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"THE LIMP CHILD"

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The clinical syndrome of congenital hypotonia of the skeletal musculature which Oppenheim (1900) entitled "myotonia congenita", and was subsequently called "amyotonia congenita" by Collier and Wilson (1908), may be produced by a variety of pathological entities. Most such cases show a progressive downhill course similar to that seen in classical cases of infantile spinal muscular atrophy of later onset (Werdnig, 1891; Hoffmann, 1893) and are found to have degenerative changes in the anterior horn cells (Beevor, 1902; Rothmann, 1909; Bibergeil, 1914; Greenfield and Stern, 1927; Grinker, 1927; Sheldon, 1929), although it has been suggested that they may also show an error in development of the upper motor neurone (Burdick, Whipple, and Freeman, 1945). Certain cases also resemble the condition referred to as "arthrogryphosis multiplex congenita" (Stern, 1923) or "amyoplasia congenita" (Sheldon, 1932), which often appears to be due to a similar spinal muscular atrophy beginning in intra-uterine life (Brandt, 1947).

That the disease in some infants with severe congenital hypotonia runs a benign course was first suggested by Oppenheim, and Batten (1910, 1911) believed that these children were suffering from a congenital non-progressive myopathy, a view which received support from Turner's (1940, 1949) follow-up of some of Batten's cases. Furthermore it has become apparent that infantile hypotonia may sometimes be symptomatic of a variety of neurological, skeletal, and metabolic disorders; the many causes of symptomatic hypotonia and their differential diagnosis have been reviewed by Brandt (1950), Tizard (1955), Sandifer (1955), and Walton (1956). Brandt (1950), as a result of an extensive follow-up study of 131 cases previously diagnosed as amyotonia congenita or infantile spinal muscular atrophy, concluded that amyotonia congenita was a syndrome which could result from a variety of diseases—some grave, some benign. After excluding all cases of spinal muscular atrophy and of symptomatic hypotonia he was left with 13 cases, of which six had recovered completely, three had shown striking improvement, three had improved but remained disabled while one had improved but died from pneumonia. Seventeen similar cases are described and discussed below.

MATERIAL AND METHODS

I have reported elsewhere (Walton, 1956) the results of a follow-up study of 109 cases in which a diagnosis of amyotonia congenita had been made previously. Fourteen were obtained from a survey of the records of the National Hospital for the years 1930-54 inclusive and 87 had attended The Hospital for Sick Children between 1940 and 1952. Six cases seen at the Royal Victoria Infirmary during 1951 and 1952 and two observed at the Massachusetts General Hospital in 1953 were added. All accessible surviving cases were examined during 1955, when it was possible to revise the original diagnosis of amyotonia congenita made from two to 25 years earlier. In 67 cases the disease process was clearly one of spinal muscular atrophy; one patient had a benign congenital "myopathy" with myasthenic features (Walton, Geschwind, and Simpson, 1956), three were suffering from progressive muscular dystrophy, and one from polymyositis in a chronic phase. The muscular hypotonia in 20 cases had clearly been a symptom of disease elsewhere than in the neuromuscular apparatus ("cerebral palsy", six cases, mental defect, eight cases, scurvy, two cases, arachnodactyly, one case, multiple congenital defects, one case, congenital dislocation of hip, one case, spinal ganglioneuroma, one case).

There remain a total of 17 cases, of which all but two were seen personally. All were limp, "floppy" children who showed a marked delay in reaching those physical milestones which can be regarded as indicative of increasing muscular activity. Certainly none of these patients are cases of spinal muscular atrophy and none of them have shown signs of the many conditions previously referred to which may give symptomatic hypotonia. Eight of them have recovered completely; the other

nine all showed some improvement in early childhood, but none of them have recovered completely and all show manifestations of a persisting, through non-progressive, muscular disorder, It is suggested that these 17 cases are examples of a distinctive clinical syndrome which may be called "benign congenital hypotonia" and that a subdivision is possible, on the basis of the natural history, into cases with complete recovery and cases with incomplete recovery. These 17 cases are the subject of the present study; two of them (Cases 7 and 8) have been reported previously (Nattrass, 1954); the other 15 are described briefly below. In order to conserve space, all negative observations concerning the patients and their relatives are omitted; for ease of reference the important clinical features of the cases are listed in Table 1.

CASE HISTORIES

A. Cases with Complete Recovery

Case 1.—C. K. was born on July 11, 1944, at term, by a normal delivery; foetal movements were normal. The child always seemed limp and "floppy" and at the age of 6 months, although she seemed to move her limbs freely, she made no attempt to sit or to hold up her head. She tended to slip through the hands and her limbs could be placed in unnatural positions, "as if she were a rag doll". There was little improvement in her activities for some months, but she was intelligent and talked at the normal age. She sat at 15 months, could stand supported at 27 months, and was able to walk a few yards with support soon after her third birthday. At this age she was seen by Dr. W. G. Wyllie at The Hospital for Sick Children; he found generalized muscular hypotonia but the tendon reflexes were normal and he made a diagnosis of amyotonia congenita. A muscle biopsy from one quadriceps showed no significant abnormality. The child remained limp and fell often, but from this time she showed slow improvement and became able to walk longer distances. Even at the age of 8 or 9 years she could not run, fell easily, and had difficulty in climbing stairs. However, in the next two or three years she showed steady improvement and became good at games and physical training.

On examination on September 8, 1955, at the age of 11, the patient was an active, intelligent, cooperative and well-developed child, who walked briskly with a normal gait and could rise quickly from the floor without using her hands. No muscular atrophy, weakness, hypotonia, or joint hypermobility could be demonstrated and there were no abnormal neurological signs.

Case 2.—A. B. was born on April 15, 1947, at term, by a normal delivery; foetal movements were normal. As a small baby he was limp and "floppy" and tended to slip through the hands, although he moved his arms and legs quite well. He held up his head a little at 4 months and could sit if supported at 10 months, but tended to flop limply forwards. He could shuffle a short distance along the floor at 15 months. Mental development was entirely normal. At the age of 2 he was seen by Dr. B. Schlesinger at The Hospital for Sick Children. He could sit firmly unaided but could not stand without support; with help he could pull himself to his feet and, if supported would make walking movements. There was extreme generalized hypotonia of all muscles, with hypermobility of joints, and the deep tendon reflexes were depressed. A diagnosis of amyotonia congenita was made. Soon afterwards the child began to improve and to walk unaided; progress was slow, but by the time he was 4 years old he could go quickly upstairs and at the age of 8 could run faster than his elder brother.

On examination on May 16, 1955, at the age of 8, the patient was active, intelligent and cooperative; he could walk, run, jump, and climb up from the floor briskly. There was no muscular atrophy, weakness, or hypotonia and no hypermobility of joints; the deep tendon reflexes were active and there were no abnormal neurological signs.

Case 3.—M. S. was born at term by a normal delivery on December 12, 1946; foetal movements were normal. He seemed to move his limbs well, but at 9 months old he had made no attempt to sit. His muscles were soft and flabby and a remarkable range of passive movement of his limbs was possible. At 9 months he was seen at The Hospital for Sick Children by Dr. B. Schlesinger, who found that the muscles of the trunk, shoulder, and pelvic girdles were weak, limp, and flabby; when he sat his body slumped forwards and there was a dorsal kyphosis. The deep tendon reflexes were normal. A provisional diagnosis of amyotonia congenita was made. The child improved slowly; he sat up at the age of a year, could crawl at 18 months, and began to walk, though clumsily and with frequent falls, at the age of 2. When seen again in November, 1950, he ran about like a normal boy of his age, but on examination some general muscular hypotonia persisted.

On May 25, 1955, the patient, now aged 9, showed no significant abnormality on examination. He walked briskly with a normal gait, his body and limb musculature was normally developed, there was no hypermobility of joints and the tendon reflexes were normal.

Case 4.—B. T. was born at term by a normal delivery on December 21, 1936; foetal movements were normal. As a baby the patient moved her limbs normally although all physical milestones were delayed and her limbs always seemed loose and limp. She sat at 1 year, crawled at 18 months, and first walked, though clumsily, at the age of 2. She tended to waddle and to fall frequently and had difficulty in rising from the floor. She could not walk upstairs until she was nearly 5 years old. She went to school at the normal age and showed slow but steady improvement. She was seen at The Hospital for Sick Children by Dr. W. G. Wyllie in 1945 at the age of 9. Dr. Wyllie found a moderate dorsal kyphoscoliosis; there was weakness and hypotonia of thigh and pelvic girdle muscles, but the tendon reflexes were normal. A diagnosis of amyotonia congenita was made. The child wore a spinal cast for a year, and improved slowly. An electromyogram in February, 1950, revealed

TABLE I

OUTLINE OF 17 CASES OF BENIGN CONGENITAL HYPOTONIA

Case No.	Sex	Age at Time of Follow-up	Clinical Features in Infancy: Muscular Weakness	Hypotonia	Hypermobility at Joints	Respiratory Weakness	Muscular Atrophy	Tendon Reflexes	Contractures, Skeletal Deformity	Associated Abnormalities	Investigations: E.M.G.	Muscle Biopsy	Natural History: Sat Up at	Walked at	Progress	Follow-up State
A. With Complete Recovery																
1	F	11	+	++	++	—	—	Normal	—	—	—	Normal	15 mth.	3 yr.	Improved—normal aged 10	Normal
2	M	8	+	+++	++	—	—	Depressed	—	—	—	—	10 mth.	2– yr.	Improved—normal aged 8	Normal
3	M	8	+	++	++	—	—	Normal	Kyphosis	—	—	—	1 yr.	2 yr.	Improved—normal aged 7	Normal
4	F	18	+	++	±	—	—	Normal	Kyphosis	—	Excess polyphasic potentials	—	1 yr.	2 yr.	Improved—normal aged 12	Normal
5	F	6	+	++	++	—	—	Normal	—	—	—	—	1 yr.	2 yr.	Improved steadily	Normal
6	M	13	+	+	±	—	—	Normal	—	Bilateral inguinal herniae	—	—	1 yr.	2 yr.	Improved—normal aged 7	Normal
7	F	16	+	++	++	—	—	Depressed	—	—	—	—	1 yr.	2 yr.	Improved—normal aged 12	Normal
8	F	18	++	±	±	—	±	Depressed	—	Webbed hands and feet	Excess polyphasic potentials	Normal	6 mth.	10 mth.	Walked clumsily, slow improvement	Normal
B. With Incomplete Recovery																
9	M	6	++	+++	+++	+	+	Absent	Kypho-scoliosis	—	—	Normal	3 yr.	5 yr.	Slow improvement but moderately disabled	Small muscles, general hypotonia
10	M	5	++	++	++	+	+	Absent	—	—	—	—	1 yr.	20 mth.	Slow improvement but moderately disabled	Muscles thin flabby, hypotonic—particularly proximal limb muscles
11	F	17	++	++	++	—	+	Absent	—	—	—	Normal	15 mth.	2½ yr.	Slow improvement — none since age of 15	Small, hypotonic muscles, shambling, awkward gait
12	M	30	++	++	±	—	+	Depressed	—	Bilateral inguinal herniae	Excess short-duration potentials	Normal	18 mth.	4 yr.	Slow improvement up to adolescence; no change since	All muscles small and weak, particularly proximal muscles of limbs. Slight hypotonia
13	M	6	++	+++	++	—	+	Normal	Genu recurvatum	—	Excess short-duration potentials	Normal	10 mth.	20 mth.	Slow improvement: recent arrest	Muscles generally small, weak, hypotonic
14	F	15	++	+++	+++	—	+	Depressed	Contracture tendo Achillis	—	—	—	10 mth.	2½ yr.	Slow improvement up to 12 years, no change since	All proximal muscles small and weak, some hypotonia
15	M	10	++	+++	+++	+	+	Depressed	Genu valgum	—	—	—	10 mth.	20 mth.	Improved up to a point	Proximal muscles small and weak, hypotonia at hips
16	F	53	++	++	++	—	+	Normal	Kypho-scoliosis	—	—	—	1 yr.	3 yr.	Slow improvement but moderately disabled	All muscles small and weak, some hypotonia
17	M	10	++	++	±	—	+	Depressed	—	—	Excess short-duration potentials	—	7 mth.	18 mth.	Slow improvement but moderately disabled	All proximal limb muscles small and weak, slight hypotonia

an excess of polyphasic potentials during voluntary contraction of the left quadriceps.

The patient was seen on May 29, 1955, at the age of 18. Slight difficulty in walking and climbing stairs had continued up to the age of 15, but then she gained strength rapidly. She was now as active as a normal girl of her age. On examination she was an intelligent girl who walked well with a normal gait and rose briskly from the floor. There was no muscular atrophy or hypertrophy, no hypotonia or hypermobility of joints, and all muscle groups in the trunk and limbs were normally powerful. The deep tendon reflexes were present, although the knee jerks were slightly depressed.

Case 5.—D. C., a girl, was born at term by a normal delivery on September 21, 1948; foetal movements were normal. She seemed to move her limbs freely, but at the age of 6 months she made no attempt to sit up and when placed in a sitting position she slumped forwards. Her limbs were loose, limp, and unusually mobile and the trunk muscles flabby. She was seen at the age of 8 months by Dr. P. R. Evans at The Hospital for Sick Children; moderate generalized hypotonia was noted but the tendon reflexes were present and equal. When a year old she was able to sit but her head tended to loll and she made no attempt to stand or crawl. The cerebrospinal fluid at this time was normal. Shortly afterwards the child began to improve and at 1 year and 10 months she could walk a few steps, though clumsily and with frequent falls. When 3 she walked and ran quite well, but could not keep up with other children of her own age. She still fell frequently and had difficulty in climbing stairs. Hypotonia of the limbs persisted.

The patient was seen on June 1, 1955, at the age of 6½. She now walked well, though there was slight difficulty in climbing a long flight of stairs. She played games and took an active part in physical training. On examination she was active, intelligent, and cooperative; she walked and ran normally and could rise briskly from the floor. There was no muscular wasting, weakness or hypotonia and no hypermobility of joints; the tendon reflexes were normal.

Case 6.—T. S. (N. H. Case 14009), a boy, was born at term by a normal delivery on June 18, 1942; foetal movements were good. All physical milestones were late; the child did not sit until he was 1 year old and did not walk until after the age of 2. His limbs were limp and flabby, but hypermobility of joints was not noted. In infancy he had bilateral inguinal herniae which resolved spontaneously. He was seen by a paediatrician who diagnosed amyotonia congenita. When he began to walk, he did so " on his toes " and had difficulty in rising from the floor. He soon became able to walk and run better but could not keep up with children of his own age. He was seen at the age of 7 by Dr. E. A. Carmichael at the National Hospital, when it was noticed that he walked with a slight waddle and made use of his hands in order to rise from the floor. There was some exaggeration of the lumbar lordosis and also bilateral genu valgum. There was a moderate reduction in power of all shoulder girdle and upper arm muscles, and some weakness of hip flexion and of dorsiflexion of the feet. All tendon reflexes were present and equal. The muscles were generally flabby but hypotonia was not severe.

The patient was seen on April 7, 1955. Since the age of 7 he had improved steadily and now walked, ran, climbed stairs, and played games as well as a normal child of his age. On examination he appeared to be a healthy, intelligent, and active child; there was no muscular wasting, weakness, or hypotonia, and no abnormal neurological signs were found.

Cases 7 and 8.—These two cases have been reported by Nattrass (1954) and will not be described in detail. Both were girls; A. T. (Case 7) was a limp, " floppy " baby who walked late and showed generalized hypotonia. When examined at the age of 16 she had recovered completely. J. W. (Case 8) had symptoms of pelvic and shoulder girdle muscular weakness; however, as in Case 6, hypotonia was never profound; she, too, recovered completely. An electromyogram showed an excess of polyphasic potentials with a shift to the right on automatic frequency analysis, and a muscle biopsy showed changes suggestive of myopathy; on review of the sections, however, much of the apparent abnormality appears to have been artefact and the muscle is probably within normal limits. It was suggested previously (Nattrass, 1954) that these two cases were possibly examples of benign congenital myopathy. However, in view of their complete recovery it seems that A. T. certainly, and J. W. probably, should be regarded as examples of benign congenital hypotonia with complete recovery.

B. Cases with Incomplete Recovery

Case 9.—R. D., a boy, was born on June 28, 1949, at term, by a normal delivery; foetal movements were normal. Next day, all four limbs were noted to be oedematous, loose and floppy and this weakness persisted. At 2 months he was seen by Mr. E. Lloyd at The Hospital for Sick Children, and was admitted to hospital. The muscles of the trunk and limbs were limp and flabby and there was striking hypermobility of all joints. Movement of the thoracic cage was poor. Despite the generalized hypotonia the baby could put his hand to his mouth and could kick. All the deep tendon reflexes were absent. Mr. Lloyd diagnosed amyotonia congenita, Dr. W. G. Wyllie Werdnig-Hoffmann disease. A muscle biopsy from the right pectoralis major was normal on section. In December, 1949, and again in January, April, and July, 1950, the patient developed severe respiratory infections, each of which responded to penicillin. He was seen again in December, 1950, and was still weak and flabby and could not sit, though he moved his limbs freely. In September, 1952, he could sit without support but tended to slump and had developed a dorsal kyphoscoliosis, for which a plaster jacket was supplied. In August, 1953, he was stronger, but still unable to walk. He was admitted to a residential school of the Shaftesbury Society on May 7, 1954, wearing a spinal jacket and below-knee calipers and sleeping in a plaster bed at night. Soon afterwards he began to walk unaided (at the age of 5) and discarded the calipers; he became able to walk long distances, to climb stairs, and to dress and feed himself.

On examination on August 8, 1955, at the age of 6 years he was a thin but intelligent child. He walked with a slight waddle and with bilateral genu valgum. He could not sit up from the supine position or rise from the floor unaided. There was a marked dorsal kyphoscoliosis and some accentuation of the lumbar lordosis on standing. The muscles of the limbs and trunk were uniformly small and felt flabby; the sternomastoids were particularly thin. The facial muscles moved normally, as did those of the eyes, tongue, palate, and pharynx. No fasciculation was seen. There was striking generalized hypotonia of all limbs, and a remarkable range of movement of all joints; the fingers could be turned back to touch the dorsal surface of the forearm and the foot could be dorsiflexed so that the toes touched the anterior surface of the leg. There were no contractures. Muscular coordination was good; the deep tendon reflexes were present but uniformly sluggish.

Case 10.—J. F., a boy, was born at term by a normal delivery on December 11, 1950. It was noted immediately that his limb movements were not vigorous. At 6 months he was unable to support his head and made no attempt to sit; all the muscles were loose and flabby. He was seen at the age of 8 months by Dr. W. G. Wyllie at The Hospital for Sick Children and a diagnosis of amyotonia congenita was made. The limbs and trunk showed striking hypotonia, there was hypermobility of all joints and the tendon reflexes were absent. The child's cough was feeble, intercostal movement was poor, breathing was almost entirely diaphragmatic, and there was recession of the lower ribs on inspiration. In October, 1951, the boy could support his head. At 1 year he could sit unsupported and his breathing had improved. He began to walk at 20 months, though weakly and clumsily with frequent falls. Subsequently there was slow but steady improvement. He was re-examined early in 1954 and still had small, hypotonic muscles. The family emigrated to Canada in late 1954 but in May, 1955, they reported that the child could now walk about 300 to 400 yards unaided, although his limbs were thin and his muscles remained small and flabby.

Case 11.—E. K., a girl, was born at term by a normal delivery on September 2, 1938. From birth it was noted that her muscles seemed weak and she did not move her limbs as well as a normal child. She did not sit up until she was 15 months old; she began to walk at the age of 2½ years, but was clumsy and fell frequently. She improved slowly but her muscles remained thin and weak. In 1944 she was seen in Vienna by a paediatrician and a neurologist who diagnosed amyotonia congenita. She came to London in 1947 and was seen by Professor A. Moncrieff at The Hospital for Sick Children. She was found to be bright and intelligent but had a shambling, awkward gait. All muscles of the limbs and trunk were small and flabby and there was hypermobility at the wrist, hip, and ankle joints. All tendon reflexes were absent. A muscle biopsy revealed no abnormality. In 1951 the family emigrated to the U.S.A. In 1955 they reported that the child had shown some further improvement in muscular power although her muscles remained small, weak, and flabby and she still had considerable difficulty in walking long distances, in lifting objects, and in climbing stairs.

Case 12.—P. T., a boy, was born at term by a normal delivery in 1925; foetal movements were normal. He had bilateral inguinal herniae at birth, and his limbs were loose and " floppy ". He did not sit until he was 18 months old and first walked, though clumsily, at the age of 4. At the age of 5, his arms were weak, he walked poorly and fell often, and had to be pushed about in a wheel chair. He had particular difficulty in climbing stairs and was never able to run or jump, although during childhood and adolescence there was some improvement. Subsequently, he became able to walk moderate distances and to climb stairs, but still had a tendency to trip and fall. For many years his condition remained stationary and he was able to work as a taxi driver.

On examination on July 16, 1955, at the age of 30, he walked with a distinct waddle and with an increase in the lumbar lordosis. He had great difficulty in climbing stairs and in rising from the floor and there was a striking contrast between his thin limbs and obese trunk. All muscles were uniformly diminished in size but there was no focal atrophy and no fasciculation. There was slight weakness of the orbicularis oculi but the lower facial and neck muscles were strong; the sternomastoids were weaker than the posterior neck muscles. All limb muscles were uniformly weak but this weakness was greater in the proximal groups; the muscles below the knee were more powerful. There was a moderate increase in passive mobility at the hip joints. All tendon reflexes were present but were uniformly depressed. An intramuscular injection of 1·5 mg. prostigmine gave abdominal colic and muscular fasciculation but no improvement in strength. An electromyogram from the left biceps muscle revealed no spontaneous activity, but on volition there were numerous polyphasic and motor unit potentials of short duration, as well as some potentials of normal duration. A muscle biopsy taken in March, 1955, at the Royal South Hants Hospital, where the patient was admitted under the care of Dr. G. S. Graveson, revealed no abnormality.

Case 13.—W. G., a boy, was born at term by a forceps delivery on August 18, 1947; foetal movements seemed somewhat weak. The child seemed lethargic, and at 6 months old he made no attempt to sit up. His muscles seemed weak and flabby, his limbs could be put into unusual positions, he tended to slump when sat up, and his head " lolled ". He sat first at the age of 10 months and took a few steps unaided at 20 months, but fell frequently and had difficulty in rising. He was seen, aged 4, at the Boston Children's Hospital by Dr. Bronson Crothers, who diagnosed amyotonia congenita. Subsequently, though continuing to fall, he became able to walk more briskly and to climb stairs, though with difficulty.

On examination on June 9, 1953, at the Massachusetts General Hospital, all the muscles of the trunk and limbs were small. The boy could not sit up from the supine position unaided and on rising from the floor he climbed up his legs. He walked well but with some accentuation of the lumbar lordosis. The facial and neck muscles

were good, but those of the limbs and trunk were uniformly reduced in bulk and power. There was marked generalized hypotonia, with considerable hypermobility of all joints; genu recurvatum was seen on standing. All tendon reflexes were active and equal. An electromyogram gave some occasional bizarre repetitive discharges on probing with a concentric needle electrode, but there was no other spontaneous activity. On volition the interference pattern was full and contained many normal motor unit action potentials, but in addition there were excessive polyphasic potentials and others of short duration. The urinary creatine output was 0·325 g. in 24 hours. A muscle biopsy from the right deltoid was normal histologically.

Case 14.—J. Y., a girl, was born one month prematurely by a normal delivery on September 8, 1940. Although weighing only 3 lb. 12 oz. she thrived, but from birth was limp and floppy " as though she had no bones ". She sat up at 10 months and walked when 2½ years old, but was clumsy and fell frequently. She improved slowly but her limbs were always loose, limp, and hypermobile, and she was unable to run, jump, or play games. She was seen at The Hospital for Sick Children, by Dr. W. G. Wyllie, in August, 1947. Dr. Wyllie found marked hypotonia of all muscles of the limbs and trunk with striking hypermobility of the joints. All muscles were small and those of the neck, upper arms, trunk, and thighs were particularly weak. The tendon reflexes in the arms were depressed and those in the legs were present only on reinforcement. There was bilateral pes cavus and some shortening of the tendo Achillis.

When seen at home on September 7, 1955, the patient had improved and could walk long distances. She fell infrequently and could run a little but had considerable difficulty in going upstairs. At the age of 11 both tendons of Achilles were lengthened at operation with benefit. The patient was the eldest of three children and the other two were normal. One daughter of a paternal great-aunt had died at the age of 21 of " muscular dystrophy "; a grand-daughter of the same aunt had had some form of muscular weakness all her life in a much milder form, but could not be traced.

On examination the patient walked with a distinct waddle and with accentuation of the lumbar lordosis. She was unable to rise from the floor without using her hands, and could not lift her head from the pillow or sit up from the supine position. There was symmetrical weakness of the facial muscles but no ptosis and the ocular movements were full. Both sternomastoids were weak and atrophic but the posterior neck muscles were relatively strong. All the muscles of the shoulder girdles and upper limbs were small and weak; weakness was more marked in the proximal groups. The abdominal and spinal muscles were also small and weak, as were those of the thighs and the anterior tibial group but the calf muscles were normal. There was some persisting hypotonia and passive hypermobility of joints, particularly at the hips. The upper limb reflexes and knee jerks were depressed but the ankle jerks were normal.

Case 15.—R. S. (N. H. Case 12794), a boy, was born at term by a normal delivery on January 10, 1945; foetal movements were normal. The child showed active spontaneous limb movements but did not sit until he was 10 months old and could almost " be tied in knots ". He began to walk a few paces at 18 months but was clumsy and fell frequently. He was admitted to the National Hospital under the care of Dr. Denis Williams in November, 1948, when it was found that he walked with an increased lumbar lordosis and could not negotiate stairs. There was striking hypotonia of all skeletal muscles in the limbs and trunk with marked hypermobility at the joints. The muscles were generally small and weak. The patient coughed poorly and there was some recession of the lower chest wall during inspiration. A diagnosis of amyotonia congenita was made. Subsequently, the child's walking and strength improved but he continued to have difficulty in climbing stairs and in rising from the floor.

On examination on April 21, 1955, at the age of 10 he walked with a waddle and rose from the floor by climbing up his legs. The upper limbs showed diffuse atrophy and decrease in strength of all muscles but no hypotonia. The neck muscles were good. In the lower limbs there was marked hypotonia of muscles about the hip joint, with an excessive range of movement at this joint. All the muscles of the lower limbs, but particularly the hip flexors and anterior tibial group, were small and weak. All tendon reflexes were depressed.

Case 16.—W. I., a girl, was born at term by a normal delivery in 1902. She was always a loose, floppy baby, was late in holding up her head and in sitting and did not walk until she was 3, when she did so with a waddle, fell frequently, and had difficulty in rising. After a few years of improvement the muscular weakness had continued unchanged. She always had difficulty in climbing stairs, but had been able to do housework. She was admitted to the National Hospital in May, 1939, under the care of Dr. Hinds Howell, when it was noted that she walked with a waddle, that there was striking hypotonia of the muscles of the limbs and trunk, and that all the skeletal muscles seemed to be weak and small; all tendon reflexes were present. No muscle biopsy was performed; a diagnosis of amyotonia congenita was made.

When seen at home on June 11, 1955, at the age of 53, there had been no deterioration in her muscular condition. On examination she was thin, walked with a waddle and accentuation of the lumbar lordosis; she could not sit up from the supine position unaided, and had to lift her legs on to the bed with her hands. There was a moderate dorsal kyphoscoliosis. She had considerable difficulty in lifting her head from the pillow and could not rise from the floor unaided. There was no fasciculation. The upper facial muscles were weak, the sternomastoids almost absent, but the posterior neck muscles were good. In the shoulder girdles and upper limbs all muscles, including the hand intrinsics, were small and weak. The abdominal and spinal muscles were also involved and there was diffuse muscular atrophy and weakness in the lower limbs. There was slight hypotonia of all muscles with some hypermobility at the joints but there were no contractures; the deep tendon reflexes were generally brisk.

Case 17.—P. S., a boy, was born at term by a normal delivery on May 14, 1945. He moved his arms and legs normally but the muscles were flabby and soft and he tended to slip through the hands. He sat at 7 months, stood at 11 months, and walked at 18 months, but his gait was clumsy and he tended to fall frequently; after falling he could not get up by himself. Soon afterwards, his arms and legs became thin and the muscles looked small. He was seen at the age of 3 by a paediatrician who diagnosed amyotonia congenita. From the age of 5 he improved slightly, began to run, though clumsily, and to climb stairs unaided.

On examination in June, 1952, in the Royal Victoria Infirmary, he was an intelligent and cooperative boy who walked with a waddle; on rising from the floor he climbed up his legs. He was unable to lift his head from the pillow or to sit up from the supine position. The muscles were generally limp and flabby and there was an unusual degree of passive mobility at the hip joints. The facial, ocular, and posterior neck muscles were normal, but the sternomastoids were weak. The muscles of the trunk and limbs were generally small and weak, but the proximal groups were more severely affected. The tendon reflexes were all present, but depressed. An electromyogram from the right tibialis anterior and right biceps showed no spontaneous activity in either situation. Volitional activity from the tibialis anterior was normal but the record from the right biceps showed an undoubted excess of polyphasic and potentials of short duration, although others of normal duration and amplitude were seen. When re-examined in December, 1955, the patient had increased his activities further, but there was no objective change.

DISCUSSION

Case Commentary

It may now be of interest to consider collectively the clinical manifestations of the syndrome which affected the above 17 patients. The cases which recovered completely will be considered separately from those in which there was residual weakness.

Foetal movements were normal in all of the patients who recovered completely. They were, however, limp, flabby babies; although muscular hypotonia varied in severity and distribution, it was usually generalized and remarkable degrees of passive movement of joints were possible. Spontaneous movements of the limbs were good, though apparently less powerful and effective than those of a normal child. All but one of these patients were late in sitting up and in walking; when they did walk, they were clumsy, fell frequently, and showed other evidence of muscular weakness, particularly of the trunk and pelvic girdle muscles. There was generally some accentuation of the lumbar lordosis, while two infants developed a moderate dorsal kyphosis. Weakness of the respiratory muscles was not a feature. The deep tendon reflexes were always present, though sometimes depressed. These children showed normal intellectual development and there were no other congenital abnormalities, save for one patient who had bilateral inguinal herniae at birth. Electrical testing of limb muscles in five of these cases, using the classical faradic-galvanic method, revealed no abnormality; in two cases, however, an electromyogram showed excessive polyphasic potentials and others of short duration during voluntary contraction. Muscle biopsy was performed in two cases only; in both, satisfactory specimens were obtained and sections stained with haemalum and eosin showed no abnormality. The progress shown by these patients was uniform. In each of them, the strength of the muscles improved steadily; they gradually became able to run, jump, and to climb stairs as well as other children of the same age and all evidence of hypotonia and joint hypermobility disappeared. They had all recovered completely at some time between the ages of 5 and 15 years.

The initial history of the cases with incomplete recovery was similar, but symptoms were generally more severe and foetal movements were reduced in one case. These children too, were limp, flaccid babies; although hypotonia varied in extent and severity from case to case it was usually generalized and there was a striking increase in the range of passive movement at the joints. Again, however, spontaneous movements of the limbs were often surprisingly good, considering the severe hypotonia. The deep tendon reflexes were absent in three cases, depressed generally in four, normally active in one case, and unusually brisk in another. One patient had bilateral inguinal herniae at birth, but associated congenital abnormalities were uncommon. Three patients showed intercostal weakness; breathing was mainly diaphragmatic, and all three suffered repeated episodes of respiratory infection in infancy. The patients were late in sitting up and did not walk until between the eighteenth month and the fifth year of life. Usually, the degree of physical retardation and the muscular disability were more severe than in the patients who recovered, while improvement was often slower and began later. Intellectual development, however, was always normal. These children, too, were even more clumsy and unsure when they did begin to walk; some were unable to climb stairs unaided for many years. In all of them, symptoms of muscular disability, indicating general muscular weakness, but particularly of the girdle and proximal limb muscles, has persisted to the present day; the patients are now aged between 6 and 53 years. It is possible that some of the children may yet recover but their recent progress has made this seem unlikely. After improving slowly at first, muscular weakness in this group of cases has seemed

to be stationary, often over a period of many years. Two patients have developed permanent kyphosis or kyphoscoliosis in the dorsal region, two have moderate genu valgum or recurvatum, and one some contracture of both tendons of Achilles; in general, however, muscular contractures and severe skeletal deformity are not prominent features of this syndrome. On examination in 1955, despite the differing ages of the subjects (between 6 and 53 years), the clinical manifestations were similar in all cases. There was always some persisting hypotonia and hypermobility of joints, usually seen best as an increase in the range of passive movement at the hips, though similar excessive movement was often seen at the knees, wrists, and ankles too. The residual hypotonia was most severe in the children, while in the patients aged 30 and 53 it was slight. All patients showed some abnormality of gait, tending to walk with a waddle and with some accentuation of the lumbar lordosis; they all had difficulty in climbing stairs, in sitting up from the supine position, and in lifting heavy objects. Every patient showed a remarkable diminution in bulk and general weakness of the skeletal musculature; the limbs were often particularly slender but in some cases the weak trunk muscles were hidden by excessive subcutaneous fat. Sometimes, as in Case 16, muscular weakness was uniform throughout the trunk and limbs but in other cases it was selectively greater in certain muscle groups; thus the upper facial muscles were weaker than the lower in two cases, while the sternomastoids were often severely affected, the posterior neck muscles being stronger. Furthermore, reduction in strength in the trunk and proximal limb muscles was often more severe than in the distal muscles, but selective involvement of individual muscles and muscle groups as observed in progressive muscular dystrophy was not seen and there was certainly no pseudohypertrophy. Electrical testing of affected muscles in four cases, by the classical faradic-galvanic method, showed no abnormality, but electromyography, which was carried out in three cases, revealed an excessive proportion of polyphasic potentials and others of short duration. Confirmatory evidence was obtained in one case by automatic frequency analysis (Walton, 1952); this showed a shift to the right of the dominant frequency. Despite this finding, sections of muscle obtained by biopsy in four cases, when stained with haemalum and eosin, revealed no abnormality. Although the muscle fibres were often somewhat slender, they did not measure significantly less than the normal in diameter and there was no undue variation in size, no degeneration of fibres, and no infiltration with inflammatory cells, fat, or connective tissue. Indeed, in all cases the muscle sampled, though reduced in overall bulk, showed no other significant macroscopic or microscopic abnormality.

It may be suggested that the children who recovered were suffering from a different disease from those who did not, but my observations have led me to believe otherwise. The initial history in cases of the two groups was strikingly similar, although the clinical manifestations were more severe and development was usually more seriously delayed in those of the second. However, it is apparent that in early infancy accurate diagnosis would be impossible and even after several years it was sometimes difficult to be certain whether complete recovery was likely or whether some disability would persist. Indeed the clinical uniformity and the identical findings on electromyography and muscle biopsy have led me to conclude that whether or not recovery occurs, all cases of this type are examples of a clinical syndrome which may reasonably be called " benign congenital hypotonia ". It will now be important to consider the relationship of this syndrome to disorders previously described.

Past and Present Concepts

The cases which recovered correspond closely to the description of " essential or primary hypotonia in young children " given by Sobel (1926). He reported 45 cases, which were brought to hospital because of delay in standing or walking and were said to show a " muscular and joint atony ", without the presence of " any basic physical or mental disturbance ". There was no apparent motor weakness, but hypotonia was severe. There was often kyphosis and scoliosis and in some cases respiratory difficulty. Many of Sobel's cases recovered in later childhood, but others had hypermobility of joints throughout life, and it seems that he probably included two separate disorders in his group of cases. He refers to Finkelstein's (1916) description of a child who had an unusual mobility of all joints, but no muscular weakness. The hips were chronically subluxated and could be dislocated and reduced at will; Finkelstein suggested that there was no muscular abnormality in his case but that the joint ligaments were congenitally lax. A similar case was described by Jahss in 1919, while in 1927, Key described a family with several affected males. These patients showed a striking hypermobility of all joints (as in contortionists), which persisted throughout life, but there was no muscular weakness or physical handicap. Sturkie, in 1941, reported a similar family, while Sutro (1947) reported five isolated cases, all with powerful muscles, and all seen between the ages of 18 and 35. Many authors

(Ford, 1952; Lidge, 1954) have classified congenital hypotonia and congenital laxity of the ligaments together. Certainly it is probable that Sobel included some cases of the latter type in his series; however, my observations suggest that benign congenital hypotonia, a condition which was probably responsible for the clinical manifestations in the remainder of Sobel's cases, is a separate disorder. Ford's Case 1, many of Brandt's (1950) 13 cases which ran a benign course, and the patient with " le retard dans l'apparition du tonus " described by Arthuis (1954) were probably of this type. These babies show marked muscular hypotonia in infancy and hypermobility of the joints is a secondary phenomenon; they also have symptoms and signs of muscular weakness, but eventually recover spontaneously. In congenital laxity of the ligaments, on the other hand, muscular weakness is not seen, hypermobility of the joints (as in contortionists) persists throughout life, and the condition may be inherited.

Turning now to the group of cases which recovered incompletely, they resemble Batten's (1910) description of " simple atrophic myopathy " and Turner's, (1940, 1949) " congenital myopathy ". A case of this type has recently been reported by Richter and Humphreys (1955). Turner's cases all presented with the clinical picture of amyotonia congenita in infancy but many years later they showed signs suggestive of a non-progressive myopathy, with marked atrophy and weakness, particularly of certain proximal limb muscles. The cases in the present report correspond even more closely to the " congenital universal muscular hypoplasia " described by Krabbe (1946). Krabbe's case was reported again by Brandt (1950) and another has been described by Ford (1952). These two cases, which appear to be the only ones recorded, were limp, hypotonic babies and were late in sitting up and in walking. In later childhood, the muscles were seen to be reduced to a fraction of the normal bulk; a striking range of passive joint movement was still possible and the tendon reflexes were sluggish. The mother of Ford's case appeared to be similarly affected and her muscular condition has remained stationary throughout life. A muscle biopsy taken from the child showed no abnormality. As Ford remarked, this condition is very like Turner's congenital myopathy, except for the fact that in one of Turner's cases muscle removed at necropsy showed focal degeneration of muscle fibres, changes which were interpreted as being myopathic in nature. However, Turner's patient was suffering from bacterial endocarditis and died after a long period of recumbency; it is possible that the histological abnormality resulted from the terminal disease and not from the long-standing muscular disorder. It seems that Krabbe's " congenital universal muscular hypoplasia ", Turner's " congenital myopathy " and " benign congenital hypotonia with incomplete recovery " may be closely related, if not identical, and that muscle taken from such a case will usually show no significant abnormality if studied by means of conventional histological techniques. Certainly there is no convincing evidence to suggest that these patients are suffering from a true myopathy or muscular dystrophy. Progressive muscular dystrophy may rarely present with the clinical picture of amyotonia congenita in infancy (Arthuis, 1954; Walton, 1956), but in such cases the muscular histology is typical of dystrophy and the patients show progressive deterioration.

The differential diagnosis of cases of infantile hypotonia has been considered elsewhere (Walton, 1956) and will not be detailed here. The relatively good spontaneous mobility of the limbs and the retention of deep reflexes which most cases of benign hypotonia show may be of great value in diagnosis from infantile spinal muscular atrophy. However, in cases of doubt, electromyography and muscle biopsy, which usually give unequivocal findings in spinal atrophy, will be justified as these conditions differ greatly in prognosis. Differentiation from cases of symptomatic hypotonia may be made through recognition of signs of the primary disease, but more often this distinction, as with that between the cases of benign congenital hypotonia which will recover and those which remain disabled, must depend upon repeated clinical observations over a prolonged period.

The Essential Pathology

Apart from histological and electromyographic evidence in a small proportion of the cases reported above, little information is available to indicate the nature of the congenital abnormality or pathological process responsible for the clinical syndrome of benign congenital hypotonia. Hence the suggestions made below are largely speculative and inferential.

It is apparent that the fault must lie either in the central nervous or peripheral (muscle spindle) mechanisms responsible for the control of muscle tone, or in the motor neurons, end-plates, or muscles. Arthuis (1954), who called the syndrome " le retard dans l'apparition du tonus ", clearly believes that it is due to late maturation of the pathways controlling tone, but the condition of the patients in this series who recovered incompletely, as well as the small amount of electromyographic evidence, points to a more peripheral neuromuscular origin.

Clearly the condition is different from the commonly-occurring types of muscular dystrophy (Walton and Nattrass, 1954), while it is evident that polymyositis could not be the cause, even though this disease in infancy may rarely give a clinical picture like that of amyotonia congenita (Bovet, 1936). Adams, Denny-Brown, and Pearson (1953) have suggested that some cases of recovery from amyotonia congenita may have been examples of infantile polyneuritis, but the cases in the present series with persisting disability show no evidence of peripheral nerve disease, and in one case the cerebrospinal fluid protein content was normal at the height of the disease. Myasthenia gravis can also be excluded as a cause, although a similar case with myasthenic features has been described (Walton *et. al.*, 1956); in Ford's (1952) case, and in three cases of this series, prostigmine had no effect on the muscular weakness.

Electromyography was carried out in five of the 17 cases, and invariably revealed an excessive proportion of polyphasic and short-duration potentials during voluntary contraction. This type of abnormality is characteristically seen in myopathic disorders (muscular dystrophy, polymyositis), in which the number of muscle fibres in each motor unit is progressively reduced. Yet in six cases, including three of those subjected to electromyography, muscle biopsy specimens were normal. Perhaps in these infants the number of muscle fibres in each motor unit was less than the normal number from birth. It may be significant that Coërs and Pelc (1954), who studied a single case which was probably of this type, found that the motor end-plates, when stained intravitally with methylene blue and with Koelle's cholinesterase technique, were abnormal. Instead of the usual terminal arborization of the nerve fibre, leading to a relatively complex end-plate, the terminal fibre was single and the end-plates consisted of a single " button ". The authors suggested that the neuromuscular apparatus was " immature ". Two similar cases are referred to by Woolf and Till (1955). It seems possible that cases of " benign congenital hypotonia " may be the result of an abnormality in neuromuscular development; the child may be born with immature motor units, perhaps populated with less than the normal number of muscle fibres. In some cases this abnormality is relatively slight and is overcome gradually by the processes of post-natal development so that the children eventually recover completely, but in other instances the defect is too severe for this process of natural compensation and the patients have small, weak muscles throughout life. In an important recent contribution, Shy and Magee (1956) report five cases, all occurring in one family, in which the clinical manifestations were identical with those noted in many of the cases with incomplete recovery reported above. Histological and histochemical studies revealed that in these individuals there was a group of aberrant myofibrils in the centre of many muscle fibres and the fibrils of the central group gave a more positive periodic-acid-Schiff reaction than did the peripheral ones, while they also stained differently with the Gomori trichrome stain. These observations suggest that in some cases the syndrome may result from a structural and biochemical abnormality of the muscle fibre; clearly many more cases must be examined with these modern techniques before we shall be able to draw definite conclusions concerning aetiology.

SUMMARY

Seventeen cases are reported, all of which were diagnosed as amyotonia congenita in infancy because of generalized hypotonia and weakness of the skeletal muscles, giving rise to an increased range of passive movement at the joints and delay in physical development. Eight cases recovered completely at some time between the fifth and fifteenth year of life while the other nine improved to some extent but have shown evidence of persisting muscular disability throughout life. The clinical syndrome observed in these 17 cases has been entitled " benign congenital hypotonia ", " with complete recovery " or " with incomplete recovery ".

Electrical testing of affected muscles gave no evidence of disease in the peripheral nerves. Electromyography in two cases of the first group and in three of the second revealed an excessive proportion of polyphasic and short-duration potentials during voluntary contraction of affected muscles. Although these findings are suggestive of a myopathic disorder, muscle biopsy specimens from two cases which recovered and from four with residual disability, when studied by conventional methods, showed no abnormality.

It is suggested that benign congenital hypotonia is a distinctive clinical syndrome which may result from a congenital neuromuscular abnormality of varying severity. In certain cases the abnormality is mild and may be overcome in time by the processes of post-natal development, while in others the defect is more severe and there is a residual disability which persists throughout life. The relationship of this syndrome to similar disorders previously described is discussed in detail. The importance of recognition of these cases and of diagnosis from infantile spinal muscular atrophy is stressed; they show that not all cases with the clinical picture of amyotonia congenita (" the syndrome of the limp child ") have a gloomy prognosis.

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