# DIABETIC AMYOTROPHY

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One half (50%) of patients suffering from diabetes mellitus have in association some form of neuropathy.[6] The neuropathies are for the most part quite independent of the hyperglycaemia, the two being separate manifestations of a generalized metabolic disorder.

## CASE REPORTS

*Case* 1

Mrs. S.M.S., aged 59, stated that she had sat in a cold draught 2 weeks previously, following on which she developed severe pain in the right eye and drooping of the eyelid. The next day she complained of double vision. For the previous few months the patient thought that the toes of both feet were becoming rather stiff. She was known to have been hypertensive for some time. On direct questioning she admitted polydipsia and polyuria, which had been increasing in severity over that past 6 months. She went through the menopause at the age of 49 years. No family history of diabetes mellitus.

*Examination.* Pulse, temperature and respiration normal. BP 180/90 mm.Hg. Cardiovascular, respiratory, gastro-intestinal and genito-urinary systems normal. The fundal vessels showed slight arteriovenous nipping and silver wiring. The right eyelid was drooping and there was an oculomotor paralysis on that side. Other cranial nerves intact. Vibration sense absent up to the knees. All other modalities of sensation normal. Coordination and muscle tone normal. Muscle power extremely weak. Reflexes markedly depressed. Plantar respond normal.

*Special investigations.* Urine contained ++++ sugar; otherwise normal. Fasting blood sugar 360 mg./100 ml. Glucose tolerance curve diabetic. WR negative. Total lipid 1,069 mg./100 ml. Serum cholesterol 318 mg./100 ml. No porphyrin or porphobilinogen in urine. Blood urea 33 mg./100 ml. Serum electrolytes normal. Fractional test meal showed free acid. Urinary estimations for 17-ketosteroids (determined as dihydro-androsterone) 6·6 mg., 17-ketogenic steroid 9·1 mg., and 17-hydroxy-corticosteroid 6·1 mg. in 24 hours. Urine examinations for heavy metals negative. Stools negative for poliovirus. ECG normal. X-rays of the chest, skull and spine normal. CSF: pressure normal, protein content 119 mg./100 ml., otherwise normal; 2 weeks later the protein 93 mg./100 ml.

*Progress.* Soon after admission condition deteriorated. Muscle weakness increased so that movement against gravity was all that could be achieved. Generalized areflexia. Breathing became mainly abdominal, respiratory rate 35/min. At no time pyrexia. Incontinence of urine developed but lasted only 2 days. Patient gradually improved and after 2½ months discharged from hospital, diabetes well controlled on 50 units of lente insulin.

Two months later readmitted and with severe pain in neck and shoulders radiating down both arms. Obvious wasting of both deltoids, supraspinati and interossei. Muscle fibrillation present. Unable to lift arms above head. No objective sensory loss. The generalized areflexia had persisted. The oculomotor nerve palsy had recovered completely. CSF protein 171 mg./100 ml.; no cells. Repeat X-rays of cervical vertebrae normal. The hyperglycaemia was still well controlled on the same dose of insulin. Random blood-sugar levels all below 160 mg./100 ml. Physiotherapy was continued. The patient improved and was discharged after 3 weeks in hospital.

Over the next 8 months muscle power had improved considerably and full range of movement had returned to all limbs. The pain in the shoulders had subsided, and the reflexes were all present but weak. The patient then developed an abducent nerve palsy of the left eye, which recovered after 6 weeks without alteration in the treatment.

*Case* 2

A.K., African girl, aged 16 years, complained of severe generalized weakness for the past 8 months. The condition was progressive and she had been bedridden for the past 2 months. Two months before the weakness began she had experienced pain in both knees, which cleared up spontaneously after 6 weeks. On direct questioning she told of increased thirst and polyuria over the past 10 months. No history of febrile illness during this period. Never menstruated. No family history of diabetes.

*Examination.* Severe generalized weakness, being unable to lift arms or legs. Bilateral foot-drop and wrist-drop, and the small muscles of feet and hands grossly wasted. Tendon jerks not elicited. No fibrillation seen and no objective sensory disturbance found Fundi normal. The breasts well developed but the pubic and axillary hair scanty. Rest of examination negative.

*Special investigations.* Fasting blood sugar 249 mg./100 ml. Over 24-hour periods an average of 230 g. of sugar was lost in the urine. CSF: pressure 120 mm. $H_2O$, no cells, protein 132 mg./100 ml. Porphyrin excretion normal. Haemoglobin 15 g./100 ml. Leucocytes 6,500/c.mm., normal differential count. Serum mucoprotein 100 mg./100 ml. WR negative. Electrolytes normal. X-rays of chest, abdomen and spine normal.

*Treatment and progress.* Insulin was started and the diabetic state brought under control. Active physiotherapy commenced. After 2½ months the CSF protein had dropped to 42 mg./100 ml. Patient discharged after 7 months, able to walk with the aid of calipers. Foot-drop had persisted. Considerable strength had returned to the upper limbs and the hands were quite useful.

When seen 4 months later, wasting of the interossei and thenar and hypothenar muscles still evident. The reflexes had not returned. There was no obvious deterioration despite the fact that the patient had discontinued her insulin for the past 6 weeks and the diabetes was now completely out of control. CSF protein, however, had

risen to 120 mg./100 ml. Insulin was recommenced and 1 month later the level of the CSF protein had returned to normal.

*Case* 3

Mr. B.I., aged 65, complained of pain in the right hip and thigh for the past week. This was a recurrence of a similar episode lasting for 2 months 2 years before. The pain was severe and cutting in nature, worse at night. The leg had become weak and he could walk only with the aid of a stick. A known diabetic of many years' standing, well controlled by dieting.

*Examination.* Well nourished. Rather deaf. BP 120/75 mm. Hg. Bilateral cataracts obscured visualization of fundi. Heart, respiratory, gastro-intestinal and genito-urinary systems normal. Mild senile tremor obvious. Dorsalis pedi pulses absent. Varicose pigmentation evident on both ankles, with varicose veins of legs. Muscle tone normal, power good with exception of muscles of right thigh. No muscle fasciculation or fibrillation. Right knee jerk absent. All modalities of sensation intact.

*Special investigations.* Blood count normal, ESR normal. Serum potassium 4·4 mEq./litre; chloride 103; sodium 138; $CO_2$ 26. Fasting blood sugar 141 mg./100 ml. Glucose tolerance curve diabetic. Urine examination normal. ECG showed an incomplete right bundle-branch block. X-rays of chest showed marked unfolding of the aorta, with normal-sized heart and clear lung fields. X-rays of lumbosacral spine and sacro-iliac joints normal.

*Progress.* Walking improved over the course of 3 weeks, the pain decreased, and the patient was discharged and maintained on active physiotherapy and a low-calorie diet. No insulin needed. No glycosuria, and blood-sugar estimations 2 hours after meals never exceeded 160 mg./100 ml.

*Case* 4

Mrs. R.P., aged 67, complained of severe pain in her left hip and thigh over the past 3 weeks. The pain was 'cramp-like' and worse at night. She had noticed weakness of the thigh for some time, which had become severe over the past 2 weeks, making walking impossible. She had experienced a similar attack of lesser severity 2 years previously, which improved spontaneously after a month. Known diabetic of many years standing, well controlled by dieting. Gall-bladder, appendix and thyroid removed 20 years previously. History of diabetes on the maternal side.

*Examination.* Well-nourished. BP 160/80 mm. Hg. Heart enlargement to 6th interspace in mid-clavicular line, predominantly left ventricular. Pansystolic blowing murmur of mitral incompetence at apex. Motor power was good with the exception of the left thigh, where wasting was obvious; 4 inches difference in girth between the two thighs 6 inches above the knee. No fibrillation of muscle. Left knee jerk diminished. Coordination normal. Loss of vibration sense up to the knees; otherwise all modalities of sensation normal.

*Special investigations.* ECG showed evidence of past posterior infarction. Urine: 12 polymorphonuclears and 4 erythrocytes per high-power field; moderate growth of coliform bacilli on culture; trace of albumin present, sugar absent. Fasting blood sugar 135 mg./100 ml., and glucose tolerance curve diabetic. Serum potassium 5·1 mEq./litre; sodium 140; chloride 108; $CO_2$ 28·6. Blood urea 29 mg./100 ml. Haemoglobin 15·5 g./100 ml. Leucocytes 7,800 c.mm., normal differential count. ESR 36 mm. in 1 hour (Westergren). CSF: pressure 120 mm. $H_2O$, protein 54 mg./100 ml. Serum cholesterol 205 mg./100 ml. Serum PB iodine 6 $\mu$g./100 ml.

*Progress.* The patient was given intensive physiotherapy and after 3 weeks could walk with the aid of a stick. Marked improvement in power and freedom from pain. Insulin not required.

*Case* 5

Mrs. L.D., aged 85, a diabetic of many years' standing. Receiving 30 units of soluble insulin twice a day at the time of admission. She complained that for the past year she had been loosing the 'feeling' of both hands. For the past few months confined to bed and unable to stand or walk because of weakness of legs. Also complained of epigastric pain, which was relieved by alkaline mixtures. Frequent attacks of palpitation associated with sweating. Angina on effort troublesome over the last 5 years. A younger brother was diabetic.

*Examination.* Well nourished, moderate hirsuties. Mild confusion, which had been present for the past month. She would answer direct questions but it was difficult to hold her attention; she knew she was in hospital and who she was, but was poor on time and day; intellect moderately impaired, arithmetic and spelling poor; relatives had noticed a gradual deterioration over the past 6 months. Appetite moderate. Marked weakness of all muscles, with slight atrophy of pelvic and shoulder girdles. No muscle fibrillation observed. She was able to move her limbs against gravity but could not hold the weight of her body. No objective sensory disturbance. Coordination normal. Fundi obscured by cataracts; iridocyclitis in right eye. BP 110/60 mm. Hg. All pulses present and vessel walls not sclerotic. Heart enlarged; left ventricular impulse. Respiratory, gastro-intestinal and genito-urinary systems normal.

*Special investigations.* Haemoglobin 14·5 g./100 ml. Leucocytes 5,900 c. mm., differential count normal. Blood urea 52 mg./100 ml; serum potassium 5·0 mEq·0/litre; sodium 135; chloride 102; $CO_2$ 25·7. Urine: +++ sugar and trace of protein; microscopy normal but on culture an abundant growth of bacillus proteus. CSF: pressure 150 mm. $H_2O$, 2 lymphocytes/c.mm. and 85 mg. protein/100 ml. The Lange colloidal gold yielded negative result. WR of blood and CSF negative. Fasting blood sugar 170 mg./100 ml. Serum PB iodine 5·1 $\mu$g./100 ml. Serum cholesterol 280 mg./100 ml. Except for a large left ventricle with unfolding of the aorta, X-ray of chest and spine showed nothing abnormal. ECG showed large left ventricle with ischaemic change.

*Treatment and progress.* Urine became sterile after a course of furadantin. The hypoglycaemic attacks stopped as the insulin was reduced. The iridocyclitis responded to hydrocortisone ointment, atropine drops and chloramphenicol. One month later the weakness was slightly improved, but the patient remained areflexic. The confusion had improved but intellectually she was unchanged.

*Case* 6

Mr. J.F.D., aged 66, was well until a year before admission, when he developed pain in his back associated with 'pins and needles' in both thighs going down to the toes. The back pain was severe and was later associated with pain in the left thigh, worse at night. At the time an orthopaedic surgeon, after X-ray, diagnosed osteo-arthritis and degeneration of disc and prescribed a corset for support. The pain persisted until admission a year later. No history of polyuria or polydipsia and no family history of diabetes.

*Examination.* BP 170/104 mm. Hg. Fundi showed arteriovenous nipping and berry aneurysms. Cardiovascular system otherwise normal. Respiratory, gastro-intestinal and genito-urinary systems normal. Both thigh muscles were a little wasted and power of movement about the hip and knee joints were reduced, most marked on the left side. All reflexes present and equal; coordination normal; no objective sensory disturbance.

*Special investigations.* Urine: + + sugar with trace of acetone; normal microscopically but moderate growth of *B. proteus* on culture. Blood urea 28 mg./100 ml.; plasma chloride 95 mEq./litre; $CO_2$ 24·7; blood sugar 218 mg./100 ml.; serum amylase 13 Street-Close units. Haemoglobin 18·5 g./100 ml. Leucocytes 5,200/c. mm., neutrophils 82%. ESR 2 mm. per hour. CSF: pressure normal; 1 lymphocyte/c.mm. and protein 50 mg./100 ml. Total serum protein 8·5 g./100 ml; $\alpha$ 2 globulin 1·42 g./100 ml. Barium meal normal. On X-ray, chest normal, and lumbar spine showed a minor degree of osteophytic lipping, with marked narrowing between L5 and S1.

*Treatment and progress.* Tolbutamide, 1g. 6-hourly; 3 days later the blood sugar taken 2 hours after meals was 120 mg./100 ml., and simultaneously the pain disappeared and for the first time in a year the patient remained free of pain.

*Case* 7

Mrs. H.C.J., aged 81, mildly obese. For the previous 4 months she had complained of severe pain in the left thigh radiating down to the knee (and now in the back and the other thigh as well); the pain was present night and day, a little worse at night. Had lost about 10 lb. in weight and both legs had become extremely weak; so that she was unable to walk. She had a right mastectomy for cancer of the breast 15 years ago but had since been perfectly well. Six months before this admission she had been admitted to hospital (after a long period of polydipsia and polyuria) in a state of hyperglycaemic coma, with severe ketosis and blood sugar of 800 mg./100 ml., and was well controlled on 40 units of lente insulin a day; after discharge she failed to report back until her present complaint of pains in the thigh developed. After enduring the pain for 2 months she was admitted to another ward, where she received X-ray therapy to the lumbar spine, a diagnosis of secondary carcinomatosis having been made in view of the previous history.

As she did not respond to this treatment she went home, and was re-admitted 2 months later to us. There was then marked atrophy of the muscle about the pelvic girdle and she was unable to rise from the sitting position. Knee and ankle jerks absent on both sides. No objective sensory loss. She had only taken her insulin intermittently. The fundi were obscured by cataract. BP 165/110 mm. Hg. Rest of examination normal.

*Special investigations.* X-ray of lumbar spine showed marked osteophytic lipping with narrowing of the intervertebral space between L5 and S1. No X-ray evidence of metastatic tumour of the skeletal system. Urine: numerous polymorphonuclear cells and abundant growths of coliform bacilli on culture; trace of albumin; acetone and sugar present. Fasting blood sugar 274 mg./100 ml. Blood electrolytes normal. Full blood count and ESR normal. Serum alkaline and acid phosphate normal. Blood urea 47 mg./100 ml.; CSF: pressure 140 mm. $H_2O$; protein 130 mg./100 ml; sugar 142 mg./100 ml. WR negative. ECG normal.

*Treatment and progress.* The pyelonephritis responded well to antibiotic therapy and the fasting blood sugar fell to 144 mg./100 ml. The diabetes was controlled by diet and 1 g. of tolbutamide 6 hourly, the blood sugar 2 hours after meals being below 160 mg./100 ml. The pain responded dramatically. The patient was given intensive physiotherapy and was ambulant after 2 weeks.

*Case* 8

Mrs. S.L., aged 65, rather obese, presented with a complaint of severe pain in the legs and back for 18 months, shooting in character and followed by a feeling of numbness. Over the last few months the legs had become extremely weak and she was bedridden. The pains were often worse at night and she had noticed some oedema of the ankles for the past 6 months. A known diabetic for 17 years; had been controlled by diet only.

*Examination.* BP 170/68 mm. Hg. Vessels sclerotic, heart enlarged (mainly left ventricle), moderate degree of mitral incompetence. Cataracts had been extracted from both eyes. The right fundus showed evidence of optic atrophy with haemorrhages and marked narrowing of the arteries. The left showed numerous berry aneurysms and marked arterial narrowing. No hepatosplenomegaly or adenopathy. Generalized areflexia. Plantar responses flexor but at times equivocal. Muscle power very weak, especially in thighs and hands, where there was considerable atrophy. Occasional fibrillation in thighs. Facial musculature normal. No objective sensory disturbance.

*Special investigations.* Urine contained protein which varied between 1 and 11 g./litre, and trace of sugar. Full blood count and ESR normal. Fasting blood sugar 200 mg./100 ml. Plasma cholesterol 210 mg./100 ml. Serum electrolytes normal. Blood urea 48 mg./100 ml. Serum PB iodine 5·0 $\mu$g./100 ml. Flocculation tests, except cephalin-cholesterol, normal. 24-hour volume of urine 1460 ml., containing total creatinine 935 mg. of which 73 mg. was creatine. Serum albumin 2·58 g.%, $\alpha$ 1 globulin 0·45 g.%, $\alpha$ 2 globulin 0·95 g.%. $\beta$ globulin 1·31 g.%, and $\gamma$ globulin 1·31 g.%. X-rays of chest showed left ventricular enlargement, lung fields clear; of skull some calcification in carotid siphon and minimal hyperostosis cranii; of cervical and lumbar region normal. ECG showed some left axis deviation with flattened T waves in standard II and III and over V 4, 5, and 6. CSF: pressure 130 mg. $H_2O$, protein 27 mg./100 ml. WR negative.

*Treatment and progress.* Blood sugar failed to respond adequately to tolbutamide and diet; with 20 units of lente insulin a day together with tolbutamide the 2-hour postprandial specimen was well under 160 mg./100 ml., but pains and muscle weakness remained unchanged. After 2½ weeks intensive physiotherapy was started; improvement has been slow but definite, with considerable relief of pain and increased muscle power.

## DISCUSSION

The frequency of neurological manifestations, which occur in some form or another in over 50% of diabetic subjects, does not seem to be related to the severity or duration of the hyperglycaemic state. If, however, we believe that the metabolic defect of diabetes mellitus is present from birth, becoming progressively more severe, or only becoming apparent late in life, then neurological complications are a comparatively late manifestation. Only one case of amyotrophy under the age of 30 years has been reported.[5] Case 2 is unusual in that neurological manifestations came on at a very early age. Nevertheless, the neurological manifestations may be the presenting feature which first draws attention to the diabetic state (cases 1 and 2).

The pure motor neurological complications that are seen from time to time have in the past received only brief attention. Rundles,[11] in a comprehensive survey, failed to mention this aspect. Jordan[7] and Woltman and Wilder[16] found that motor disturbances were rare and mostly associated with some sensory abnormality. Bruns[1] (1890), in elderly diabetics, described the association of muscle weakness with pain in the hip and thigh and without objective sensory loss. This syndrome was reintroduced into clinical medicine by Garland and Travener[3] (1953) as diabetic myelopathy. Garland[4] (1955) has described numerous cases and now groups them under diabetic amyotrophy. This terminology is satisfactory and is not meant to pin-point the lesion, which may vary from the muscle itself to the spinal cord, producing the picture of muscular weakness and wasting, which are constant findings in this condition. Cases 3, 4 and 6 are typical examples. In cases 1, 2, 5, 7 and 8, the motor involvement is symmetrical In cases 1, 2, 5 and 8 the condition is generalized as well as symmetrical and is accompanied by areflexia. Because of the absence of objective sensory disturbance, these cases cannot be classified as diabetic polyneuritis, of which only a few true examples have been described.[2,9,10,14] Occasionally in other syndromes involving the nerve roots rather than the peripheral nerve, as in infective or febrile polyneuritis or the Landry-Guillain-Barré syndrome, the sensory disturbance may be minimal, and the possibility of coincidental pathology in our cases was considered. The absence of pyrexial illness or any other known cause of polyradiculitis such as porphyria, heavy-metal poisoning, malnutrition, sarcoidosis, polyarteritis nodosa, scleroderma, or amyloid disease, together with the fact that most of these are characterized by both sensory and motor change, minimizes the possibility of double pathology. The presence of diabetes mellitus, the cyclical nature of the neurological manifestations in cases 1, 3 and 4, and the lowering of the CSF protein with insulin therapy in cases 1 and 2, makes the diabetic aetiology fairly certain.

Of the 8 cases recorded, 5 required insulin, 1 tolbutamide and 1 a combination of both. The neurological response in 3 of the 5 cases treated with insulin was not dramatic; cases 6 and 7, however, responded rapidly to lowering of the blood-sugar level. Cases were considered controlled when this level fell below 160 mg./100 ml. 2 hours after meals. In 6 cases no correlation between diabetic control and neurogical improvement could be demonstrated. The varying manifestations of case 1 recurred despite adequate control, and improved spontaneously. Cases 3 and 4 gave histories of spontaneous improvement on previous occasions, and case 11 seemed no worse off neurologically for her insulin having been stopped, although a rise in CSF protein occurred.

These therapeutic results are somewhat similar to those of Hirson *et al.*[6] who described, amongst other cases, 12 manifesting as weakness and wasting of the quadriceps femoris; foot drop was observed in 6 cases, being bilateral in 1; weakness and wasting of the hands were seen in 4; in 1 case only did the condition recover with hyperglycaemic control. These results are disappointing when compared to the dramatic improvement with insulin reported by Garland,[5] who has

pointed out that the hyperglycaemia may be intermittent, as in cases of rapid absorption following gastrectomy, and comments on the possibility that hypoglycaemia may be an aetiological agent in the production of amyotrophy. Amyotrophy in cases of pancreatic insulin-secreting adenomata have been recorded.[13,12,15] In our cases we consider that intermittent hypoglycaemia was a factor contributing to the mental deterioration in case 5. Muscle fibrillation was seen in cases 1 and 8, which also demonstrated the unusual features of atrophy and weakness affecting the upper limbs, in case 8 as much as, and in case 1 more than, the lower extremities. The CSF protein in cases with diabetic neurological manifestations may vary from normal to marked increase without increase in cells. High protein levels have been reported.[7,8,11]

It was most encouraging to see the excellent progress in the rehabilitation of these cases brought about by intensive physiotherapy directed by a persistent and interested physiotherapist.

Electromyographical studies in these cases of amyotrophy (Fig. 1) reveal a reduction in motor unit activity on maximum contraction. Fibrillation potentials may occur and the degree of synchronization recorded by different electrodes in the same muscle may be marked. The motor unit potentials may have an unusually high voltage, suggesting together with other features that the lesion in some cases may lie in the spinal cord or motor nerve root. In case 8 the muscle showed marked irritability and exhibited bursts of myotonic activity. This has been classified as pseudomyotonia (as may be seen in cases of polymyositis). The possibility of an unsuspected polymyositis in case 8 was ruled out by the muscle biopsy findings, which were typical of a lower motor-neurone lesion. The muscle histology in diabetic amyotrophy is consistent with the atrophy following on nerve degeneration; bundles of fibres may be atrophic, reduction and thinning of individual fibrils may be seen, and loss of myohaemoglobin and transverse striation may occur. The histological features of muscle atrophy of varying degree was present in all 8 cases.

The muscles mainly involved are the proximal ones, the pelvic girdle being almost invariably involved and less commonly the shoulder girdle. The muscles are involved in groups and do not tend to follow any neural pattern. In some cases distal muscles are involved as well, when there may be some similarity to the group of motor-neurone diseases. The weakness and wasting may be either mainly unilateral or symmetrical; so also may be the distribution of pain, which is almost invariably present and is not characteristically asymmetrical as has been stated.[3,4] Although amyotrophy is more commonly found in elderly mild diabetics, it is not confined to this group. Many cases are seen where severe weakness and muscle atrophy are associated with objective sensory disturbance, some showing more motor than sensory involvement and others *vice versa*. Other cases, though rare,

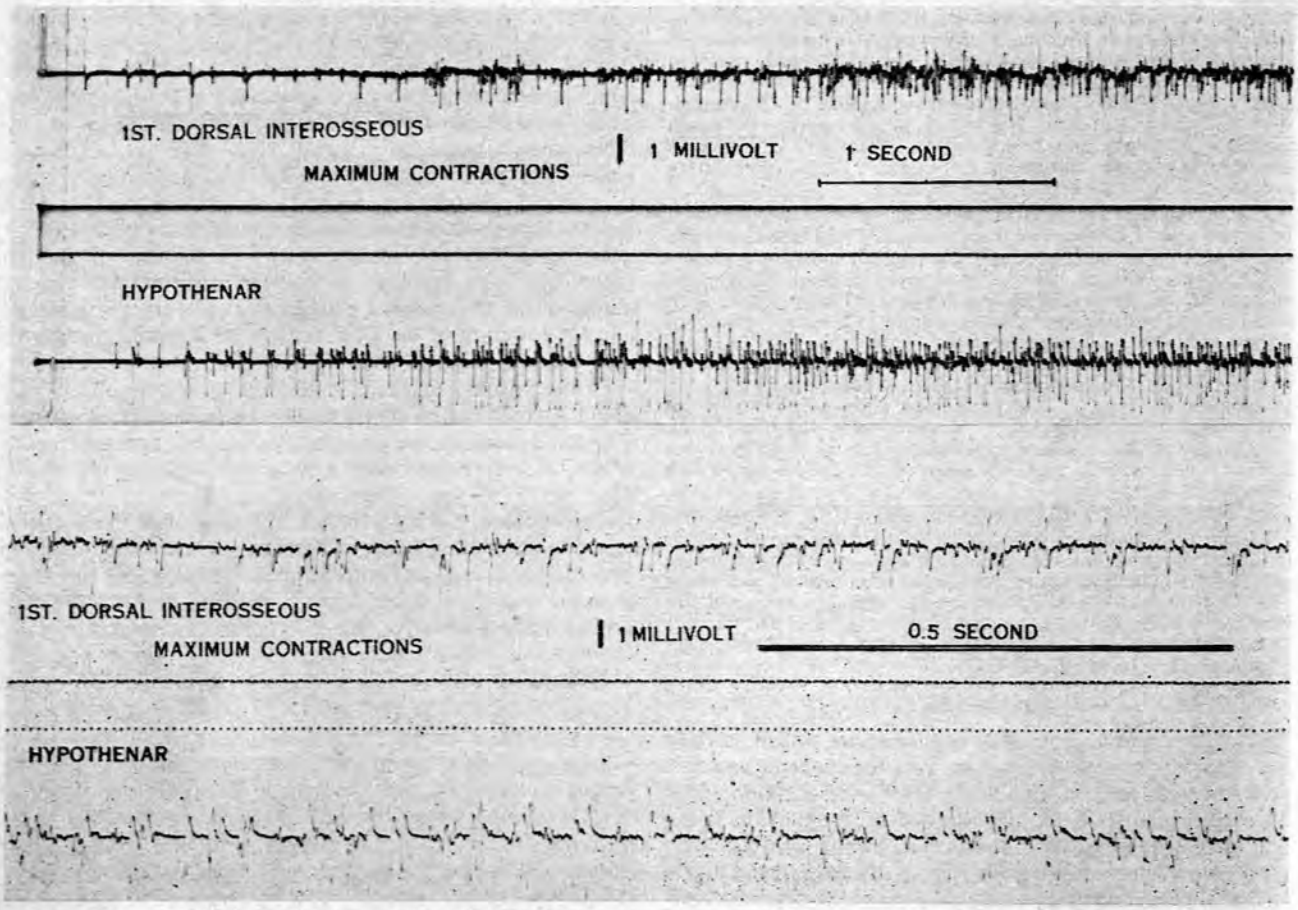


*Fig.* 1. Case 8. Electromyographic studies showing single motor unit potential and mixed patterns on maximum contraction.

may present with involvement of the sympathetic nervous system marked by severe postural hypotensions. Diabetes mellitus may then be associated with neurological manifestations which vary markedly from case to case. The decade now ended has rightly seen emphasis laid on the much neglected aspect of motor involvement, and the pattern can now fall into place leaving us with a clearer conception of the neurological manifestations of diabetes mellitus.

SUMMARY

Eight cases of diabetic amyotrophy are presented. Four cases are unusual in that they demonstrate severe generalized symmetrical motor weakness. Control of hyperglycaemia led to rapid relief of pain in 2 cases only. One case was of particular interest in that pseudomyotonia was demonstrated on electromyography.

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