Congenital myotonic dystrophy in Britain

I. Clinical aspects

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Harper, P. S. (1975). *Archives of Disease in Childhood*, **50**, 505. **Congenital myotonic dystrophy in Britain. I. Clinical aspects.** A clinical and genetic study of congenital myotonic dystrophy in Britain has been carried out in 70 patients from 54 sibships. The clinical aspects are analysed here, and the existence of a syndrome clinically distinct from myotonic dystrophy of later onset is confirmed. Characteristic features include neonatal hypotonia, motor and mental retardation, and facial diplegia. A high incidence of talipes occurs at birth together with hydramnios and reduced fetal movements during pregnancy, factors suggesting prenatal onset of the disorder in many cases. Prolonged survival is the rule after infancy, but the occurrence of numerous neonatal deaths in the sibships suggests the existence of unrecognized cases dying in the neonatal period.

Myotonic dystrophy (*dystrophia myotonica*) is generally considered to be a disease of adult life or adolescence, and in these age groups it shows characteristic diagnostic features including myotonia and progressive muscle degeneration affecting in particular facial, jaw, neck, and distal limb muscles.

Vanier (1960) first reported the occurrence of this disorder in early childhood, and recognized that the clinical features might differ considerably from those seen in later life. Subsequent reports (Dodge *et al.*, 1965; Watters and Williams, 1967; Aicardi, Conti, and Goutières, 1974) have defined the clinical picture of myotonic dystrophy presenting in infancy, and have emphasized that hypotonia, rather than myotonia is the dominant feature, and that it may result in severe, even fatal, respiratory problems in the newborn period. The frequent occurrence of mental retardation and the striking facial diplegia have also been recognized (Parker, 1963; Calderon, 1966; Gordon and Hilson, 1967).

In addition to these case reports, studies in the United States (Harper and Dyken, 1972; Dyken and Harper, 1973) have attempted to analyse the clinical features of larger series of patients, and to explain the unexpected finding that in the majority of cases showing congenital onset of the disease the mother is found to be the affected parent. The hypothesis has been proposed that congenital myo-

tonic dystrophy may result from an intrauterine maternal factor acting upon the fetus carrying the gene for myotonic dystrophy (Harper and Dyken, 1972).

The present study attempts to investigate the aetiology of congenital myotonic dystrophy, and in particular to test the above hypothesis, by analysis of clinical, genetic, and biochemical data based on as complete and unbiased a series of cases as possible from a defined population. In this paper the clinical data are analysed with special reference to the neonatal and antenatal periods. Subsequent papers (see following article) will discuss the genetic and biochemical data.

Method of study

An attempt was made to obtain data on all patients in Britain presenting with myotonic dystrophy in childhood in whom there was evidence of onset at or around birth. A letter requesting information was sent to all paediatricians in Britain (excluding Ireland) and to all neurologists and physician superintendents of mental subnormality hospitals. A positive response was followed by a more detailed questionnaire, and by a personal visit to the patient and family in nearly all cases. Cases ascertained purely through family studies were not accepted, nor were those in whom details of infancy were lacking or were completely normal. The study was carried out during the period April 1973–April 1974.

In addition to genetic data, information was collected on the pregnancy and neonatal period, and all available

TABLE I
Clinical features of patients with congenital myotonic dystrophy

Family no.*	Case no.	Sex	Gestation (w)	Birthweight (kg)	Hydramnios	Reduced fetal movements	Talipes at birth	Neonatal hypotonia	Neonatal respiratory distress	Facial diplegia	Motor delay	Mental retardation	Affected parent	Affected grandparent	Severity of parental disease†
1	1	M	39	3.2	N	-	+	+	+	+	+	+	Mother	?G-mother	1
	2	M	37	3.25	-	-	-	+	+	+	+	+	"	"	1
2	3	M	38	3.5	-	+	-	N	N	N	N	N	"	"	1
3	4	M		2.8	N	N	+	+	+	+	+	+	"	"	3
4	5	M	40	3.3	N	N	+	+	+	+	+	+	"	"	3
	6	M	40	2.7	+	N	+	+	+	+	+	+	"	"	1
5	7	M	40	3.2	+	+	-	+	+	+	+	+	"	"	4
6	8	M	42	3.9	+	-	-	N	N	+	+	+	"	"	4
	9	M	42	4.1	+	-	-	N	N	+	+	+	"	"	4
	10	F	40	2.6	+	-	-	N	N	+	+	+	"	"	2
7	11	F	40		+	-	-	+	+	+	+	+	"	"	1
8	12	F	40	3.2	+	+	-	+	+	+	+	+	"	"	2
9	13	M	34	2.0	+	N	-	+	+	+	+	+	"	G-father	1
10	14	M	34	2.3	-	+	+	+	+	+	+	+	"	"	
11	15	M		3.7	N	N	+	+	+	+	+	+	"	"	
12	16	F	43	3.0	-	-	+	+	+	+	+	+	"	G-mother	2
	17	M	40	3.9	-	N	+	N	-	+	+	+	"	"	1
13	18	F	43	4.0	+	+	+	+	+	+	+	+	"	"	4
	19	F	42	4.5	+	+	-	-	+	+	+	+	"	"	4
14	20	M	40	3.4	+	+	-	+	+	+	+	+	"	"	3
15	21	M			+	+	-	+	N	+	+	+	"	"	4
	22	M	40	4.1	-	+	-	N	N	+	+	+	"	"	4
	23	M			+	+	+	N	N	+	+	+	"	"	2
16	24	F	42	3.3	+	+	-	-	+	+	+	+	"	?G-father	5
17	25	M	32	2.5	+	+	-	+	+	+	+	+	"	"	1
18	26	F	43	3.2	+	-	-	-	+	+	+	+	"	"	1
	27	M	40	3.4	+	-	+	N	+	+	+	+	"	"	2
19	28	F	38	2.6	+	+	+	+	+	+	+	N	"	"	1
20	29	F		3.5	N	N	+	+	+	N	N	N	"	"	1
21	30	M	40	3.1	+	-	-	+	+	+	+	+	"	? G-mother	1
22	31	M	40	2.5	+	-	+	+	+	+	+	+	"	"	3
	32	F	40	2.2	-	-	-	+	+	+	+	N	"	"	3
23	33	F	39	2.2	-	-	-	+	+	+	+	+	"	? G-father	2
24	34	M	41	3.5	-	+	+	-	+	+	+	+	"	"	1
25	35	F	40	2.8	-	+	-	+	+	+	+	+	"	G-father	2
26	36	M	40	3.4	-	+	-	+	-	+	+	-	"	? G-mother	2
	37	M	41	3.6	-	+	+	+	-	+	+	-	"	"	2
27	38	F	40	3.8	-	+	+	+	-	+	+	+	"	G-mother	2
	39	M	40	4.5	+	-	+	+	+	+	+	+	"	"	2
28	40	F	40	3.1	+	+	-	N	+	+	+	-	"	"	1
29	41	F	40	2.8	N	+	+	+	+	+	+	N	"	G-father	3
30	42	M	36	2.4	+	+	+	+	+	+	+	+	"	G-mother	3
32	43	M	39		+	+	+	+	+	+	+	+	"	"	3
33	44	F	40		-	-	+	+	+	+	+	+	"	G-mother	1
	45	F	36		-	-	-	N	+	+	+	+	"	"	1
34	46	F	40	4.1	-	-	-	N	-	+	+	+	"	? G-mother	1
35	47	F	43	3.65	-	+	-	+	-	+	+	+	"	? G-father	4
36	48	F	40	3.1	-	-	+	-	+	+	+	+	"	"	2
37	49	F	40	4.3	+	-	+	+	+	+	+	+	"	G-father	1
38	50	F	40	2.9	+	-	-	+	+	+	+	+	"	"	1
	51	M	40	2.7	+	-	-	+	+	+	+	+	"	"	1
39	52	M	39	2.7	N	N	-	+	+	+	+	+	"	G-mother	1
40	53	F	41	4.55	-	-	+	+	+	N	+	N	"	? G-mother	3
41	54	M	40	3.0	-	-	+	+	+	-	+	-	"	? G-father	1
	55	M	42	3.1	-	+	+	+	+	+	+	+	"	"	1
42	56	F		3.0	N	+	-	+	+	+	+	N	"	G-father	2
43	57	M	41	3.4	+	-	+	+	+	+	+	+	"	"	1
44	58	F	34	2.2	-	-	+	+	+	+	+	+	"	"	2
45	59	F	38		N	N	-	+	+	+	+	N	"	? G-father	
46	60	M	36	2.0	N	N	-	+	+	-	+	-	"	"	2
47	61	F			N	N	N	N	+	N	+	+	"	G-father	
48	62	M	39	3.1	N	N	-	+	+	+	+	+	"	G-mother	1
	63	M	40	3.9	-	+	+	+	+	N	N	N	"	"	1
49	64	M	40	3.7	N	N	-	+	+	+	N	N	"	"	3
50	65	M	43	3.7	+	-	+	+	+	+	+	+	"	G-mother	2
51	66	F	38	3.2	N	N	-	+	+	+	+	+	"	"	1
52	67	F	40		N	N	+	+	+	+	+	+	? Mother	"	1
53	68	M	40		+	+	+	+	+	+	+	+	?	"	
	69	M	37	2.3	+	N	+	+	+	+	+	+	Father	G-mother	4
54	70	M	40	3.4	-	-	-	-	-	+	-	N			

*Family numbers refer to Fig. 1-3 in subsequent paper, pp. 515 and 516. †See Table V of following article for grading, p. 516.
+ Present; -, absent; N, not noted.

family members were examined for the presence of myotonia and other neurological abnormalities. The presence of lens opacities was investigated by ophthalmoscopy and by a portable slit-lamp microscope (Kowa Ltd.).

Results

Data were obtained on 70 patients with congenital myotonic dystrophy from 53 kindreds. In all but four instances the families were visited personally. A further 9 patients with myotonic dystrophy were excluded because onset was not in the neonatal period or because of lack of details concerning early childhood, and 2 more patients were considered to have myotonia congenita (Thomsen's disease) and were therefore excluded. Details on individual patients and their families are given in Table 1.*

Main clinical features. The incidence of the major clinical features in the newborn period is given in Table II, and is similar to that reported in previous studies. The majority of patients presented as floppy infants with delayed motor development, and in a number of cases no specific diagnosis was made at this stage, erroneous diagnosis being

neonatal life, despite other clear evidence of congenital involvement. Talipes was present at birth in 33 of the 70 patients, varying from a mild degree in which no treatment was required to more severe deformity requiring casts or surgery.

The above features provide positive diagnostic evidence of myotonic dystrophy in the infant in whom it is suspected. Equally important is the absence in infancy of some of the cardinal features of the adult form of the disease, notably the myotonia which is such an obvious clinical sign in most adult or adolescent patients.

TABLE III
Incidence of clinical myotonia

Age group (years)	Present	Absent	% Present
<1	0	4	0
1-5	2	15	12
6-10	9	3	75
11+	25	0	100

Table III shows the incidence of myotonia, elicited clinically by percussion of thenar and limb muscles and by grip, in relation to age at the time of examination. The absence of myotonia during infancy contrasts with its consistent presence in patients in their second decade of life at the time of this study. In no case was there a record of these same patients with myotonia having myotonic symptoms or objectively documented myotonia during infancy. In contrast, myotonia was the major feature during infancy in the 2 patients considered to have myotonia congenita and not included in the present series; in neither of these were other features of myotonic dystrophy present in the patient or in other family members.

Cataract is another feature of adult myotonic dystrophy that is generally absent in the congenital form. One patient in the present series was born with unilateral congenital cataract; no lens opacities were seen in any patient under 10 years of age examined with the portable slit-lamp; the examination in younger children was frequently unsatisfactory, however.

Antenatal abnormalities. Previous reports of children with congenital myotonic dystrophy have given few details about the antenatal period, and in view of the possible involvement of a maternal intrauterine factor the presence or absence of such antenatal abnormalities becomes of considerable significance.

TABLE II

Clinical features in the neonatal period (70 cases)

	Present	Absent	Uncertain
Facial diplegia	61	4	5
Hypotonia	47	7	16
Respiratory problems	33	31	6
Talipes	33	36	1
Delayed motor development	60	3	7

frequent (discussed below). Facial diplegia was a consistent and often striking abnormality, and in only 4 patients was absent. It was frequently visible in early photographs even when other evidence in infancy was lacking.

Respiratory problems occurred particularly during the first days of life; in some cases there was failure to establish adequate respiration immediately after birth; in others apnoeic or cyanotic attacks occurred, being misinterpreted as congenital heart disease in two instances. The possible relation of these respiratory problems with subsequent mental retardation and with the neonatal death of sibs not recognized as being affected will be discussed later. In contrast to these infants, almost one-half of the 70 cases had no evidence of respiratory problems in

*Summarized case histories are available on request from the author.

The presence of congenital talipes in a considerable proportion of cases, discussed previously, suggests *in utero* involvement of affected infants; so to a lesser extent does the presence of static mental retardation. Two other factors, the occurrence of hydramnios and the reduction in fetal movements felt by the mother, were found in the present study and provide more direct evidence. The data on these and other factors are given in Table IV; out of the 54 cases where information

TABLE IV
Intrauterine involvement

	Present	Absent	Uncertain
Hydramnios			
Definite (18)			
Probable (7)	25	29	16
Reduced fetal movements	24	28	18
Talipes	33	36	1
Maternal drug therapy	11	49	16
Maternal infection	8	51	11
Birthweight (kg) (no. = 68)	3.22		
Mean			
SD	0.64		
Gestation (w) (no. = 63)	39.5		
Mean			
SD	2.2		

was available, hydramnios was recorded in 25 pregnancies, being graded as 'definite' (medical record) in 18, and 'probable' (present according to mother) in 7 cases. Hydramnios was severe enough to require amniocentesis in some instances. Reduced fetal movements were noted in 24 out of the 52 pregnancies for which information was available, again supporting the existence of intrauterine muscle involvement.

Other factors studied in pregnancy have proved to be largely negative. The instances of maternal infection in pregnancy (Table IV) are largely accounted for by urinary tract infections (5 cases) and those of drug therapy by antibiotic treatment (6 cases). Neither prematurity nor reduced birthweight were found, suggesting that defective placentation cannot be blamed for the specific features of congenital myotonic dystrophy, in particular the mental retardation.

Associated congenital malformations. Some previous reports of congenital myotonic dystrophy have suggested that there is an increased incidence of other malformations in these children (Pruzanski, 1965). Information on this is given in Table V, those defects in which *in utero* muscle involvement could be considered responsible being

TABLE V
Associated malformations

<i>Possibly attributable to muscle involvement (12)</i>	
Inguinal hernia	2
Undescended testis	4
Congenital dislocation of hip	2
Strabismus	2
Hiatus hernia	1
Torticollis	1
<i>Not attributable to muscle involvement (10)</i>	
Congenital heart defect (unconfirmed)	2
Hydrocephalus	2
Spasticity	1
Blocked nasolacrimal duct	1
Hydronephrosis	1
Congenital cataract	1
Transverse palm crease	1
Cleft lip	1

separated from those which seem to be entirely unrelated. It can be seen that the majority of malformations can be related to fetal muscular development; the present study does not support the existence of a true increase in unrelated malformations in congenital myotonic dystrophy.

Mortality and prognosis. The ages of patients seen in the study varied from under 6 months to over 30 years. The year of birth of patients in the present study is shown in Fig. 1, and the absence of still older patients probably reflects the lack of early data on such patients and the predominantly paediatric mode of ascertainment in this study, rather than their death before this age.

Information was requested and received on past as well as present patients, but only 4 deaths are known to have occurred in the 70 cases studied, 3 occurring in the first year of life. Full necropsy details are available for only one case, whose older brother had already been recognized as having congenital myotonic dystrophy. The younger sib

FIG. 1.—Age distribution of patients with congenital myotonic dystrophy.

was seen by the author 4 hours after birth and died aged 48 hours. Despite investigation for muscle and brain abnormalities (Dr. K. M. Laurence), none could be found.

The prolonged survival of nearly all individuals reaching the age of one year has important practical consequences as to prognosis which parents should be made aware of, particularly in view of the high proportion of patients who subsequently prove to be mentally retarded. No patient in the study had failed to walk or was confined to a wheelchair, and most parents of older cases reported a steady improvement during the first decade of life, but subsequently a gradual increase in muscle weakness and wasting, together with the appearance of myotonia. The outlook remains uncertain, and no patient in the present series had married or reproduced. Likewise no case of completely transient congenital involvement was seen, all individuals of sufficient age having ultimately developed myotonia, progressive muscle wasting, and other features of the adult form of myotonic dystrophy.

Mortality among sibs. Despite the relatively good prognosis for life among patients in the present series, there was heavy infant mortality in the sibs. Excluding the diagnosed cases of myotonic dystrophy who died, 24 deaths occurred in the first year of life in the apparently unaffected sibs, 16% of all live births in the sibships. The overall infant mortality rate for England and Wales in 1965, the median year of birth for patients in the present series, was 19/1000 live births, while the corresponding rates for 1943 and 1972, the outer limits of births in the series, were 49 and 17.2, respectively. Two-thirds of deaths occurred in the first 24 hours of life; only 2 deaths occurred after the first week.

Table VI shows the causes of death of these infants, with further details in Table VII. In 3 of the cases where post-mortem reports were available no conclusive structural changes were found to account for death; no note was made of any muscular abnormality except for the one

instance of diaphragmatic hypoplasia. However, in 8 of the pregnancies hydramnios was present, and 7 infants were born with talipes, suggesting that a significant proportion of these deaths may have been due to unrecognized congenital myotonic dystrophy.

Mental retardation. No attempt at detailed assessment of mental function was made in the present study, but this had been done previously in many cases, while in others an approximate assessment could be made from the need for institutional care to attendance at a school for the educationally subnormal. Of the 70 patients studied 48 were considered to be definitely mentally retarded, while in 9 there was no evidence of mental retardation. In a further 13 the existence of mental retardation was uncertain either because of the young age of the patient or because of incomplete assessment. Fig. 2 shows the distribution of IQ scores where these were available. The

FIG. 2.—Distribution of IQ in congenital myotonic dystrophy.

mean IQ of those tested was 66 (SD 16). Since the results are highly heterogeneous both in method of testing used and in age at testing, they should not be considered as more than an approximate guide.

The incidence of mental retardation in the present series is similar to that previously reported (Dyken and Harper, 1973), but two points deserve further mention. Firstly, the retardation appears to be static and to be present from birth; secondly in this series it is not correlated with the occurrence of definite respiratory problems and possible consequent anoxia in the newborn period. The mean IQ for those cases with neonatal respiratory distress was 66 (SD 15); for those without neonatal respiratory distress the mean IQ was 65 (SD 20).

TABLE VI

Early deaths among sibs (known cases of congenital myotonic dystrophy excluded)

Cause of death	No.
Atelectasis, respiratory distress syndrome*	9
Cerebral haemorrhage, tentorial tear*	7
Prematurity	4
Cot death	1
Congenital eventration of diaphragm	1
Uncertain	4

*2 deaths recorded as due to both cerebral haemorrhage and atelectasis.

TABLE
Neonatal deaths in sibs of patients

Case no.	Family no.	Sex	Age at death	Birthweight (kg)	Gestation (w)	Hydramnios	Talipes
71	4	M	2 d	1.9	36		
72	6	F	Few hours	1.4	36	+	
73	7	M	"		34	+	
74	8	F	2 h	3.3	38	+	
75	9	M	6 h		34		
76	11	F	1 h	3.1	38		
77	11	F	3 d	2.7	36		
78	15	M	Few hours				
79	15	F	"				
80	17	M	1½ h	2.2	34		
81	17	F	Few hours	2.0	34		
82	19	F	15 min	1.4	32	+	
83	19	F	10 h	2.0	37	+	
84	19	F	24 h	2.5	36	+	
85	23	M	4 h	3.2	40		
86	27	M	24 h	3.3	40	+	
87	28	M	11 d	3.2	43		
88	28	F	6 h	4.0	40	+	
89	30	M	2 d	1.6	27		
90	38		45 min	1.6	34		
91	39	F	1½ h		32		
92	40	F	5 d				
93	42	M	3 m	3.4	40		
94	53	F	3 d	1.8	36		

Discussion

The present study confirms the existence of congenital myotonic dystrophy as a clinical syndrome with characteristic diagnostic features, many of which differ from the disease when onset is in later childhood or adult life.

In the present series hypotonia was found to be the dominant feature of those cases presenting in the neonatal period, while clinical myotonia was absent, agreeing with previous reports (Bell and Smith, 1972; Aicardi *et al.*, 1974) in which the disorder was recognized shortly after birth.

Respiratory problems are also a prominent feature of the congenital cases, occurring in almost half of the present series, and accounting for neonatal death in at least 2 cases, apart from the undiagnosed sibs who may have been affected. Hypoplasia of the diaphragm has been recognized

in necropsy reports of 2 fatal congenital cases (Bossen, Shelburne, and Verkauf, 1974; Aicardi *et al.*, 1974) and was present in one neonatal death in an undiagnosed sib in the present study. Diaphragmatic hypoplasia may also have been responsible for the radiographic appearance of diaphragmatic elevation, sufficient to be mistaken for diaphragmatic hernia in one patient, while surgery was actually undertaken for this diagnosis in one of the patients of Aicardi *et al.* Histology of diaphragmatic muscle in one case (Bossen *et al.*, 1974) has shown a marked increase in central nuclei in addition to a diminution of fibre size.

The diagnosis of myotonic dystrophy in infancy may be difficult, especially in the neonatal period. The absence of clinical myotonia may mean that the disorder is not even considered, particularly in those cases where neither parent is already known

VII
with congenital myotonic dystrophy

Necropsy	Cause of death	Details
+	Uncertain Cerebral haemorrhage Prematurity Cerebral haemorrhage	Rapid delivery; hypotonic, cyanosed, bilateral talipes; subtentorial tear with haemorrhage into posterior fossa; no note of muscle abnormality
+	Respiratory distress Cerebral haemorrhage	Bilateral talipes; born severely asphyxiated; extensive tentorial tear and cerebral haemorrhage; no gross abnormality of other internal organs
+	Respiratory distress syndrome	Apnoea at birth; died on respirator; lungs completely unexpanded, congested; other organs normal
+	Uncertain Uncertain Tentorial tear: atelectasis	Lungs atelectatic, 2 small tentorial tears without bleeding; other organs normal
+	Prematurity; atelectasis	Lungs imperfectly expanded; other organs normal
+	Cerebral haemorrhage; atelectasis	Small left-sided intraventricular haemorrhage, pulmonary atelectasis; normal placenta
+	Respiratory distress Cerebral haemorrhage; hypoxia	Small tentorial tear, slight bleeding
+	Cerebral haemorrhage Respiratory distress syndrome	Severe hydramnios; difficult forceps delivery; incomplete aeration of lungs; brain normal; no note of muscle abnormality
+	Congenital eventration of diaphragm	Limp and cyanosed at birth, postural talipes, unable to suck; progressive respiratory deterioration; dome of right diaphragm raised with reduced muscle; lungs poorly aerated, other organs normal, including motor nerve end plates
+	Respiratory failure Prematurity Uncertain Respiratory distress Respiratory failure	
+	Cot death Prematurity	

to be affected. The differential diagnosis at this stage is principally from other forms of infantile hypotonia (Dubowitz, 1969; Tizard, 1974), including the severe Werdnig-Hoffmann type of spinal muscular atrophy, various congenital myopathies (such as central core disease, nemaline myopathy, and myotubular myopathy), and the hypotonia that may be associated with cerebral anoxia or other damage. Even in the absence of a family history of myotonic dystrophy, the combination of hypotonia with facial diplegia and such factors as talipes and hydramnios should allow a clinical diagnosis to be made in most cases; electromyography will exclude the spinal muscular atrophies even if myotonic discharges cannot be shown, while muscle biopsy may likewise distinguish both the spinal muscular atrophies and the congenital myopathies, as well as show the positive features of

congenital myotonic dystrophy discussed below. Careful examination of the mother will confirm the diagnosis of myotonic dystrophy in most cases; however, despite the almost invariable maternal transmission of congenital myotonic dystrophy (see following article), the lack of an affected mother does not rule out the diagnosis since a few paternally transmitted cases, though atypical, do exist (Parker, 1963; Dyken and Harper, 1973). In later infancy delayed motor and mental development are prominent features, and the hypotonia is generally less marked. At this stage, and in later childhood, the facial diplegia is often striking, and may be accompanied by weakness of jaw and palatal muscles. An initial diagnosis of Möbius syndrome was made in 2 of the present patients (Cases 1 and 62). Previous authors (Vanier, 1960; Dodge *et al.*, 1965) have stressed the

possibility of this misdiagnosis, and the heterogeneity of facial diplegia in childhood.

Mental retardation is often the presenting problem in children approaching school age. The present study has confirmed previous reports (Calderon, 1966) that this is usual in myotonic dystrophy of congenital onset, and that it is generally moderate or mild ($IQ > 40$). There is no doubt, however, that some individuals are of normal or near normal intelligence, and in the testing of these children other factors such as facial immobility and speech impairment resulting from involvement of palatal and lip muscles must be taken into account if a correct assessment is to be made. The apparent lack of correlation of mental retardation with neonatal anoxia in the present study differs from that found in the American study of Dyken and Harper (1973) and suggests that the onset of the cerebral defect is likely to be at least in part prenatal; it supports the indications of prenatal muscle involvement from the high incidence of talipes and hydramnios, and from the reduction in fetal movements.

In late childhood and adolescence features of the adult form of the disease usually become apparent, in particular myotonia. Wasting of temporal, sternomastoid, and small hand muscles may be seen, and gradually increasing weakness may develop, contrasting with the general improvement of muscle power noted in most patients during the first decade of life. Diagnosis at this stage is not difficult, though a number of older patients may remain undiagnosed in mental subnormality hospitals (Calderon, 1966). Failure of ascertainment and lack of details from the neonatal period is likely to have resulted in under-representation of such patients in the present series.

Histological and histochemical studies of biopsied muscle in cases of congenital myotonic dystrophy have recently been reported by Karpatis *et al.* (1973), Dubowitz and Brooke (1973), and Farkas *et al.* (1974). The changes were less marked than in the adult disease, and the selective atrophy of type 1 muscle fibres was not always seen. Histochemistry showed a peripheral zone deficient in oxidative enzymes, which was associated on microscopical studies with a lack of mitochondria.

The occurrence of nonmuscular abnormalities in congenital myotonic dystrophy has been noted by some authors (Pruzanski, 1965; Caughey and Myrianthopoulos, 1963; Bell and Smith, 1972). Most of the defects noted in this study and by other workers can, however, be related to a prenatal failure of muscle action and development and there seems no need to invoke a separate teratogenic

mechanism in these cases. Nevertheless, if a maternal factor is operating in the production of the congenital form of the disease, the occurrence of more general abnormalities would not be unexpected, being well documented in the case of offspring of maternal phenylketonurics (Stevenson, 1973).

The occurrence of hydramnios in pregnancies resulting in a child with congenital myotonic dystrophy has been noted previously (Bell and Smith, 1972; Aicardi *et al.*, 1974). Its occurrence in more than one-third of pregnancies in the present series not only indicates the prenatal onset of the disorder but may provide a warning sign in the pregnancies of affected women.

The frequent occurrence of hydramnios should also be considered in interpreting fetal maturity and gestation in these pregnancies, so that the risk of premature induction of labour is not added to the other neonatal problems of congenital myotonic dystrophy. The simplest explanation for the occurrence of hydramnios is a neuromuscular failure in fetal swallowing *in utero*, and evidence supporting this has come from a recent report (Dunn and Dierker, 1973) of a woman with recurrent hydramnios in two pregnancies, in both of which the infant died shortly after birth and in which intra-amniotic injection of contrast medium showed delayed fetal swallowing. Though undiagnosed at the time, the mother was later shown to have myotonic dystrophy, and there is little doubt that the infants were affected with the congenital form of the disease. The occurrence of hydramnios in other neuromuscular disorders of prenatal onset has not been well documented, but it is of interest that it has not been noted in Werdnig-Hoffmann disease, though the incidence of reduced fetal movements is similar in this condition (one-third) to that in congenital myotonic dystrophy (Pearn, 1973).

The incidence of congenital myotonic dystrophy in relation to the adult form remains conjectural. If the present survey represented total ascertainment it would suggest only about 5 affected children born each year in Britain, but the occurrence of unrecognized neonatal deaths and the incomplete, though increasing awareness of the condition among clinicians makes this likely to be a considerable underestimate. Equally unknown is the proportion of children born to all affected women who are congenitally affected; the present study, in which ascertainment was through the children, not the parent, can give no information on this important point. The genetic analysis of the families and its interpretation in the light of the hypothesis of a maternal intrauterine factor are discussed in the following article.

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