. With the inevitable increase in the use of this important procedure such consequences should be borne in mind.

We acknowledge the help of Dr R W Whittlesey and thank Dr R L'E Orme and Mr D W Sykes for allowing us to report this case.

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Spinal muscular atrophy associated with HLA-B7

The spinal muscular atrophies are familial disorders characterised by degeneration of the anterior horn cells of the spinal cord or bulbar motor nuclei but with no disease of the pyramidal tract or peripheral nerves. Although the characteristic neuronal changes can be determined only at necropsy, diagnosis of the secondary muscular changes on clinical, electrodiagnostic, and histological grounds is

clear. The disorders are highly heterogeneous in the age of onset, severity, and distribution of the predominant muscle weakness. The distal, bulbar, scapuloperoneal, and facioscapulohumeral forms seem to be distinct entities, but usually the weakness is generalised or mainly proximal. Acute Werdnig-Hoffmann disease, which is of early infantile onset and has a rapidly progressive course, seems to be a specific autosomal recessive disorder within this group.¹ In most of the more chronic cases inheritance appears to be recessive.² Yet the great variation in severity and age at onset within sibships, the characteristically intermittent progression of the disease, and the low segregation ratio² suggest that the genetic element might consist of a predisposition to the disease, which requires a trigger to become manifest. Thus a possible association with the HLA system is reasonable.

Subjects, methods, and results

We identified those patients with spinal muscular atrophy living in the Northern Region whose records were at the Regional Neurological Centre, Newcastle, and who satisfied the diagnostic criteria of having a predominantly proximal distribution of muscle weakness, a clinical diagnosis supported by results of electromyography and muscle biopsy, and having survived beyond the age of 2 years.

Patients aged over 17, or the parents of younger patients, were asked whether they and their families would participate in the investigation. Altogether, 55 patients from 50 families took part; 26 had spinal muscular atrophy type II and 23 type III,³ while in six patients the onset had occurred after the age of 30. In three families two sibs were affected, and in a fourth family three sibs were affected. Controls comprised 110 healthy unrelated medical students and subjects attending the Regional Genetic Advisory Service. Specimens were HLA typed by the microcytotoxicity method standard in this laboratory.⁴ We examined 15 specificities at the HLA-A locus, 16 at the HLA-B locus, and four at the HLA-C locus, using a minimum of 73 different antisera, at least two for each specificity.

A significantly higher incidence of B18, a highly significant increase in B7, and a barely significant increase in A10 and decrease in A2 were apparent in the patients compared with controls (table). Since 31 antigens were studied, some apparently significant association is likely to occur by chance. When correction was made for this only the association with B7 remained highly significant. Since bias may be introduced by including several patients from a particular family, one patient was randomly selected from each family. B7 was then the only antigen that was significantly more common in patients than controls before and after correction. The incidences of the antigens were similar in patients with type II and type III disease.

No (%) of patients and controls positive for each antigen

HLA antigen	No (%) of patients (n=55)	No (%) of controls (n=110)	χ^2	P
A1	26 (47.3)	37 (33.6)	2.34	
A2	16 (29.1)	51 (46.4)	3.84	
A3	14 (25.5)	30 (27.3)	0.004	
A9 (incl 23, 24)	16 (29.1)	24 (21.8)	0.34	
A10 (incl 25, 26)	7 (12.7)	4 (3.6)		0.044
A11	8 (14.5)	13 (11.8)	0.01	
A28	4 (7.3)	3 (2.7)		0.142
A29	1 (1.8)	8 (7.3)		0.097
AW30	2 (3.6)	6 (5.5)		0.263
AW31	0	2 (1.8)		0.422
AW32	0	1 (0.9)		0.651
B5	1 (1.8)	11 (10.0)		0.079
B7	36 (65.5)	26 (23.6)	21.53	
B8	16 (29.1)	34 (30.9)	0.004	
B12	16 (29.1)	42 (38.2)	0.96	
B13	1 (1.8)	3 (2.7)		0.388
B14	0	4 (3.6)		0.176
B15	2 (3.6)	9 (8.2)		0.138
BW16	1 (1.8)	5 (4.5)		0.244
B17	4 (7.3)	8 (7.3)		0.245
B18	10 (18.2)	7 (6.4)	5.33	
BW21	1 (1.8)	3 (2.7)		0.399
BW22	0	4 (3.6)		0.194
B27	4 (7.3)	8 (7.3)		0.245
BW35	1 (1.8)	7 (6.4)		0.135
B37	0	0		
B40	3 (5.5)	12 (10.9)	0.97	
CW1	0	5 (4.5)		0.113
CW2	0	5 (4.5)		0.113
CW3	3 (5.5)	7 (6.4)		0.259
CW4	1 (1.8)	8 (7.3)		0.097

Comment

These results indicate that the HLA system is implicated in this group of disorders. This is the third disorder of the central nervous system to be associated with the B7 antigen (the others being multiple sclerosis and paralytic poliomyelitis, though the strengths and existence of the associations are not consistent in all the series). The

B7 antigen may perhaps be as specific for neurological disorders as the B8 antigen appears to be for the autoimmune disorders, and the B27 antigen for the arthropathies.

These findings, which are important for understanding the aetiology of the disease, relate to nearly all cases of spinal muscular atrophy in this region but should obviously be confirmed by other studies.

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Peripheral skin necrosis complicating beta-blockage

Cold extremities and Raynaud's phenomenon are reported as complications of most beta-blocking drugs used in hypertension.^{1 2} Peripheral gangrene complicating the use of propranolol and metoprolol has been reported in two hypertensive patients with peripheral vascular insufficiency.^{3 4} We describe three hypertensive patients who developed painful ischaemic lesions of the feet during treatment with beta-blockers, prompt and complete recovery occurring when treatment was stopped.

Case reports

Case 1—A 71-year-old man treated for moderate hypertension with propranolol 80 mg four times daily, clonidine, and hydrochlorothiazide-K complained in February 1976 of cold extremities; oxprenolol 80 mg thrice daily was substituted for propranolol. In December 1977 he complained of severe pain in both feet and was found two months later to have multiple areas of skin necrosis on the toes and soles of both feet (see figure). Foot pulses remained palpable throughout. Oxprenolol was stopped and he was treated with aspirin 300 mg twice daily and dipyridamole 25 mg four times a day. The ischaemic lesions resolved completely within one month. Erythrocyte sedimentation rate, cryoglobulin determination, and tests for rheumatoid factor and DNA-binding antibodies were all normal.

Case 1. Area of skin necrosis on fifth toe of right foot.