Congenital fibre type disproportion myopathy

A histological diagnosis with an uncertain clinical outlook

N. P. C. CAVANAGH, B. D. LAKE, AND P. MCMENIMAN

Departments of Neurology, Histopathology, and Orthopaedics, The Hospital for Sick Children, and The Institute of Child Health, London

SUMMARY Nine children with congenital fibre type disproportion (CFTD) are described. Their muscle biopsies contained type 1 fibres which were smaller than the largest type 2 fibres by at least 13·5%. Attention is drawn to the variable natural history of this disorder which generally carries a good prognosis but may sometimes be associated with fatal respiratory problems. For important therapeutic, genetic, and prognostic reasons CFTD must be distinguished from other conditions with similar histochemical or clinical features.

In 1969, Brooke and Engel reported the histographic analysis of muscle fibre types from 180 children and distinguished five separate groups of biopsies. One of these was characterised by relatively small, and sometimes excessively numerous, type 1 fibres and large type 2 fibres. Clinically the children in this group had been floppy infants whose condition generally improved as they grew older. Brooke (1973) subsequently described a further 12 cases to which he gave the name congenital fibre type disproportion (CFTD). In the interim period other cases were recorded (Caille et al., 1971; Noronha, 1973), although probably the earliest descriptions of this disorder were by Farkas-Barrier et al. (1968) and Dubowitz (1969).

Since 1973 there have been a few similar reports (Fardeau et al., 1975; Lenard and Goebel, 1975; Serratrice et al., 1975), and Spiro et al. (1977) described 3 infants who died of respiratory failure all of whom had small type 1 muscle fibres.

We present a further 9 patients whose muscle biopsies showed the presence of type 1 fibres which were smaller than the largest type 2 fibres by more than 13·5%. We think that these children could be said to have CFTD and that this has important genetic and therapeutic implications which are of interest to paediatricians. We also wish to stress the difficulties of making this diagnosis and the need for further debate to delineate more fully the natural history and histochemical features of the disorder. The case histories of 2 children are given in full in order to give the range of clinical symptoms; the histories of all the children are summarised in Table 1.

Case histories

Case 1. Pregnancy was normal and there were normal intrauterine movements. The baby, a girl, was born at term by breech delivery with forceps to the aftercoming head, and weighed 2·8 kg. In the newborn period she was noted to be floppy and to have a left 'clicking' hip. There were no respiratory or feeding difficulties.

In the family history her mother had been a 'bottom shuffler'.

The child was first seen at this hospital aged 6 weeks, by which time she was smiling. On examination she was visually alert. She had a circumflex-shaped mouth but no obvious facial weakness. There was no tongue fibrillation and no fasciculatory finger movements. She was markedly hypotonic and could just move her limbs against gravity. She was areflexic. She was nursed in double nappies because of her hip.

Investigations at that time showed a CPK high on one occasion and normal on others. Electromyography of her right tibialis anterior muscle was myopathic. A muscle biopsy of her left quadriceps showed type 1 fibres which were smaller than type 2 ones (Table 1), and a small proportion (41%) of fibres which might be considered as type 2C.

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The Hospital for Sick Children, London
Department of Neurology
N. P. C. CAVANAGH, senior registrar

Department of Morbid Anatomy
B. D. LAKE, reader

Department of Orthopaedics, Adelaide Children's Hospital, Australia
P. MCMENIMAN, senior registrar
Table 1  Summary of some of the clinical features of 9 cases of congenital fibre type disproportion

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Family history</th>
<th>Delivery</th>
<th>Presenting symptoms</th>
<th>Milestones</th>
<th>Operative procedures</th>
<th>Age when last seen (years)</th>
<th>Centile</th>
<th>Height</th>
<th>Weight</th>
<th>Other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>Mother had weak legs in childhood: now normal</td>
<td>Breech: forces to the after coming head</td>
<td>Hypotonia. CDH</td>
<td>M: Delayed Sp: Slight delay S: Normal</td>
<td>R. femoral osteotomy</td>
<td>2½</td>
<td>10th</td>
<td>10th</td>
<td>See full history</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>Parents were 2nd cousins. Two maternal cousins 'doubled jointed'</td>
<td>Forceps because of toxaemia</td>
<td>Hypotonia. Weakness</td>
<td>M: Delayed Sp: Normal S: Normal</td>
<td>L. adduction rotation osteotomy</td>
<td>2½</td>
<td>10th</td>
<td>&lt;3rd</td>
<td>Contracts at 2 months. Hypermobile hand joints. Improved with age</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>None</td>
<td>Normal</td>
<td>Fixed dorsiflexed position of feet. Poor sucking</td>
<td>M: Delayed Sp: Delayed S: Delayed</td>
<td>Elongation of extensor tendons</td>
<td>2½</td>
<td>&lt;3rd</td>
<td>&lt;3rd</td>
<td>Improving with age</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>Two paternal cousins had CDH</td>
<td>Breech</td>
<td>Hypotonia, Bilateral talipes, CDH</td>
<td>M: Delayed Sp: Normal S: Normal</td>
<td>Derotation osteotomy. L. innominate osteotomy. Posterior medial release of both feet. Bilateral extension tendon achillis</td>
<td>3½</td>
<td>10th</td>
<td>10th</td>
<td>Improving with age</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>None</td>
<td>Breech</td>
<td>Dyspnoea</td>
<td>M: Delayed Sp: Not reliably assessed S: assessed</td>
<td>Tracheostomy Died aged 1½</td>
<td>15th</td>
<td>15th</td>
<td>See full history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>None</td>
<td>Normal</td>
<td>Stridor. CDH</td>
<td>M: Delayed Sp: Normal S: Normal</td>
<td>Open reduction L. hip</td>
<td>3½</td>
<td>&lt;3rd</td>
<td>&lt;3rd</td>
<td>Frequent chest infections, stridor improving with age</td>
<td></td>
</tr>
</tbody>
</table>

M = Motor, Sp = speech, S = social, CDH = congenital dislocation of hip.
At follow-up there was concern about the instability of her right hip which tended to sublux and at age 2 years a right varus derotation osteotomy was performed.

Although she could sit at 7 months she was still not walking alone at 2½ years when last seen. She was reluctant to bear weight, could not pull to stand, and could take only 2 steps holding. She shuffled on her bottom. Her social responses were appropriate for her age and she had good comprehension, but her speech was confined to single words. Her height and weight were on the 10th centile.

Case 8. Pregnancy and intrauterine movements were normal. Delivery was by breech at 36 weeks and Apgar score at one minute was 8. Birthweight was 3·7 kg. There were no problems in the newborn period and the baby, a boy, sucked well. He smiled at 6 weeks.

There were no worries about him until age 4 months when during a period of 2 days he became ill with a cough and fever. On admission to hospital he was found to be dyspnoeic and to have a collapsed left lung. Within a few hours his condition deteriorated and he required high concentrations of oxygen to maintain his blood oxygen (Po₂) levels. 4 ml of pleural fluid was aspirated which later grew a coagulase-positive staphylococcus.

On transfer to this hospital 4 days later he was noted to be hypotonic with normal reflexes. Closer questioning of the parents disclosed that head raising in the prone and supine positions had always been poor. There were no cranial nerve abnormalities. There were no dysmorphic features and no skeletal abnormalities. Bronchoscopy did not show any significant abnormality. A barium swallow showed incoordinate swallowing with reflux into the posterior nasopharynx; the lowest portion of the oesophagus was dilated, and normal oesophageal stripping waves were ineffective. Pulmonary arteriography and left ventricular angiography were normal.

Six days after admission, assisted ventilation became necessary because of persistent respiratory failure secondary to left-sided collapse, and subsequently he developed a right upper lobe pneumonia and a right tension pneumothorax. 10 days after admission his liver function was first assessed and his liver enzymes were found to be raised (alanine amino transferase 150 IU/1 and aspartate amino transferase 104 IU/1). His liver edge felt firm but there was no hepatomegaly. These enzyme abnormalities gradually improved during the next months.

Three weeks after admission his CPK was estimated and found to be raised (14·6 μmol/ml per hour at 37°C, normal <3·6). In view of a recent history of intramuscular injections, the significance of this finding was uncertain. However, subsequent estimations showed a persistent abnormality and, in view of this, electromyography and muscle biopsy were performed. Sampling with a concentric needle electrode in right deltoid and vastus medialis did not show any abnormality, but his biopsy from left tibialis anterior when he was 6 months showed the presence of type 1 fibres which were smaller than the type 2 with no other abnormality (Table 2). Three months after admission, a tracheostomy was performed and he continued to require assisted ventilation until the time of his death at 14 months. Repeat contrast investigations of the upper alimentary tract confirmed that reflux into the respiratory tract continued, so that it was difficult to be certain to what degree his respiratory difficulties were a reflection of this or of his myopathy. He continued to remain very hypotonic and weak and be unable to sit alone. Two weeks before he died he developed fits which were generalised and left focal. Epilepsia partialis continua down the left side was resistant to anticonvulsant treatment. His clinical condition after the onset of these fits deteriorated rapidly and computerised axial tomography (CAT) of his brain showed pronounced cerebral, cerebellar, and brain stem atrophy. He died from bronchopneumonia and congestive cardiac failure.

### Table 2 Summary of muscle biopsy features

<table>
<thead>
<tr>
<th>Case</th>
<th>Age at biopsy (months)</th>
<th>Muscle biopsied</th>
<th>Fibre types percentage</th>
<th>Fibre size (μm)</th>
<th>Percentage difference by which type 1 is smaller</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1  2A  2B  2C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>Vastus lateralis</td>
<td>37-5 29 13-5 4-5</td>
<td>14·25±2-2 17·6±2-2 16±2-2</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>Vastus lateralis</td>
<td>51 29 20</td>
<td>13 ±0·15 18·5±4 19·5±4</td>
<td>29±7 33</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>Vastus lateralis</td>
<td>33 24 43</td>
<td>14·5 16·5 17·5</td>
<td>12±1 17·1</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>Vastus lateralis</td>
<td>44 34 22</td>
<td>11 ±1·7 16·5±1·7 22 ±2</td>
<td>33·3 50</td>
</tr>
<tr>
<td>5</td>
<td>18</td>
<td>Tibialis anterior</td>
<td>51-1 33 15-5</td>
<td>18 ±2·4 21 ±2·9 26 ±2·2</td>
<td>18·2 30·7</td>
</tr>
<tr>
<td>6</td>
<td>18</td>
<td>Gastrocnemius</td>
<td>50-5 37 12-5</td>
<td>13·5±1·4 17·2±2·1 21·5±4·4</td>
<td>20±6 37·2</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>Vastus lateralis</td>
<td>50 27 23</td>
<td>18·6±3·6 28·7±4·8 29·4±5·4</td>
<td>35 36·6</td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td>Peroneus</td>
<td>55 31-5 13-5</td>
<td>28·5±6·7 40±4·9 43±4·9</td>
<td>28·7 33·7</td>
</tr>
<tr>
<td>9</td>
<td>27</td>
<td>Tibialis anterior</td>
<td>37-5 42 20-5</td>
<td>13·5±4 27±4 24·5±4</td>
<td>50 44·9</td>
</tr>
</tbody>
</table>

Normal fibre diameters are from about 14 μm at birth to about 21 μm at 2½ years.
Investigations found to be normal were: sweat test, blood viral antibody screen, absence of vacuolated lymphocytes, urine mucopolysaccharides, blood copper, and zinc. Urine amino- and organic acids on some occasions were normal and at other times showed a raised glycine and taurine and raised parahydroxyphenyllactic and parahydroxyphenylacetic acid. These abnormalities were considered to be a reflection of his impaired liver function. He was shown to have a low IgG (26 IU/ml) and a high IgM (>170 IU/ml) at 4 months. His height and weight were both on the 15th centile.

Investigations

Electromyography was performed in all but one patient. The findings suggested a myopathy in Cases 1, 3, 4, and 5, were normal in Cases 2, 8, and 9, and suggested denervation but with normal nerve conduction studies in Case 6. CPK estimations were slightly raised in Cases 4, 5, and 6, significantly raised in one (Case 8), slightly raised on one occasion and normal on another in Case 2, and normal in the others.

One (Case 5) was extensively investigated on account of her low height and weight. The following investigations were normal: sweat test, barium meal and follow through, barium enema, jejunal biopsy, duodenal enzymes on aspiration. No organism was found in the pancreatic juice although she had been treated several months previously with metronidazole for giardia infection of the gut. Her serum albumin was normal.

Other investigations which were performed and found to be normal are shown in Table 3.

A muscle biopsy was obtained in all cases and treated as described previously (Lake and Wilson, 1975). In addition, muscle tissue was obtained from some patients during the course of orthopaedic surgery. The least diameter of a minimum of 50 fibres of each type covering several muscle fascicles was measured in the acid preincubated ‘ATPase’ preparations using a calibrated eyepiece graticule. Most muscle fibres do not show a uniform shape and, for this reason, the minimum diameter was measured as this gives the best approximation to the true diameter regardless of the plane of section. An indication of the diameters measured is shown in Fig. 1. The mean diameter and SD for each type is shown in Table 2. The fibre type percentage is calculated from a fibre type analysis of several muscle fascicles containing at least 200 muscle fibres, using the acid preincubated ‘ATPase’ preparations to define the three main fibre types.

Muscle tissue was obtained at necropsy from Case 8 and frozen for cryostat sectioning. Samples were taken from left and right tibialis anterior, vastus lateralis, psoas, diaphragm, rectus abdominis, sternomastoid, biceps brachialis, sartorius, and trapezius.

Pathology

The only change noted in each of the (in vivo) biopsies was a disproportion in size of type 1 and type 2 fibres. There was no increase in numbers of central nuclei, endomyosial connective tissue, degeneration, or other nonspecific features associated with denervating or myopathic conditions. The more specific features of nemaline myopathy or central core disease were not seen. In one biopsy (Case 7) many of the type 1 fibres showed 'moth eaten' characteristics.

The disproportion of the size of type 1 and the largest type 2 fibres (Table 2) was always greater than 13.5% and in 7 out of 9 patients the 2B fibres were larger than the 2A ones. The proportion and size of type 1 fibres were in most cases within the normal range. The coefficient of variability of the type 2 fibres was less than 250 in all patients.

In Cases 2 and 9 a biopsy of sartorius taken during reduction of the dislocated hips did not show disproportion of fibre diameters, although biopsies of vastus lateralis taken earlier (Case 9), or later (Case 2), showed the characteristic disproportion.

The muscles sampled at necropsy of Case 8 showed pronounced intersample differences and had changed remarkably since the biopsy taken at age 6 months. In each muscle examined from this patient there was an increase in endomyosial connective tissue, a greater number of central nuclei, and pronounced variation in fibre diameters which did not correlate with fibre type. Cytoplasmic bodies, staining bright red in the trichrome preparations, were present even in the more mildly affected muscles. Considerable infiltration by histiocytes showing acid phosphatase activity was noted with only little evidence of regenerative

<table>
<thead>
<tr>
<th>Investigation</th>
<th>No. of patients investigated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood thyroxine</td>
<td>5</td>
</tr>
<tr>
<td>Thyroid stimulating hormone</td>
<td>1</td>
</tr>
<tr>
<td>Pyruvate and lactate</td>
<td>4</td>
</tr>
<tr>
<td>Urine amino- and organic acids</td>
<td>5*</td>
</tr>
<tr>
<td>Blood amino-acids</td>
<td>6</td>
</tr>
<tr>
<td>Urine mucopolysaccharides</td>
<td>2</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>2*</td>
</tr>
<tr>
<td>Blood chromosome analysis</td>
<td>2</td>
</tr>
<tr>
<td>CAT of the skull</td>
<td>2</td>
</tr>
<tr>
<td>Congenital infection screen</td>
<td>3</td>
</tr>
</tbody>
</table>

*The urine of Case 8 intermittently contained raised glycine and taurine.
†Serum alanine and aspartate aminotransferase levels were raised in Case 8.
changes although some of the central nuclei were plump and occasionally several were present in one fibre. The degree of involvement could be roughly graded from the least affected muscle to the most affected in the following order: tibialis anterior, sternomastoid, sartorius, biceps brachialis, psoas, rectus abdominis, vastus lateralis, trapezius, and diaphragm. In Figs 1–4 the biopsy findings are compared with those found at necropsy.

The lungs showed bronchopneumonic changes and some hyaline membrane formation. Other tissues appeared normal or showed only slight changes. In particular there was no evidence of any abnormality of anterior horn cells, nor was there evidence of storage disease.

Discussion

Some of the clinical features of our 9 cases are shown in Table 1. A family history of neuromuscular problems was present in only 2 children (Cases 2 and 7); in one the parents were second cousins and two maternal cousins were said to be ‘double jointed’, and in the other case two paternal cousins had had CDH but no other neuromuscular problems. Six of the 9 patients were girls.

Pregnancy was normal in all but one instance in which there was terminal toxæmia, and intrauterine movements were experienced normally by all mothers.

Delivery was complicated in 6 out of 9 patients: Cases 1, 7, and 8 were breech presentations, Cases 3 and 6 were caesarean sections, one electively and the other for placenta praevia, and forceps was used in Case 2.

Generalised hypotonia and weakness were noted early in 6 children and became evident within the subsequent 2 years in the remaining 3 (Cases 5, 6, 9) although in Cases 5 and 9 these symptoms were only slight. There was no significant deterioration in any patient after age 2 years and in 3 there was greater improvement in strength than might have been anticipated from natural maturation alone.

Respiratory difficulties were present in the newborn period in only one child (Case 9) who had laryngeal stridor. One other patient (Case 5) sucked poorly.

Congenital dislocation of the hip was noted in about one-third of our cases. Other skeletal abnormalities were not uncommon and included deformities of the feet in 3 children (Cases 3, 5, and 7), scoliosis and high arched palate in Cases 3 and 6. Cases 2, 4, and 8 had no skeletal deformities. Muscle contractures commonly developed and reflexes were depressed or absent. Height and weight tended to be about or below the 3rd centile in most instances. Motor milestones were delayed in all patients, but speech and social development was normal in all except Cases 1 and 5.

These clinical features are very like those described by Brooke and Engel (1969) and Brooke (1973) in the majority of their patients. In their series there was a slight preponderance of females, and in ours there were twice as many females as males, but the numbers are too small to form any valid conclusions. Delivery was complicated in 6 out of our 9 cases whereas it was normal in all but 2 of Brooke and Engel’s cases. Half their patients had high arched palates whereas this was a feature in only 2 of ours. Brooke commented that recurrent respiratory infections ‘may be a problem’. This was true of Case 9 in our series, and in Case 8 the clinical picture was dominated from age 4 months onwards by persisting and very severe respiratory difficulties necessitating continued assisted ventilation. This child is reminiscent of those described by Spiro et al. (1977) and leads us to confirm their impression that respiratory failure is a rare but definite feature in CFTD.

Although the clinical features of CFTD are distinctive they are by no means exclusively diagnostic and may also be present in several other congenital myopathies—such as nemaline myopathy and infantile myotonic dystrophy. A disproportion in fibre sizes, type 1 fibres being smaller than type 2, may also be present in these two conditions with the result that it may be difficult to distinguish them one from another and from CFTD. This difficulty is illustrated by the report of Caille et al. (1971) where it is clear that their Case 1 had CFTD and their Case 2 nemaline myopathy.

None of the biopsies of our patients contained nemaline rods whereas they were present in 2 of the cases of Brooke and Engel (1969), and it is interesting that these 2 patients had very high arched palates—a feature characteristic of nemaline myopathy. We feel that these patients could more properly be said to have had nemaline myopathy. Although we recognise that nemaline bodies may be found in a variety of conditions (Dubowitz and Brooke, 1973) and that therefore the presence of such bodies does not necessarily imply the diagnosis of nemaline myopathy, nevertheless it would appear to us more logical to call the association of nemaline bodies and type 1 fibre atrophy, nemaline myopathy, than to attempt to extend the histochemical picture of CFTD to include the presence of nemaline bodies.

The distinction between CFTD and neonatal myotonic dystrophy may be difficult on both histochemical and clinical grounds in the early stages. However in over 90% of cases of Neonatal myotonic dystrophy, myotonia can be clinically
Fig. 1  Biopsy of L. tibialis anterior at 6 months (Case 8). Haematoxylin and eosin preparation showing two populations of fibres without other myopathic features. An indication of the fibre diameters measured is also shown for four fibres. Scale mark 50 μm. × 700

Fig. 2  Biopsy L. tibialis anterior (Case 8). 'ATPase' preparation after preincubation at pH 4.3 showing that the small fibres are all of type 1. Scale mark 50 μm. × 950
Fig. 3 Necropsy diaphragm muscle (Case 8). Haematoxylin and eosin preparation showing pronounced variation in diameter of fibres, increase in connective tissue, central nuclei, and whorled fibres. Scale mark 200 $\mu$m. $\times$ 200.

Fig. 4 Necropsy trapezius muscle (Case 8). 'ATPase' preparation after preincubation at pH 4·3 showing that the orderly pattern of the biopsy (Fig. 2) has been replaced and that the large fibres are now mainly type 1. Scale mark 100 $\mu$m $\times$ 400.
elicited in the mother. None of the mothers of our cases had myotonia.

The significance of the presence of 'motheaten' type 1 fibres in Case 7 is uncertain, but it is interesting that this patient was the only one in whom bilateral talipes equinovarus was present; this association was reported previously by Dubowitz and Sharrard (1968).

The absence of fibre type disproportion in sartorius muscle in 2 patients confirms the impression of Spiro et al. (1977) that there may be 'striking intersample differences', and this is also seen in the marked differences between the muscles sampled at necropsy of Case 8.

The appearances of the muscle at necropsy in Case 8 are very similar to those of congenital muscular dystrophy and it could be speculated that some cases of congenital muscular dystrophy may arise from a fibre type disproportion at birth. However Case 8 presented with respiratory failure at 4 months of age, and the absence of severe neuromuscular problems in the early months of life makes the clinical diagnosis of congenital muscular dystrophy unlikely.

The clinical differential diagnosis of CFTD includes a number of other conditions. The picture initially may suggest a severe form of spinal muscular atrophy. In view of the very different prognosis in these two conditions it is clearly important to distinguish them, even to the extent of performing a muscle biopsy.

The combination of foot deformities, congenital dislocation of the hip, and flexion contractures often leads to a diagnosis of arthrogryposis multiplex congenita. This condition is a clinical definition of what is probably a heterogeneous group of disorders (Wynne-Davies and Lloyd-Roberts, 1976), some of which are myelopathic in origin presenting as 'wooden dolls' (Brandt, 1947), and others myopathic with weakness, hypotonia, and flexion contractures (Adams, 1975). Muscle biopsy may be the only way of distinguishing CFTD from this latter group.

Although none of our patients had contractures at birth, several soon developed them. These contractures present a different clinical problem from the rigid contractures of arthrogryposis multiplex congenita, and we feel the combination of weakness, hypotonia, and posture are significant aetiological factors.

Only one child (Case 7) had bilateral congenital talipes equinovarus at birth, which contrasts with its more usual incidence in arthrogryposis multiplex congenita (Lloyd-Roberts and Lettin, 1970). Calcaneo-valgus deformity of the feet was seen in 3 patients, requiring elongation of the extensor tendons and dorsal capsulotomy of the ankle joint in one.

Finally in the clinical differential diagnosis, is the syndrome of multiple congenital dislocations associated with characteristic facial abnormality (Larsen et al., 1950). This diagnosis was initially given to 2 of our patients before muscle biopsy and it is important to distinguish this condition from CFTD as the management of the congenital dislocated hip is different. In Larsen's syndrome reduction of the dislocated hips has proved to be unrewarding (G. Lloyd-Roberts, personal communication), whereas in CFTD it is worth while.

Approximately one-third of our cases had dislocated hips and this is similar to the incidence reported by Brooke (1973). In his series good results were obtained with conservative treatment. This has not been our experience. All hips which were dislocated have required open reduction.

One of our patients was immobilised for a prolonged period after fracturing her tibia and a consecutive operation on her tendon achillis. She became noticeably weaker after this. Brief periods of immobilisation for operative procedure in the other patients has not been followed by any physical deterioration.

Extensive investigations of the gastrointestinal tract in one patient did not show any abnormality. As yet there is no explanation for the observation that many children with CFTD have heights and weights below the 3rd centile.

The question of inheritance of CFTD is an interesting one. None of our cases had an affected parent or sibling, but Case 6 of the series of Brooke and Engel (1969) had an elder brother with similar clinical features, and the father of these 2 boys was also said to have been weak as a child but to have outgrown the condition. Neither the brother nor the father of the index patient was biopsied and we feel from the information presented that the father did not have the same condition as his 2 sons. Fardeau et al. (1975) also reported a father and 2 siblings. However the father had at no time had any muscle weakness and his biopsy contained nemaline bodies and these features lead is to suspect that he too did not have the same condition as his children. Kinoshita et al. (1975) reported a boy and his mother who both had type 1 fibre atrophy and also nemaline bodies present on muscle biopsy. Although the authors felt that these patients had CFTD, we think their condition should be more properly called nemaline myopathy. It seems likely therefore that CFTD is inherited as a recessive trait.

From our experience of these 9 cases we agree with the general opinion that CFTD is a histological diagnosis which is usually associated with a clinical presentation having a favourable prognosis. However the progressively deteriorating clinical and biochemical features of our Case 8 lead us to agree with
Spiro et al. (1977) that a benign outlook is not invariable.

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References

Correspondence to Dr N. Cavanagh, Department of Neurology, Hospital for Sick Children, Great Ormond Street, London WC1N 3JH.

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N P Cavanagh, B D Lake and P McMeniman

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