Correspondence

Archives of Disease in Childhood, 1972, **47**, 836.

Screening for Cystic Fibrosis

Sir,

In their Short Report on screening for cystic fibrosis, Vol. 47, pages 131–134, Drs. Cain, Deall, and Noble expressed the hope that their trial would stimulate other maternity units to carry out similar surveys so that the efficiency of the method could be more rapidly assessed.

In 1969 we started developing an immunochemical method to analyse meconium for albumin, and since August 1971 we have conducted a screening programme for CF in newborns at the University Hospital, Uppsala, Sweden. So far 2073 newborn infants have been screened and two cases of CF have been found.

A specimen of meconium is collected from the napkin, freeze-dried, and an aliquot is dissolved. After centrifugation the concentration of albumin in the supernatant is determined by single radial immunodiffusion technique. The results are given in the Table.

TABLE

Albumin in Meconium

(expressed as mg albumin/g dry weight meconium)

	<5 mg/g*		5–20 mg/g†		>20 mg/g†	
	Total No.	Thereof CFs	Total No.	Thereof CFs	Total No.	Thereof CFs
Included in the screening programme	2057	0 (?)	12	0	4	2
Clinically suspected (not included in screening programme)	23	0 (?)	2	0	8	7

*In this group only sibs of CF children and children with otherwise strong suspicion of CF have been sweat tested.

†In these groups all children have been sweat tested. The diagnosis of CF is based on pathological sweat test (pilocarpine-iontophoresis method), and one of the clinical signs of meconium ileus, lung involvement and/or malnutrition.

In the screening programme there were four meconiums with more than 20 mg albumin/g dry weight. Two of these came from newborns who were subsequently diagnosed as CF (22 mg and 160 mg albumin/g meconium respectively), one came from a child with melaena neonatorum (150 mg albumin/g meconium), and one from a child who is still perfectly healthy (80 mg albumin/g meconium).

In addition, we have analysed 33 meconiums from newborns who were clinically suspected of CF. 8 of these specimens had more than 20 mg albumin/g meconium, 7 of which were from children later diagnosed as CF by pathologically raised sweat electrolytes. Six of the children had meconium ileus and the seventh was a sib of a known CF child. The eighth meconium in this series with raised albumin concentration (52 mg albumin/g meconium) came from a child with atresia of the small bowel (normal sweat test). The 25 clinically suspected children with albumin concentration under 20 mg/g meconium included 10 sibs of known CF children, 4 children with bowel obstructions, and 11 children with delayed passing of meconium or with unusually viscous meconium.

In order to establish the diagnostic value of the present screening method, it would be advantageous for us to receive meconiums from patients with a clinical suspicion of CF, e.g. patients with meconium ileus, sibs of CF children, or patients with positive findings by other screening programmes.

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Spontaneous Femoral Artery Thrombosis and Intermittent Claudication in Childhood Nephrotic Syndrome

Sir,

The report in this journal of femoral artery thrombosis after femoral vein puncture in a nephrotic child (Cameron *et al.*, 1971) prompts us to report a case in which a similar thrombosis occurred spontaneously. We wish to draw attention to factors that may have contributed to an increased risk of arterial occlusion.

A boy aged 3 years presented with generalized oedema, oliguria of 48 hours' duration, and ascites. The blood pressure was 110/70 mmHg, and there was heavy proteinuria. The blood urea and electrolytes were normal, total plasma protein 4·2g/100 ml, βIC globulin 80 mg/100 ml, and creatinine clearance 20·3 ml/min per m^2. The ratio of the clearance of IgG to the clearance of transferrin was 0·2, indicating moderately nonselective proteinuria. Urinary microscopy showed hyaline and granular casts, but no growth on culture.

Prednisone 40 mg/day was started after a 36-hour

period of anuria. 48 hours later only 230 ml urine had been passed, and two intramuscular injections of frusemide 20 mg were given 18 hours apart, resulting in a diuresis of 1200 ml.

Four hours after the second dose of frusemide, while he was asleep leaning forwards over his left thigh, with his left leg bent up beneath him, a circulatory change was observed in the left leg. There was purplish discoloration extending to midcalf, the skin was cold, and no pulses were palpable below the femoral. He was treated with continuous intravenous heparin for 48 hours, followed by phenindione for 4 weeks. No further deterioration in the leg circulation occurred, and during convalescence, though the left leg was colder than the right, the collateral circulation opened up and all pulses were palpable, but of poor volume. As he became more mobile intermittent claudication developed. Pain recurred in the left calf after running 25 metres and he had to sit down until it had worn off. This symptom has improved but not disappeared and occasional pain has occurred in the calf at night. The nephrotic syndrome relapsed after an initial course of prednisolone, but eventually went into remission with tetracosactrin (Synacthen) and cyclophosphamide. Temporary hypertension occurred during the use of tetracosactrin. Renal biopsy which was deferred until he was normotensive, showed glomerulonephritis with predominantly mesangial proliferation and few capsular adhesions.

Both hypercoagulability and hypovolaemia occur in the nephrotic syndrome, and the blood volume may fall still further during diuretic therapy, and also on standing (Garnett and Webber, 1967). Frusemide gives a maximum diuresis of 14–30 ml/min, which is equivalent to 10 to 20% of the glomerular filtration rate. The duration of action of a single dose is 2 to 6 hours (Robson *et al.*, 1964). In this case frusemide had been given 4 hours before the first signs of occlusion and had already produced a diuresis of 500 ml. High doses have been recommended in the nephrotic syndrome and considered to be safe (Snashall, 1971). This may not be so, if steroids, which also increase coagulability (Ozsoylu, Strauss, and Diamond, 1962) are already being given. Use of the thromboplastin generation test before the use of diuretics might be useful to predict those susceptible to acute arterial occlusion, particularly if steroids are used (Mukherjee *et al.*, 1970).

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Artificial Grunting in Respiratory Distress Syndrome

Sir,

Infants suffering from idiopathic respiratory distress syndrome (RDS) show the grunting type of respiration illustrated in the Fig. It has been shown that grunting is an effective means of raising arterial oxygen tension (P_{aO_2}) in RDS (Harrison, Heese, and Klein, 1968), and the ability to simulate this pattern of respiration during mechanical ventilation might therefore be useful in the treatment of RDS.

We have modified a simple ventilator to produce this pattern, which Gregory *et al.* (1971) would describe as continuous positive pressure breathing (CPPB), in the treatment of infants with RDS.

The East-Radcliffe ventilator* has been adapted for use in the neonate to produce intermittent positive pressure ventilation (IPPV) (Tunstall *et al.*, 1968). It was further modified to produce CPPB by the addition of a gate-clamp to the expiratory tubing distal to the 'dummy lung'. With this arrangement the pressure changes may be monitored continuously on the manometer of the ventilator itself. The infant can then be supplied via a nasotracheal tube with oxygen-enriched heated, humidified air at any preselected pressure.

In the Fig., pressure-volume tracings obtained during artificial grunting are compared with tracings obtained during IPPV. During IPPV, airway pressure falls to zero midway through the ventilator cycle because of negligible resistance during the expiratory phase, possibly allowing further alveolar collapse to take place. With CPPB on the other hand there is continuing positive pressure during the expiratory phase, producing volume changes similar to grunting in RDS but with positive airway pressure remaining at the end of each cycle. This presumably increases the infant's functional residual capacity and helps to prevent alveolar collapse.

When CPPB is applied as described, the ventilator minute volume is considerably reduced and may even

*Type P.N.A. 1 H.G., East & Co., Oxford.