

THYROTOXIC MYOPATHY

BY

RAGNAR HED, LENNART KIRSTEIN, and CURT LUNDMARK

From the Medical Department IV, the Departments of Clinical Neurophysiology and Pathology, Södersjukhuset, Stockholm, Sweden

It has long been recognized that there is a connexion between the function of the thyroid gland and muscular strength.

Both Graves (1835) and von Basedow (1840), in their original studies, called attention to muscular weakness as an important symptom in thyrotoxicosis. This weakness is usually localized to the proximal muscle groups, primarily to the lower extremities, and is manifested in difficulty in going up and down stairs and in arising from a sitting position. In its milder forms this muscular weakness is a common symptom, although it is perhaps rarely noted in the case history and examination, being instead attributed to general asthenia. In a more advanced form, including pronounced paresis and atrophy, the symptom seems to be less common. About 40 such cases are described in the literature under the title of chronic thyrotoxic myopathy.

In 1955, two cases of so-called chronic thyrotoxic myopathy were treated in this hospital. Taking these two cases as the point of departure, we have undertaken a more systematic investigation of the musculature in thyrotoxicosis and have thus far examined 20 patients. The investigations included, in addition to the routine clinical examination procedures and functional tests, electromyography, and studies of biopsy specimens from the muscles. The following is a report of the series investigated, the methods used, and the results obtained, as well as a discussion of the observations.

Materials and Methods

Material.—The material comprised a series of 20 patients. Eleven (Cases 1 to 11) presented pronounced symptoms of either atrophy or muscular weakness. Ten of these patients (Cases 1 to 10) suffered a high grade of disability. The clinical picture in these 10 cases agreed completely with the condition described as chronic thyrotoxic myopathy. In Cases 12 to 20 the atrophy and muscular weakness was only slight or moderate. Table I shows the sex and age distribution in the series.

The diagnosis of thyrotoxicosis was established on the basis of both the clinical picture and the results of prevailing examining methods such as tracer iodine

studies, determination of protein-bound iodine in serum, basal metabolism, serum cholesterol, and the 24-hour excretion of creatine in urine. In all cases the diagnosis was also confirmed by the results of the treatment.

Methods.—In the tracer iodine tests (0.08 m.c. iodine¹³¹ by mouth) the uptake in the thyroid gland after three and 24 hours and the excretion in the urine during the first 24 hours were determined. The approximate normal limits taken were 50% for the uptake in the thyroid gland after 24 hours and 30% for excretion in the urine during the first 24 hours. The protein-bound iodine in serum was determined according to the method of Barker, Humphrey, and Soley (1951). A value of 4 to 8% was considered as normal.

Creatine and creatinine were determined according to Folin (1904).

In the glucose tolerance test the patients received 1 g. glucose per kilogram of body weight by mouth, and the blood sugar was determined after 30, 60, 90, 120, 150, and 180 minutes.

For the electromyographic examination concentric needle electrodes were used (platinum wire 0.20 mm. in diameter, insulated from a cannula of stainless steel having an outer diameter of 0.5 mm.). The action potentials were led off to a differential amplifier (time constant 30 m.sec.) connected to an oscilloscope which recorded the time in milliseconds or 1/100 second. The output of the amplifier was also fed to a loudspeaker. Measurements from tracings were made in all cases.

All the patients were examined with electromyography (E.M.G.). In three cases only the gluteal muscles were examined. In all these cases changes were found which were characteristic of myopathy. A similar picture—patchily distributed areas from which a large number of rapid diphasic and polyphasic potentials were recorded—was, however, also observed in two patients suffering from duodenal ulcer and in one patient with acute nephritis. Neither of these three patients had any symptoms or signs of thyrotoxicosis nor were the gluteal muscles paretic. Because of these findings the activity from the gluteal muscles was not recorded in the remaining 17 cases with thyrotoxicosis. In 17 patients the quadriceps muscles on both sides were examined, in seven cases also the deltoid muscles. The muscles were systematically searched, the point of the needle, inserted in several different areas, being moved from superficial to deeper parts of the muscle.

TABLE I
VALUES FOR THYROID FUNCTION

Case No.	Sex and Age	¹³¹ I Accumulation in Thyroid (%)	Protein-bound Iodine (γ%)	B.M.R.	Creatine Excretion (mg./24 hr.)	Duration of Symptoms (yr.)	Muscular Weakness		Atrophy	
							Upper Extremity	Lower Extremity	Upper Extremity	Lower Extremity
1	F 48	72	24.5	+22	435	1½	++	+++	++	+++
2	M 50	70	21.5	+77	689	2	++	+++	++	+++
3	F 61	—	28.0	+56	410	3	++	+++	++	+++
4	F 54	—	16.0	+50	440	3	++	+++	++	+++
5	F 61	61	7.0	+42	200	2	++	+++	++	+++
6	F 70	80	7.5	+48	640	15	+++	+++	+++	+++
7	M 51	74	9.4	+21	96	1	+++	+++	+++	+++
8	F 67	69	10.5	+32	310	3	+++	+++	+++	+++
9	M 67	65	11.6	+29	200	6	+++	+++	+++	+++
10	F 66	76	8.9	+80	600	4	+++	+++	+++	+++
11	M 55	69	11.2	+59	430	1	+++	+++	+++	+++
12	M 60	59	19.0	—	100	1	+++	+++	+++	+++
13	F 45	60	12.0	+32	1,224	½	+	+	0	+
14	F 47	78	11.0	+60	570	½	0	+	0	+
15	F 37	70	12.8	+36	0	½	0	+	0	0
16	F 61	60	9.2	+44	0	1	0	+	0	+
17	F 54	73	16.0	+46	730	1	+	+	+	+
18	F 66	68	8.6	+23	0	1	0	+	0	0
19	F 39	79	8.9	+33	1,240	½	0	+	0	+
20	M 38	—	29.0	+88	520	½	0	+	0	+

+ = slight
++ = moderate
+++ = considerable

Muscle tissue was examined histologically in 18 cases. The biopsy material was taken from the quadriceps muscle in 12 cases, from the gluteus maximus in four, from the supraspinatus in one, and from the extensor musculature of the forearm in one.

The excised muscle tissue was fixed in 10% formalin solution or in Bouin's fluid. In two cases basic lead acetate was used as well. The preparations were stained with eosin and haematoxylin and according to van Gieson's method. Those fixed in basic lead acetate were stained with toluidine blue solution.

Results of the Investigation

Age and Sex Distribution.—In Cases 1 to 10 the age ranged between 48 and 70 years. This group included seven women and three men. In Cases 11 to 20 the ages lay between 37 and 66 years, and the group comprised seven women and three men.

Signs of Thyrotoxicosis.—Thyrotoxic eye symptoms were entirely absent in Cases 1 to 10. In three patients (Cases 1, 6, and 7) finger tremor was also absent. On the other hand, tachycardia was found in all cases. An appreciable loss of weight, ranging from 20 to 30 kg., was observed. In Cases 11 to 20 thyrotoxic eye symptoms were more or less pronounced in all but two cases (14 and 16), and finger tremor was present in all cases. The duration of the symptoms in Cases 1 to 10 varied between one and 15 years. In seven cases the symptoms had been present for more than three years and in only three cases for shorter periods. In Cases 11 to 20 symptoms had been apparent only six months to one year. The laboratory values obtained for the function of the thyroid gland are presented in Table I.

Muscular Weakness and Atrophy.—In all except Case 7 the muscular weakness was localized mainly to the proximal muscle groups. In six patients (Cases 1, 2, 3, 4, 5, and 8) the weakness was principally localized to the lower extremities. These patients were unable to go up and down stairs or to arise from a sitting position. They were not even able to walk on level ground without assistance. In Cases 6, 7, 9, and 10 there was pronounced weakness in the upper extremities as well. Patients 6 and 10 were able only with the greatest difficulty to raise the arms above the horizontal plane, and patient 9 was only able to abduct the arms about 30 degrees. Patient 7 was unable to raise his arms at all and differed otherwise from the other patients in that he had pronounced weakness in the hands and fingers as well. The muscular weakness in Case 7 started proximally as in the other cases, however, and only later did the peripheral paresis occur. Patient 6 had paresis even in the pharyngeal musculature and in both sternomastoid muscles. Two patients (Cases 8 and 10) had earlier been admitted to nursing homes because of pronounced muscular weakness. One patient (Case 6) had received an invalid's pension because of the muscular symptoms. Two patients (Cases 1 and 5) had previously been interpreted as hysterical disturbance of walking. Patients 11 to 20 had only slight to moderate muscular weakness, localized principally to the lower extremities. In three patients (Cases 3, 4, and 5) the muscular weakness started before other signs of thyrotoxicosis were observed.

The atrophy was most pronounced in the quadriceps and the gluteal musculature, but in five cases

appreciable atrophy was observed in the musculature of the shoulder and upper arm as well. In Case 6 there was also marked atrophy of both sternomastoid muscles. Table I gives the localization of the muscular weakness and atrophy as well as the duration of both muscular and other thyrotoxic symptoms.

Neurological Investigation.—In three patients (Cases 1, 4, and 5) both knee and ankle jerks were absent, in one (Case 3) only the ankle jerks. Otherwise the neurological examination showed normal conditions in all cases.

Carbohydrate Metabolism.—Before treatment two patients (Cases 1 and 2) presented signs of diabetes with elevated fasting blood sugar levels and glycosuria. Three patients (Cases 3, 8, and 10) had diabetic glucose tolerance curves.

Electromyography.—In the 17 cases in which the quadriceps and the deltoid muscles were examined every muscle explored showed in different areas one to several spots in which 75 to 100% of the recorded potentials were diphasic with a duration of 1 to 4 milliseconds and polyphasic with a duration of 3 to 6 milliseconds. The polyphasic potentials would in several cases best be described as “notchy diphasic”. The amplitude varied between 100 microvolts and 3 millivolts, the lowest voltages being observed in considerably atrophic and weak muscles. On maximal contraction a “dense” or “scanty” interference activity was recorded, depending on the degree of paresis: a greater number of different potentials was led off from stronger than from weaker muscles. No statistical analysis of the mean duration of the potentials was made.

Fig. 1 (Case 15) shows the activity from such an abnormal area in a slightly paretic quadriceps muscle. In *A* is seen the activity on a moderate contraction. Seventy-five per cent. of the potentials were notchy diphasic (*B*), polyphasic (*C*), and diphasic of abnormally short duration (*D*).

The potentials in Fig. 2 (Case 12) were led off from a moderately weak quadriceps muscle. *A* shows the pattern on a weak contraction. No potentials with a duration above 5 milliseconds could be observed with the needle in this spot, only diphasic (*B* and *C*) with a duration of 2 to 2.5 milliseconds, triphasic (*D*) and polyphasic (*E*) at 3.5 to 4 milliseconds. The amplitude varied from 1 to 3 millivolts.

The records from a conspicuously atrophic and moderately paretic deltoid muscle are seen in Fig. 3 (Case 11). In *A* the activity on a weak contraction is illustrated. No “normal” potentials could be led off from this particular area, only notchy diphasic

(*B*), polyphasic (*C* and *D*), and rapid diphasic (*E*).

In one patient (Case 6) both sternomastoid muscles were highly atrophic and paretic. On maximal contraction of the right sternomastoid muscle (Fig. 4) an interference activity was seen (*B*). No di- or triphasic potentials with a duration above 4 milliseconds could be observed in this muscle, but only di- or triphasic with a duration of 1.5 to 2 milliseconds (*C*, *D*, and *E*) and polyphasic at 5 milliseconds (*F*). The amplitude did not exceed 200 microvolts.

In none of these cases were fibrillations observed.

Two patients (Cases 5 and 7) showed a dissimilar electromyographic picture. From the quadriceps muscles of one of these patients (Case 7) a pattern was seen which was quite characteristic of myopathy, with scattered areas from which a considerable number of rapid diphasic and polyphasic potentials were recorded. The activity of the extensor muscles of the forearms and of the first interosseus muscles of the hands was, on the other hand, without any doubt consistent with a lesion of the peripheral motor neurones: only single discharges of diphasic action potentials with a duration of 6 to 7 milliseconds and an amplitude of 2 millivolts were recorded. The frequency on maximal contraction was 30 per second. Fibrillary action potentials were found in all the muscles examined in large numbers, thus also in the quadriceps muscles. In Fig. 5 are shown the activity of the extensor muscles of the right forearm on maximal voluntary contraction (*A*), spontaneous fibrillations (*C*), and sharply rising positive potentials (*D*) from the same muscles (Kugelberg and Petersén, 1949; Jasper and Ballem, 1949).

The other patient (Case 5) showed a considerable weakness of the quadriceps muscles. On voluntary contraction only polyphasic action potentials were recorded, the duration varying from 3 to 6 milliseconds and the amplitude between 500 microvolts and 2 millivolts. The frequency was not higher than 8 per second. Fibrillation potentials as well as sharply rising positive potentials (Fig. 6, *A*, *B*, and *C*) were observed in all regions of the muscles. It is somewhat difficult to interpret this pattern: it may equally be the expression of a myopathy as of a neurogenic disorder.

Histological Examination.—The histological examination of the musculature was entirely negative in one patient (Case 20). In the other 17 cases investigated histologically it showed widely varying degrees of atrophy of the muscle fibres. In seven patients (Cases 2, 3, 4, 6, 7, 8, and 19) there was an increase in the number of sarcolemmal nuclei, sometimes diffusely, sometimes only in spots. In some of the muscle specimens studied the nuclei formed

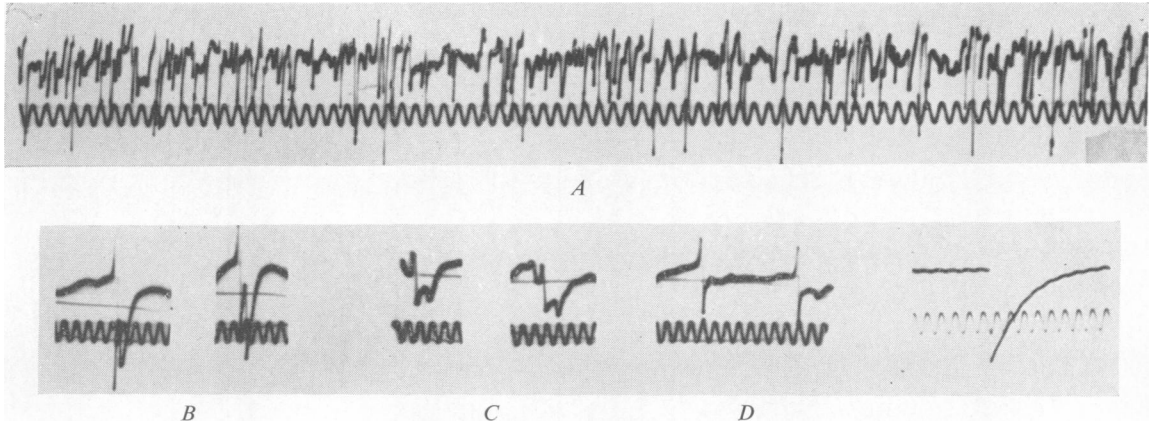


FIG. 1.—Records from a slightly paretic quadriceps muscle. Calibration 1 millivolt. *A*. Moderate contraction gives rise to a scanty interference activity (time, 1/100 sec.). *B-D*. Detailed pictures of different potentials. In this and the following records the duration of the potentials is shown in parenthesis. *B*. Notchy diphasic (5 m. sec.). *C*. Polyphasic (5 m.sec.). *D*. Diphasic (1 m.sec.). Time, 1/1,000 sec.

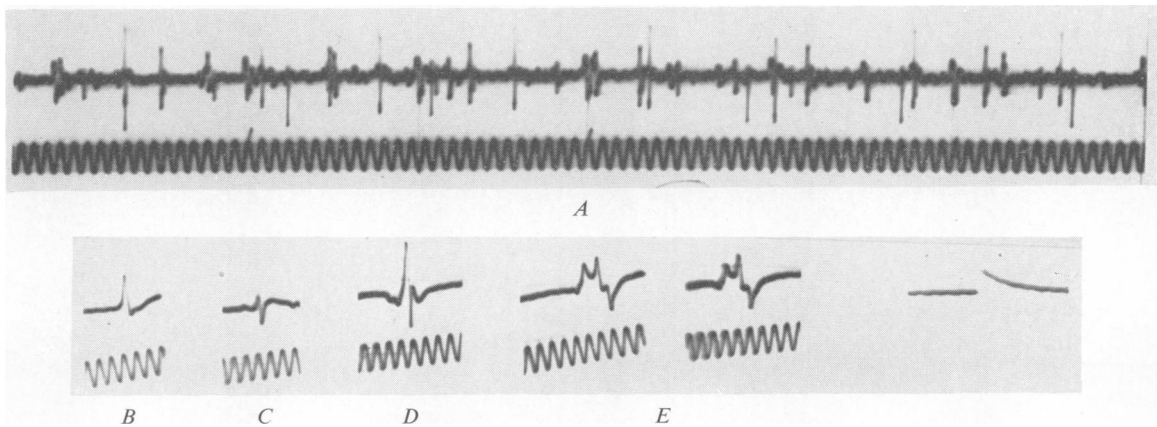


FIG. 2.—Records from a moderately paretic quadriceps muscle, Calibration 1 millivolt. *A*. Weak contraction (time, 1/100 sec.). *B-E*. Detailed pictures of different potentials. *B*. Diphasic (2 m.sec.). *C*. Diphasic (2.5 m.sec.). *D*. Triphasic (3.5 m.sec.). *E*. Polyphasic (4 m.sec.). Time, 1/1,000 sec.

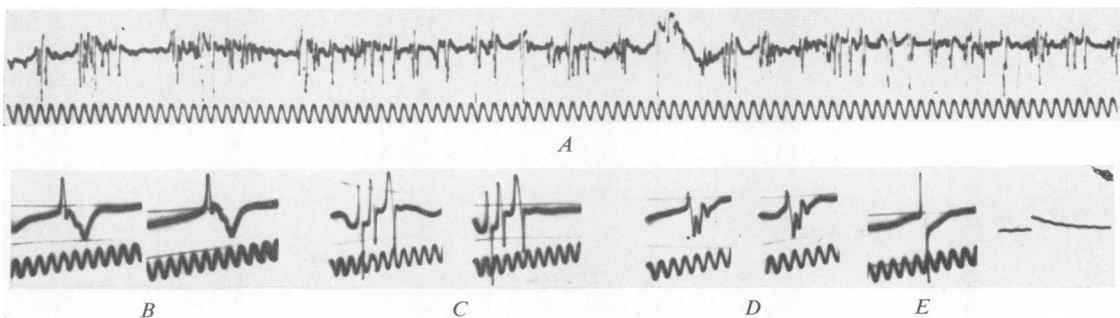


FIG. 3.—Records from a considerably atrophic and moderately paretic deltoid muscle. Calibration 100 microvolts. *A*. On a weak contraction single discharges of different potentials with varying frequency are recorded. Time, 1/100 sec. *B-E*. Detailed pictures of different potentials. *B*. Notchy diphasic (4 m.sec.). *C*. Polyphasic (5 m.sec.). *D*. Polyphasic (3.5 m.sec.). *E*. Diphasic (2.5 m.sec.). Time, 1/1,000 sec.

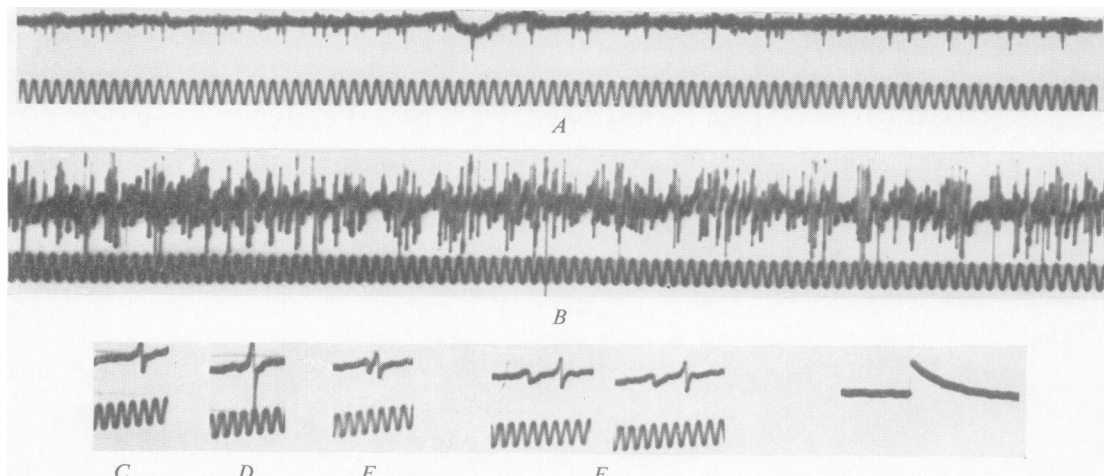


FIG. 4.—Records from a conspicuously atrophic and paretic sternomastoid muscle. Calibration 100 microvolts. *A*. Weak contraction. *B*. On strong voluntary contraction an interference activity is led off. Time, 1/100 sec. *C-F*. Detailed pictures of different potentials. *C*. Diphasic (1.5 m.sec.). *D*. Diphasic (2 m.sec.). *E*. Triphasic (2 m.sec.). *F*. Polyphasic (5 m.sec.). Time, 1/1,000 sec.

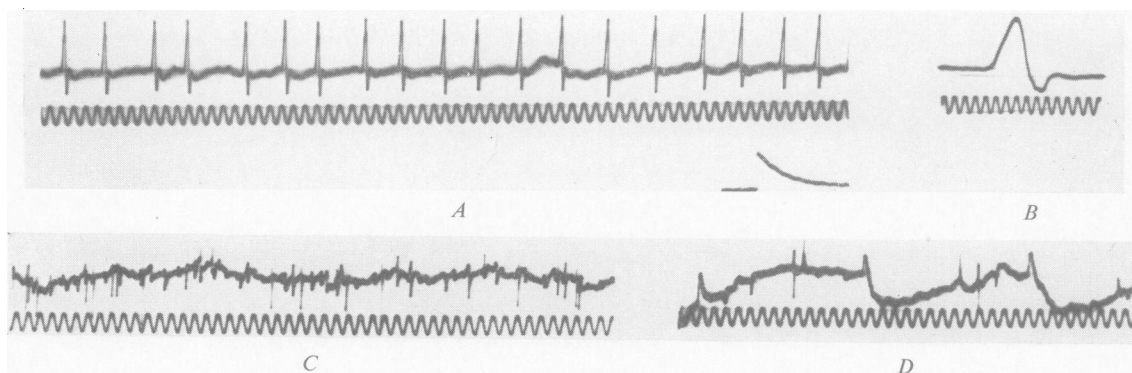


FIG. 5.—Activity from extensor muscles of the right forearm indicating a partial denervation. Calibration in *A* and *B* 1 millivolt. *A*, maximal voluntary contraction gives rise to high amplitude single discharges. Detailed picture of action potential (7 m.sec.) in *B*. *C*. Spontaneous fibrillation activity. *D*. Fibrillations and sharply rising positive potentials.

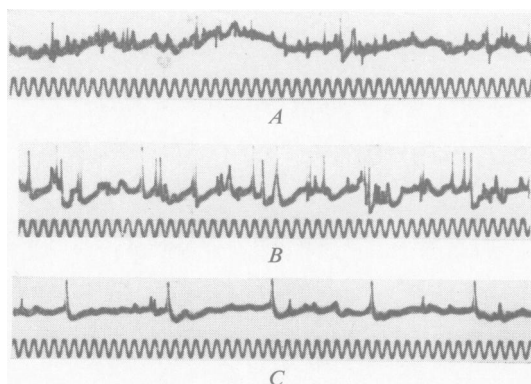


FIG. 6.—Involuntary activity from the right quadriceps muscle. Fibrillation activity and sharply rising positive potentials immediately after insertion of the needle (*A*); five seconds later (*B*); 10 seconds later (*C*).

continuous rows or small conglomerates. In two patients (Cases 7 and 19) an appreciable swelling of the sarcolemmic cells was observed. In five patients (Cases 2, 4, 6, 11, and 19) thin, basophilic muscle fibres with densely packed nuclei were a characteristic feature of the picture. The number of such muscle fibres varied from case to case. In only four patients (Cases 3, 4, 6, and 8) obliteration of the cross striation and a more or less distinct waxy degeneration were observed. In addition, in one patient (Case 6) a breakdown of isolated muscle fibres was demonstrated. As a whole, necrobiotic changes in the musculature were very slight or entirely absent. In two patients (Cases 3 and 8), however, relatively large necroses were observed in the musculature. In Case 3 the necrotic regions presented comparatively abundant inflammatory cells and so-called myocytes (Fig. 7). In Case 8 new connective tissue and an accumulation of iron-pigment-loaded phagocytes were observed as well in connexion with the necrosis (Fig. 8). An observation common to these two cases was the hyalinized muscle fibres and greater or lesser conglomerates of nuclei in the margin of the necroses (Fig. 9). Such nuclear conglomerates were found to a slight extent in two other patients (Cases 4 and 19). In some patients (Cases 3, 6, 8, and 11) small accumulations of lymphocytes, resembling those occurring in myasthenia gravis, were seen in the interstitial tissue (Fig. 10). No increase in adipose tissue in the musculature of a magnitude having pathological significance was observed.

In a number of cases the biopsy material included minor nerves. Only in Case 7 changes of single nerves were observed in the form of demyelination and vacuolization; the biopsy specimen was taken from the extensor musculature of the forearm.

Treatment.—In all cases muscular strength improved appreciably after two months' treatment of the thyrotoxicosis. To a certain extent Case 7 was an exception. Even in this patient the proximal muscular weakness disappeared after two months' treatment, but the peripheral paresis in the hands and fingers had not disappeared until after an additional five months. In all cases muscular strength was fully restored with the exception of Case 6, in which the patient died of cholangitis before completion of the treatment.

Electromyograms during the course of treatment showed a decrease in rapid diphasic potentials, but the number of polyphasic potentials seemed to be unchanged.

Discussion

It is evident from the foregoing report that clinical signs of thyrotoxicosis were but slight and

thyrotoxic eye symptoms entirely absent in the 10 patients with crippling paresis. In consequence, the diagnosis in these cases was not established until after the disease had been in progress for several years, and in one patient (Case 6) only after a period of 15 years. In the mild cases (11 to 20), on the other hand, thyrotoxic eye symptoms were present in all except two, and the duration of the symptoms was only from six months to one year. It seems probable, judging from our material, that the existence of thyrotoxicosis for a long period without treatment is one of the main factors in the origin of disabling thyrotoxic myopathy. It is therefore natural that the mean age of the patients with crippling paresis in our series should be high inasmuch as thyrotoxicosis in older persons frequently presents with an atypical clinical picture and is therefore difficult to diagnose.

In contrast to the reports in the literature, where chronic thyrotoxic myopathy is said to be considerably more common in men than in women, our 10 severe cases show a sex distribution largely the same as that for thyrotoxicosis in general, *i.e.*, seven women and three men. In the series of 10 mild cases (11 to 20) as well, the sex distribution was the same, seven women and three men.

In some of the patients the muscular weakness began several years before definite thyrotoxic symptoms were observed. The weakness and atrophy in six of Cases 1 to 10 was primarily localized to the proximal muscles in the lower extremities, in four cases to the upper extremities as well. In one patient (Case 7) there was distal muscular weakness and atrophy in addition to proximal. Electromyography in this case showed a typical neurogenic picture in the peripheral muscle groups but myogenic in the proximal muscles. As in the other cases the paresis first appeared proximally and only later peripherally. When treatment was instituted, the paresis in the proximal muscle groups disappeared very quickly while that in the peripheral persisted much longer. In this case neuropathy was probably present as well as myopathy. Whether or not thyrotoxicosis can give rise to both myopathy and neuropathy cannot of course be established definitely on the basis of this case alone. It is possible, however, that neuropathy has occurred in other cases; areflexia in cases from the literature as well as in our own material supports this assumption.

Whether or not the impaired carbohydrate metabolism in five cases has any pathogenetic significance in the origin of the paresis or if it is only an expression of the duration of the thyrotoxicosis cannot be determined.

Pathological creatinuria has been pointed out in the literature as a constant and typical observation

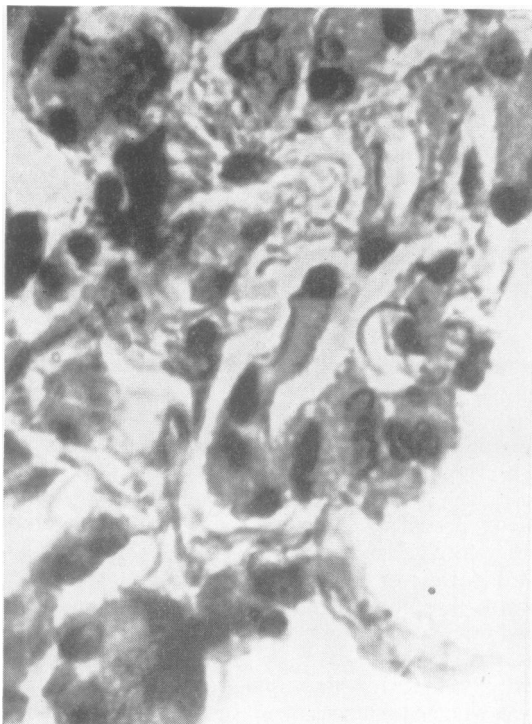


FIG. 7.—Case 3: Necrotic region of muscle with collections of "myocytes". $\times 1,100$.

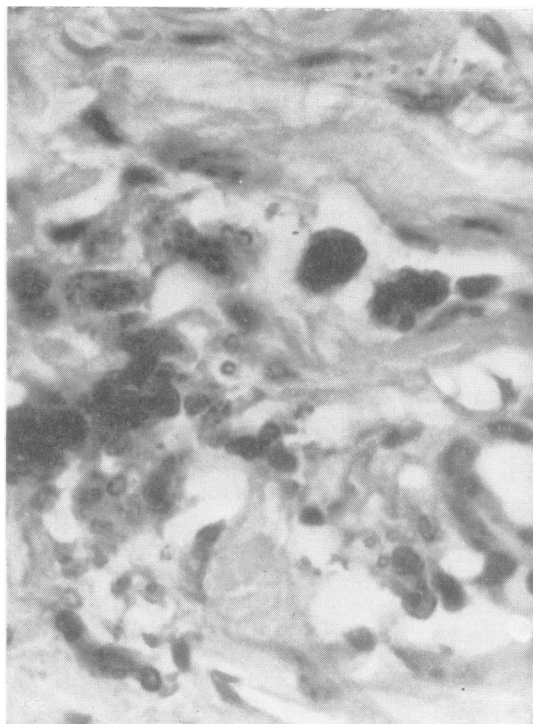


FIG. 8.—Case 8: Muscle with newly-formed connective tissue in necrotic area. Some phagocytes loaded with iron pigment are seen $\times 1,100$.

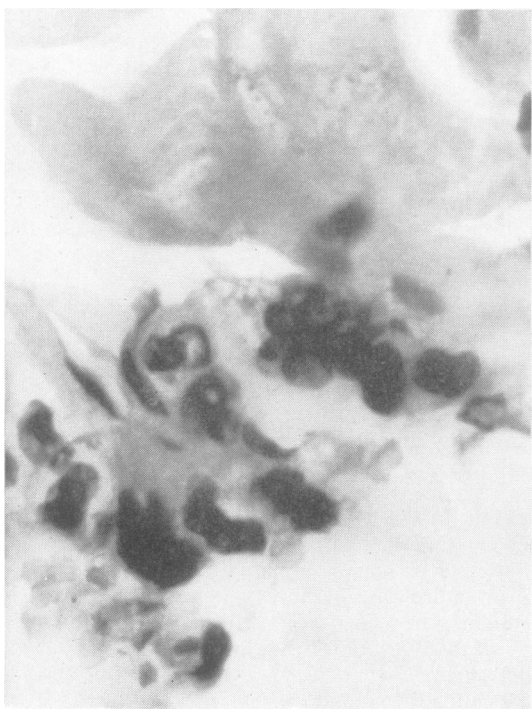


FIG. 9.—Case 3: Necrotic region of muscle with conglomerates of nuclei in the margin of the necrosis. $\times 1,100$.

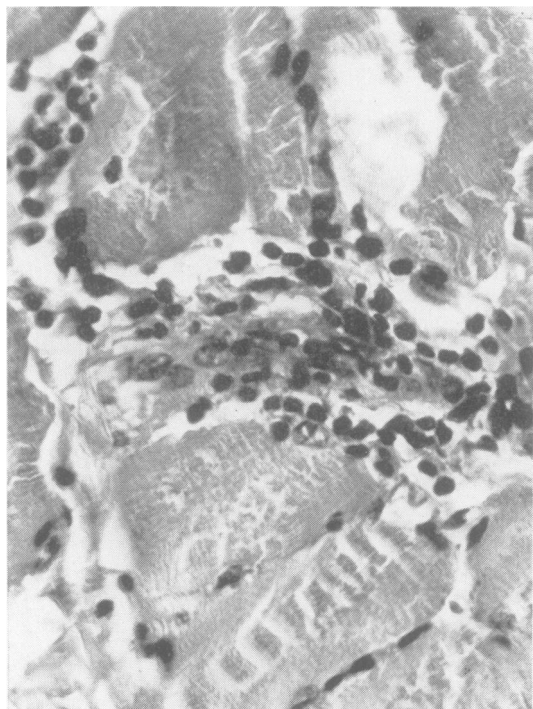


FIG. 10.—Case 6: Muscle with small accumulation of lymphocytes, resembling those occurring in myasthenia gravis. $\times 625$.

in thyrotoxic myopathy. However, Zierler (1951) found only inappreciable spontaneous creatinuria in his cases but extremely pathological tolerance values. He interprets this as being due to reduced creatine synthesis in the liver. All our cases of chronic thyrotoxic myopathy, however, presented definitely pathological spontaneous creatinuria. On the other hand, there was no parallelism between the quantity of creatine excreted in the urine and the degree of severity of the paresis. The largest amount of creatine, in excess of 1,000 mg. per 24 hours, was excreted in two patients (Cases 15 and 18) with only inconsiderable muscular weakness. In both these cases the condition appeared clinically to be relatively toxic, but the symptoms of the disease had been of only brief duration.

Our investigation has shown that electromyographic signs of myopathy occur even in patients with only slight muscular weakness. There is therefore reason to assume that the muscular weakness in almost all cases of thyrotoxicosis, and often interpreted as asthenia, is caused by a true myopathy. It is probably only a question of difference in degree between thyrotoxicosis with only slight muscular weakness and the disabling forms, so-called chronic thyrotoxic myopathy.

The electromyographical picture of myopathies was first described by Kugelberg (1947, 1949). He showed that the typical sign of proximal and distal muscular dystrophies, myotonic dystrophy, and myasthenia gravis was the occurrence of spike potentials with an abnormally short duration and a significant increase of polycyclic action potentials, the duration of which was mostly below that for the normal action potential. These findings have been confirmed by Walton (1952) by audiofrequency analysis. The same picture was observed in cases of dermatomyositis by Lambert, Beckett, Chen, and Eaton (1950), by Guy, Lefebvre, Lérique, and Scherrer (1950), and by Buchthal and Pinelli (1953), and in thyrotoxic myopathy by Sanderson and Adey (1952). Millikan and Haines (1953) reported on nine patients with chronic thyrotoxic myopathy. An E.M.G., performed in three cases, was normal.

In the present investigation the E.M.G. was abnormal in all the 17 cases examined. The pattern was quite characteristic of myopathy with patchily distributed small areas of abnormal potentials—rapid diphasic and polyphasic potentials lasting up to 6 milliseconds. The number of abnormal areas varied according to the degree of paresis—a greater number of such spots was observed in markedly weak than in slightly paretic muscles. No statistical analysis of the mean duration of the potentials was made since these abnormal potentials were not

uniformly distributed. This may also be the case in progressive muscular dystrophy, according to Kugelberg (1953), where “the pathological changes often have a patchy distribution and vary with the severity of the disease”. He adds further: “The difficulty of obtaining statistically valid values of mean durations of potentials is well understood.”

Fibrillation potentials, a common sign in lesions of peripheral neurones, was observed by Kugelberg and Petersén (1949) in cases of hereditary distal myopathy. This sign of increased excitability has also been found in myositis by Lambert *et al.* and by Guy *et al.* In the present cases fibrillations have only been observed in two patients (Cases 5 and 7): in one patient (Case 7) such potentials were led off both from those muscles showing signs of peripheral neuropathy and from the quadriceps muscles, the electromyographic picture of which was typical of myopathy. The electrographic pattern of the quadriceps muscles in the other patient (Case 5) was somewhat difficult to interpret; it was not quite clear if it was due to a lesion of the peripheral motor neurones or to myopathic changes. As all the other clinical signs pointed to thyrotoxicosis, so the aetiology, “primary” myositis, could be discarded in both these cases.

As a rule, the histological changes in the musculature were slight, and in the majority of patients no definite pathological changes were observed other than a certain degree of atrophy of the muscle fibres. This would seem to agree on the whole with the reports in the literature with the exception of Askanazy's study (1898), which is based on necropsy material. The change that appears to be the most constant according to the literature, namely adipose infiltration in the muscles, was not observed in our material. In only two cases were relatively pronounced histological changes with necroses in the musculature recorded. The semilunar accumulations of metachromatic substance inside the sarcolemma described by Asboe-Hansen, Iversen, and Wichmann (1953) were not encountered in the two patients examined for them.

Summary

In 20 cases of thyrotoxicosis systematic studies of the musculature, including electromyography and muscle biopsy, were performed in addition to the usual clinical examinations. Of these 20 patients, 10, seven women and three men, were severely disabled by pronounced muscular weakness. The other 10 patients had only slight to moderate muscular weakness.

Clinical signs of thyrotoxicosis in the 10 cases presenting high-grade muscular weakness were only slightly pronounced; thyrotoxic eye symptoms were

completely absent. In consequence many of these cases had remained untreated for many years.

In a number of cases the muscular weakness began several years before definite clinical signs of thyrotoxicosis were observed. In all cases but one the weakness was principally localized to the proximal muscle groups and then primarily to the lower extremities.

Five of the 10 patients with crippling muscular weakness had impaired carbohydrate metabolism of diabetogenous type. Pathological spontaneous creatinuria occurred in all of these 10 cases. No correlation was demonstrated between the degree of muscular weakness and the creatinuria.

Electromyographic examination showed signs of myopathy in the 17 cases in which the quadriceps or deltoid muscles were examined. There is therefore reason to assume that the muscular weakness in almost all cases of thyrotoxicosis and interpreted as asthenia is caused by true myopathy. Probably there is only a difference in degree between thyrotoxicosis with only slight muscular weakness and the disabling forms, so-called chronic thyrotoxic myopathy.

The histological changes in the musculature were slight as a rule. No pathological increase in adipose tissue in the musculature was observed. In only two cases were relatively pronounced histological changes with necrosis in the musculature recorded.

In one case both neuropathy and myopathy were demonstrated electromyographically. Histologically, signs indicating myopathy and degenerative changes in single nerves were observed.

Our material indicates that thyrotoxicosis untreated for a long period is probably one of the principal factors in the origin of disabling thyrotoxic myopathy.

Our thanks are due to Professor Eric Kugelberg for much valuable criticism of the electromyographic part of this work.

REFERENCES

- Asboe-Hansen, G., Iversen, K., and Wichmann, R. (1953). *Ugeskr. Laeg.*, **115**, 889.
- Askanazy, M. (1898). *Dtsch. Arch. klin. Med.*, **61**, 118.
- Barker, S. B., Humphrey, M. J., and Soley, M. H. (1951). *J. clin. Invest.*, **30**, 55.
- Basedow, C. A. von (1840). *Wschr. f.d. ges. Heilk.*, **6**, 197.
- Buchthal, F., and Pinelli, P. (1953). *Neurology*, **3**, 424.
- Folin, O. (1904). *Hoppe-Seyl. Z. physiol. Chem.*, **41**, 223.
- Graves, R. J. (1835). *Lond. med. surg. J. (Renshaw)*, **7**, 516.
- Guy, E., Lefebvre, J., Lericque, J., and Scherrer, J. (1950). *Rev. neurol. (Paris)*, **83**, 278.
- Jasper, H., and Ballem, G. (1949). *J. Neurophysiol.*, **12**, 231.
- Kugelberg, E. (1947). *J. Neurol. Neurosurg. Psychiat.*, **10**, 122.
- (1949). *Ibid.*, **12**, 129.
- (1953). *Progress in Neurology and Psychiatry*, Vol. 8, p. 264.
- , and Petersén, I. (1949). *J. Neurol. Neurosurg. Psychiat.*, **12**, 268.
- Lambert, E. H., Beckett, S., Chen, C. J., and Eaton, L. M. (1950). *Fed. Proc.*, **9**, 73.
- Millikan, C., and Haines, S. F. (1953). *Res. Publ. Ass. nerv. ment. Dis.*, **32**, 61.
- Sanderson, K. V., and Adey, W. R. (1952). *J. Neurol. Neurosurg. Psychiat.*, **15**, 200.
- Walton, J. N. (1952). *Ibid.*, **15**, 219.
- Zierler, K. L. (1951). *Bull. Johns Hopk. Hosp.*, **89**, 263.