Achilles Tendon Reflex in Accidental Hypothermia and Hypothermic Myxoedema

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Summary

The photomotogram (P.M.G.) of the Achilles tendon reflex was studied in 26 patients with hypothermia (rectal temperature 33·3°C or less), 10 of whom also had myxoedema (serum protein bound iodine 2·8 μg/100 ml or less). No reflex could be elicited in eight (31%) of these patients, including three of those with myxoedema. Hypothermia increases both the contraction and the relaxation times of the reflex, the relaxation phase being particularly prolonged in those with myxoedema. In those patients from whom the reflex was elicited the ratio of the contraction time to the "half-relaxation time" in the P.M.G. was less than unity in six of the seven with myxoedema, and considerably greater than unity in eight of the 11 (73%) who were euthyroid. Thus, analysis of the Achilles tendon reflex P.M.G. correctly predicted the thyroid status in 14 of the 18 hypothermic patients in whom the Achilles tendon reflex was present (78%). The wider use of this rapid test of thyroid function would allow a more rational use of thyroid hormones in hypothermic patients and so lead to a better assessment of their value.

Introduction

Hypothermic myxoedema usually involves a very grave prognosis (Asher, 1960). Its immediate recognition is difficult, for many of its clinical features are shared by cases of accidental hypothermia uncomplicated by hypothyroidism (Duguid *et al.*, 1961; Mathews, 1966; Cooper, 1968; Hockaday and Fell, 1969).

The place of rapidly acting thyroid hormone preparations in the treatment of hypothermic myxoedema is controversial, but their use may sometimes be beneficial. During spontaneous rewarming the patient's body temperature often fails to rise at the satisfactory rate of 0·55-0·83°C per hour (Cooper, 1968; Burton and Edholm, 1955; Rees, 1958; Hardwick, 1962; *British Medical Journal*, 1964; Taylor, 1964), so vital organs are subjected to increasing risks of damage as the hypothermia is prolonged (Davies *et al.*, 1967). Active external rewarming may be dangerous (Duguid *et al.*, 1961), but rapidly acting thyroid hormone preparations may quickly stimulate the endogenous production of heat (Cooper and Ross, 1960; Davies *et al.*, 1967). In those with severe myxoedema coma and carbon dioxide retention the respiratory centre may resume its normal function only after treatment of the myxoedema has been started (Nordqvist *et al.*, 1960). Thyroid hormone replacement will also correct any impaired adrenocortical function in these patients (Hubble, 1955). When there is hypotension the early administration of triiodothyronine is necessary before vasopressor drugs become effective (Catz and Russell, 1961). In these patients the loss of muscle enzymes into the plasma, which may be associated with poor myocardial function, may gradually be stopped by the use of thyroid hormone (Griffiths, 1965; Maclean *et al.*, 1968; Hurwitz *et al.*, 1970). In selected cases of hypothermic myxoedema, therefore, the careful use of a rapidly-acting preparation of thyroid hormone may help to improve the patients' chances of survival.

Treatment by triiodothyronine of euthyroid patients with accidental hypothermia is both illogical and of doubtful value (Zingg, 1967). Most euthyroid hypothermic patients rewarm spontaneously at a satisfactory rate once further heat loss is stopped (Maclean *et al.*, 1968).

Biochemical indices of the state of thyroid activity in patients with accidental hypothermia may be difficult to interpret (Mathews, 1966, 1967; Hockaday and Fell, 1969; Rosin and Exton-Smith, 1964; Sprunt *et al.*, 1970) and are unlikely to be immediately available. Clearly there is a need for a quick, simple test that would allow a more rational use of thyroid hormone preparations and a better assessment of their value.

We therefore studied the photomotogram (P.M.G.) of the Achilles tendon reflex in patients with accidental hypothermia and collected serum for the later determination of the protein

TABLE I—*Clinical Data Relating to the 26 Hypothermic Patients Under Study*

Case No.	Age and Sex	Rectal Temperature °C	Serum P.B.I. (μg/100 ml)	Relevant Associated Conditions	Achilles Tendon Reflex P.M.G. (msec) C	(msec) ½R	C/½R
1 ..	78 F.	29·4	1·3	None	70	210	0·33
2 ..	85 F.	27·8	0·5	Malnutrition	275	290	0·95
3 ..	89 M.	28·9	< 2·0	C.C.F.	160	640	0·25
4 ..	80 F.	30·0	1·2	P.A.	365	675	0·54
5 ..	67 M.	33·3	< 2·0	None	160	990	0·15
6 ..	79 M.	29·4	2·6	Diabetes mellitus	165	360	0·46
Cases 1–6: Mean ± S.D.					199 ±104	528 ±294	0·45 ± 0·28
7*..	71 F.	32·0	2·8	Uraemia	165	70	2·36
8 ..	87 F.	29·4	2·8	P.A.	‡	‡	‡
9 ..	63 F.	30·0	2·8	None	‡	‡	‡
10 ..	78 F.	33·3	< 2·0	P.V.D.	‡	‡	‡
11 ..	87 M.	27·8	4·0	C.C.F.	415	205	2·05
12 ..	86 M.	29·4	7·4	Stroke, P.V.D., (?)luetic aortitis	265	155	1·71
13 ..	84 M.	31·1	5·0	None	360	135	2·67
14 ..	65 M.	25·6	6·5	Glutethimide poisoning	425	160	2·66
15 ..	77 F.	31·1	6·4	(?)CO poisoning	250	140	1·79
16 ..	97 F.	33·3	6·2	Malnutrition	280	110	2·55
17 ..	81 F.	25·2	6·1	Stroke	340	220	1·55
18 ..	70 M.	33·3	> 16·0†	Uraemia	470	205	2·29
Cases 11–18: Mean ± S.D.					351 ± 82	166 ± 39	2·16 ± 0·45
19 ..	89 M.	32·2	5·0	None	60	360	0·17
20 ..	79 M.	29·9	5·9	None	165	185	0·89
21 ..	83 M.	32·8	5·0	Rectal carcinoma	160	370	0·43
Cases 11–21: Mean ± S.D.					290 ±127	204 ± 86	1·71 ± 0·88
22 ..	70 F.	31·7	7·1	Diabetes mellitus	‡	‡	‡
23 ..	84 F.	30·6	7·0	(?)CO poisoning	‡	‡	‡
24 ..	80 F.	26·7	7·1	None	‡	‡	‡
25 ..	80 M.	28·9	4·0	Stroke	‡	‡	‡
26 ..	60 F.	31·7	6·8	Carcinomatosis	‡	‡	‡

*Excluded from mean because of probable associated central nervous system damage.
†Recent I.V.P. elsewhere. Not myxoedematous.
‡Reflex absent.
C.C.F. = Congestive cardiac failure. P.A. = Pernicious anaemia. P.V.D. = Peripheral vascular disease. Stroke = Affecting opposite side.

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bound iodine (P.B.I.) level. Our results suggest that the Achilles tendon P.M.G. will quickly distinguish between the patients who are probably euthyroid and those who probably have myxoedema, although in some hypothermic patients the Achilles tendon reflex is absent.

Subjects and Methods

Twenty-six hypothermic and 30 euthermic patients were studied (tables I and II).

The Achilles tendon reflex was elicited in the usual manner by a tendon hammer. The displacement of the foot was recorded by an optical system involving the light-source and photoelectric cell technique previously described for recording cardiac and venous pulsations (Berry, 1966; Berry and Mago, 1967). The system has the advantage that no part of the apparatus is actually attached to the foot (Gilson, 1959). A multichannel oscilloscopic recorder (Cambridge Instrument Co. Ltd.) was used to make records of the P.M.G. on photographic paper.

TABLE II—*Clinical Data Relating to the 30 Euthermic Patients Under Study*

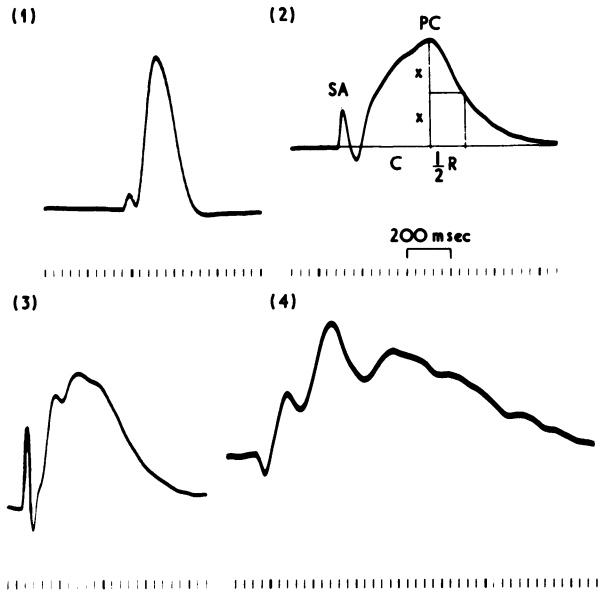
Case No.	Age and Sex	Serum P.B.I. (μg/100 ml)	Associated Conditions	Achilles Tendon Reflex P.M.G. (msec) C	½R	C/½R
1 ..	83 F.	2·1	Myxoedema	265	135	1·96
2 ..	58 F.	2·3	Myxoedema	290	155	1·87
3 ..	80 F.	2·0	Myxoedema	270	220	1·23
4 ..	52 F.	< 2·0	Myxoedema	280	190	1·47
5 ..	79 F.	1·9	Myxoedema	175	145	1·21
6 ..	60 M.	< 2·0	Myxoedema	285	240	1·19
7 ..	54 F.	1·8	Myxoedema	360	360	1·00
8 ..	12 F.	1·8	Myxoedema	245	220	1·11
9 ..	70 M.	2·0	Myxoedema	200	150	1·33
10 ..	46 F.	3·1	Myxoedema	200	85	2·35
11 ..	51 F.	2·9	Myxoedema	250	110	2·27
12 ..	76 F.	3·0	Myxoedema	305	140	2·18
13 ..	79 F.	1·7	Myxoedema	275	125	2·20
14 ..	81 F.	3·2	Myxoedema	190	290	0·66
15 ..	73 F.	< 2·0	Myxoedema	220	400	0·56
Cases 1–15: Mean ± S.D.				254 ± 50	198 ± 92	1·51 ±0·59
16 ..	76 F.	5·3	None	205	260	0·79
17 ..	83 F.	5·4	None	190	145	1·31
18 ..	62 F.	6·4	Stroke	195	80	2·44
19 ..	87 F.	5·4	None	240	105	2·29
20 ..	79 F.	4·3	None	240	185	1·30
21 ..	74 M.	4·4	Bronchial carcinoma	205	100	2·05
22 ..	66 M.	5·0	Chronic bronchitis	200	120	1·67
23 ..	71 M.	4·4	Ischaemic heart disease	220	120	1·83
24 ..	71 M.	4·5	Ischaemic heart disease	200	120	1·67
25 ..	75 M.	5·3	Diabetes mellitus	120	290	0·41
26 ..	57 M.	5·5	Myelomatosis	185	90	2·06
27 ..	71 F.	5·0	None	195	210	0·93
28 ..	87 M.	3·8	Erythroderma, Congestive heart failure	200	65	3·08
29 ..	45 M.	5·7	None	245	90	2·72
30 ..	50 M.	6·0	None	185	80	2·31
Cases 16–30: Mean ± S.D.				202 ± 30	137 ± 68	1·79 ±0·74

The serum P.B.I. levels were estimated by an autoanalyser technique (Technicon Instruments Corporation, 1964).

The chart shows a typical P.M.G. at (2), the way in which it was analysed, and the terminology used. Any late periodic oscillations do not interfere with the measurements. In each case the P.M.G. used for the final results was the one out of 10 successively recorded tracings which had the shortest contraction plus half-relaxation time.

Results

In our preliminary study of the 30 euthermic patients, we confirmed the findings of many previous workers that hypothyroidism prolongs both the contraction and the relaxation phases of the Achilles tendon reflex (Ord, 1884; Lambert *et al.*, 1951; Fogel *et al.*, 1962; Sherman *et al.*, 1963; Miles and Surveyor, 1965; Abraham *et al.*, 1966; Nuki and Bayliss, 1968). The relaxation phase was prolonged more than the contraction phase, the mean (± 1 S.D.) for the ratio of the contraction time to the half-relaxation time (C/½R) in the P.M.G. being 1·51 ± 0·59 in those with myxoedema and 1·79 ± 0·74 in those who were euthyroid (table II).



Achilles tendon P.M.G.: effects of hypothermia and hypothyroidism. (1) Euthyroid, euthermic. (2) Euthyroid, hypothermic. (3) Hypothyroid, euthermic. (4) Hypothyroid, hypothermic. SA = Stimulus artefact. PC = Peak contraction. C = Contraction time. ½R = Half-relaxation time. x = Half peak contraction amplitude.

Ten of the hypothermic patients (table I) had serum P.B.I. levels of 2·8 μg/100 ml or less and so were considered to be cases of hypothermic myxoedema (Sprunt *et al.*, 1970). In three of them the Achilles tendon reflex could not be elicited, but in six of the other seven the ratio C/½R was less than unity (mean ± 1 S.D. = 0·45 ± 0·28). The remaining hypothermic patients all had serum P.B.I. levels of 4·0 μg/100 ml or more and so were regarded as being euthyroid. In five of them the Achilles tendon reflex was absent; the ratio C/½R was considerably greater than unity in eight (mean ± 1 S.D. = 2·16 ± 0·45) and less than unity in only three (overall mean ± 1 S.D. for euthyroid group = 1·71 ± 0·88). One of the three patients had a rectal carcinoma and may have had carcinomatous neuromyopathy and in one the thyroid gland was found at necropsy to be normal.

In the 10 patients with hypothermic myxoedema the Achilles P.M.G. had correctly predicted the diagnosis in six of the seven in whom the reflex was present and allowed us to decide on their management before the P.B.I. results became available. One patient (case 1) spontaneously became euthermic and did not receive thyroid hormone until she had completely recovered from the hypothermic episode. Another (case 2) failed to become warmer, but died six hours after admission. In case 3 the patient's temperature spontaneously rose to 32·2°C within 12 hours and so he did not receive treatment; he achieved a body temperature of only 34·4°C over the next seven days before his death and ought therefore to have been given thyroid hormone once the good initial response was not maintained. The next three patients all failed to gain heat adequately and so were given triiodothyronine or thyroxine or both, after which slow rewarming began. The first two of these patients survived, but the other died four hours later (body temperature 32·8°C), death probably being due to associated pancreatitis accompanied by the acute onset of severe diabetic ketoacidosis. The other patient in this group did not have the P.M.G. findings indicative of myxoedema,

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perhaps because of coexistent damage to the central nervous system, but although she died before treatment would have been considered (11 hours after admission) her temperature had already risen to 35·0°C.

The three patients with hypothermic myxoedema in whom the serum P.B.I. results were necessary for confirmation of the diagnosis all died. One (case 8) had spontaneously regained normal body temperature within 16 hours, but died the same day. The other two patients did not have a satisfactory rise in their temperature and so received both triiodothyronine and thyroxine once the P.B.I. results became available. Slow rewarming followed this treatment in both patients, but they died before normal body temperature had been reached (case 9 reached 34·3°C in seven days; case 10 reached 35·1°C in five days).

None of the three patients in whom the P.M.G. results gave a false diagnosis of myxoedema actually received thyroid hormone because in two their temperatures rose spontaneously at a satisfactory rate and they survived and the other was known to have an inoperable rectal carcinoma.

Discussion

Slow ankle jerks are characteristic of myxoedema (Ord, 1884) and they have often been studied (Fogel *et al.*, 1962; Sherman *et al.*, 1963; Miles and Surveyor, 1965; Abraham *et al.*, 1966; Nuki and Bayliss, 1968). Indeed, delayed relaxation of the ankle jerk has routinely been used in the Mayo Clinic for about 50 years as an aid in the diagnosis of myxoedema (Lambert *et al.*, 1951).

Much less attention has been paid to the ankle jerks in hypothermia. Emslie-Smith (1958) made the clinical observation on three patients with accidental hypothermia, two of whom probably also had myxoedema, that the muscles contracted slowly during the ankle jerk; he did not specifically comment on the relaxation phase. Subsequently, muscular relaxation during the tendon jerk in hypothermic euthyroid patients was commented on by a number of workers (Mathews, 1966, 1967; Hockaday and Fell, 1969; Rosin and Exton-Smith, 1964; Gooding, 1969), but the effect of hypothermia on the P.M.G. seems to have been investigated only twice before (Lambert *et al.*, 1951; Petajan and Watts, 1962).

In descriptions of the P.M.G. the term "half-relaxation time" has been used to refer to different features. Petajan and Watts (1962) defined it as the time from stimulation to half-relaxation, which they found to be prolonged in hypothermia. We adopted the definition of Buller (1963) and Moulopoulos *et al.* (1964)—that is, the time from peak contraction to half-relaxation—because that measurement is not affected by factors such as the influence of the stimulus artefact and polyphasic after-oscillations. The stimulus artefact, however, does interfere with the measurement of contraction times.

Myxoedema and hypothermia each prolongs both the contraction and the relaxation phases of the tendon jerks; cooling affects the two phases more uniformly than myxoedema, which prolongs the first half of the relaxation phase relatively more than it prolongs the contraction phase (Lambert *et al.*, 1951).

It has been shown experimentally that temperature is one of the principal variables affecting the duration of all phases of the Achilles tendon reflex, the increase in its duration paralleling the decrease in temperature by 0·023-0·028 sec/°C, irrespective of the patient's thyroid status (Lambert *et al.*, 1951). In normal subjects a calf-muscle temperature of 25-28°C was required to produce a prolongation of the Achilles tendon reflex comparable to that found in some patients with myxoedema in whom the calf-muscle temperature was above 34°C (Lambert *et al.*, 1951). Cooling of a limb leads to a linear increase in the time from the stimulus to half-relaxation time, and to a decrease in the amplitude, of the ankle jerk (Petajan and Watts, 1962).

According to the "sliding filament" hypothesis the contraction and relaxation of skeletal muscle both involve the movement of actin and myosin myofilaments past one another. However, the physicochemical events that lead to relaxation are not simply the reverse of those that produce contraction. There is therefore no theoretical reason why the kinetics of contraction and relaxation should be identical.

The ankle jerk may not be elicited in severely hypothermic patients. It may be prolonged in the elderly (Mathews, 1967). Many elderly patients with accidental hypothermia have other associated conditions which are known to prolong the jerk, including diabetes mellitus, neurosyphilis, hypokalaemia, oedema, peripheral vascular disease, sprue, pernicious anaemia, and Parkinsonism. The drugs propranolol, procainamide, quinidine, reserpine, bromides, and the antithyroid preparations also prolong the ankle jerk (Nuki and Bayliss, 1968; Waal-Manning, 1969).

Prolongation of the tendon reflexes has been regarded as unhelpful in differentiating hypothermia from hypothyroidism (Mathews, 1967). The results of our study, however, have suggested that in those from whom the Achilles tendon reflex can be elicited the P.M.G. may rapidly indicate which patients are probably euthyroid and which probably have myxoedema—the accuracy of the test in this series being 78%. Moreover, in those who have myxoedema the P.M.G. may show a characteristic series of peaks (see (4) in chart), since the various muscles may not always be equally affected in this disease (Jellinek, 1960). In our series the frequent absence of the reflex restricted the value of the test and allowed the correct assessment of thyroid status to be made in only 14 of the 26 (54%) hypothermic patients. Occasionally brisk relaxation is noted in the tendon reflexes elicited in hypothermic patients—for example, case 7, table I. This may result from damage to the central nervous system.

Because the precise requirements of, and the least hazardous way of using, thyroid hormone in hypothermic myxoedema have yet to be established, we restricted their use to those patients who had not begun to rewarm spontaneously within 12 hours of their admission to hospital, and to those in whom rewarming did not continue. Other complications of myxoedema, as mentioned above, which threatened the patients' chances of survival would provide additional indications for their use.

Nevertheless, the Achilles P.M.G. enabled the treatment of the patients to be decided before the serum P.B.I. results became available and no serious harm resulted from misdiagnosis. The study and fuller statistical evaluation of such results in a much larger series of patients with accidental hypothermia and hypothermic myxoedema will decide whether or not this form of earlier diagnosis is regularly confirmed by the serum P.B.I. results or other tests of thyroid function and will determine the effect of the earlier use of thyroid hormone on the overall prognosis of these patients.

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Interaction between Levodopa and Methyldopa

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Summary

The interaction between methyldopa and levodopa was studied in 18 patients with Parkinsonism. Together they produced a fall in blood pressure in doses which when given alone had no effect or only a slight hypotensive effect. Severe hypotension never occurred. It is reasonable to give methyldopa to hypertensive patients on levodopa but the regimen should be initiated in hospital.

Introduction

Since the introduction of levodopa for the treatment of patients with Parkinsonism a variety of interactions between levodopa and other drugs have been reported (Hunter *et al.*, 1970).

Theoretically, an interaction between levodopa and methyldopa could be envisaged since methyldopa can cause Parkinsonism by inhibiting decarboxylase, thus preventing the conversion of dopa to dopamine.

Although levodopa has been reported to cause postural hypotension (Barbeau, 1969; Calne, 1969; Calne, 1970; Duvoisin, 1970; McDowell and Lee, 1970) the hypotension is not related to the dose. In the past, it has been thought inadvisable to give methyldopa and levodopa together. However, many patients with Parkinsonism have hypertension and are effectively controlled on methyldopa. Fermaglich and O'Doherty (1971) reporting on patients with Parkinsonism who received both drugs found that Parkinsonism was improved by adding methyldopa to levodopa. The average dose of levodopa was reduced from 3·244 g to 0·96 g when methlydopa was added. However, careful assessment of the blood pressure was not made.

In this study the interaction between the two drugs on the blood pressure is investigated.

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Method

Eighteen inpatients with Parkinsonism were investigated as follows. While not receiving treatment, lying and standing blood pressure measurements were recorded at 6 a.m., 11 a.m., 1 p.m., and 3 p.m. The effect of a single dose of 250 mg methyldopa was assessed by administering the drug at 6 a.m. and measuring lying and standing blood pressures at 6 a.m., 11 a.m., 1 p.m., and 3 p.m. The patients were then started on treatment with levodopa until two weeks later, with the patient on a mean dose or 1·5± 0·5 g levodopa a further 250 mg of methyldopa was administered and lying and standing pressure again monitored at 6 a.m., 11 p.m., 1 p.m.; and 3 p.m.

Three of the patients were also given methyldopa 250 mg twice a day for one day while on a dose of 1·75-2·5 g levodopa.

Results

Results of the standing blood pressure are shown in the table. Four comparisons were made. First between a control period and methyldopa, second between a control and

Results of Standing Blood Pressure Measurements in the Study Groups

	Standing Blood Pressure (mm Hg)	
	Systolic	Diastolic
Mean control	136·1	90·0
Mean methyldopa	134·7	77·2
Difference of mean	1·4	12·8
No. of readings	18	18
Significance	P >0·50	0·01 < P <0·02
Mean control	136·1	90·6
Mean levodopa	135·6	80·6
Difference of mean	0·5	10
No. of readings	18	18
Significance	P >0·05	0·1 < P <0·5
Mean methyldopa	134·2	77·8
Mean methyldopa and levodopa	120·3	71·1
Difference of mean	13·9	6·7
No. of readings	44	44
Significance	P <0·01	<0·01
Mean levodopa	135·3	80·0
Mean levodopa and methyldopa	123·3	74·7
Difference of mean	12	5·3
No. of readings	18	18
Significance	0·02< P <0·05	0·1< P <0·5

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