than by any other physiological variable. This is not to say, however, that there are not other factors (such as acid–base balance and congenital anomalies) which affect this process, just as there are many influences besides parathyroid hormone which determine plasma calcium.

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The Achilles tendon reflex as an index of thyroid function

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THIS PAPER is dedicated with affection to John McMichael who so rightly taught one of us that in the practice of medicine mensuration was often the great corrective to that important but potentially misleading entity known as 'clinical impression'.

Introduction

In 1884 William Ord reported that the tendon reflexes elicited on clinical examination were prolonged in patients with myxoedema. Not until 40 years later was this prolongation recorded graphically (Chaney, 1924); the converse shortening of the reflex time in thyrotoxic patients was first demonstrated in 1929 (Fournier). Subsequently a number of workers using various recording devices have measured the tendon reflexes in patients with thyroidal dysfunction (Harrell & Daniel, 1941; Lambert *et al.*, 1951; Lawson, 1958; Gilson, 1959; Sharpe, 1961; Fogel *et al.*, 1962; Fejer & Kun, 1963; Sherman, Goldberg & Larson, 1963; Smart & Robson, 1963; Moulopoulas, Koutras & Kralios, 1964; Reinfrank *et al.*, 1967).

Today two main techniques are used, the photomotogram (Gilson, 1959) and the kinemometer (Lawson, 1958). In the former the movement of the sole of the foot, after percussion of the Achilles tendon, interrupts a light path which transmits a signal via a photo-electric transducer to an electrocardiographic (ECG) machine and writes a tracing as shown in Fig. 1(a). Thyroidal function has been assessed from either the 'half-relaxation time' or the 'relaxation time' (Fig. 1a). The kinemometer is an electromagnetic device. A magnet is attached to the sole of the patient's foot and on percussion this moves into an electrical field inducing a current which is transmitted to an ECG machine. A tracing is written as shown in Fig. 1(b). The time from stimulation to the end of contraction or from maximal contraction to maximal relaxation ('the valley-to-peak time') is used as an index of thyroidal function.

There is no general agreement as to the usefulness of these measurements as an index of thyroidal activity and it is appreciated that a variety of non-thyroidal conditions such as neurological disorders and ankle oedema may falsify the results.

The purpose of this paper is to relate our experience with the photomotographic method in all patients referred to an outpatient clinic for assessment of thyroid function over a period of 4 years.

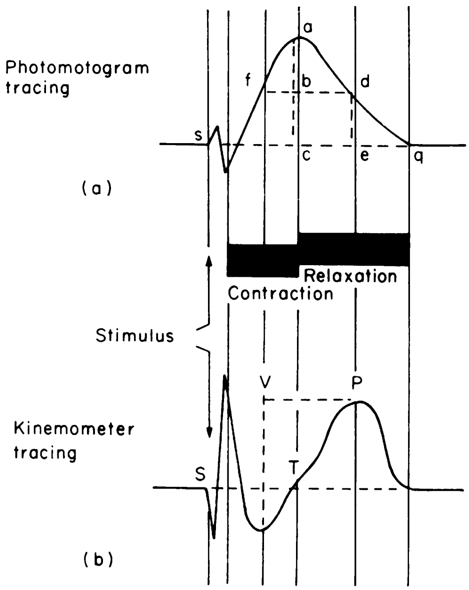

FIG. 1. Diagrammatic representation of the Achilles tendon reflex recorded by photomotography (a) and by kinemometry (b). ab = bc. The 'half-relaxation-time' is represented by se; the 'relaxation time' by sq and the 'half-contraction-to-half-relaxation time' by fd. The 'valley-to-peak' time is represented by VP and the 'contraction time' by ST.

Methods and patients

The Achilles tendon reflexes were recorded by one observer (R.I.S.B.) with the patient kneeling on a pillow covering the seat of a wooden chair. An ordinary patellar hammer was used. The photomotographic machine was made by the Department of Clinical Measurement and the tracing recorded on an ECG machine calibrated to give 1 cm deflection with 1 millivolt and at a paper speed of 25 mm/sec. About ten tracings were made from each patient. The first three or four tracings and any showing artefacts were discarded; thereafter three to five tracings were mounted on a card for later measurement.

The measurements were all made by another observer (G.N.) to the nearest 10 msec on the shortest of the mounted tracings. This was done without knowledge of the clinical state of the patient or of results of the other tests of thyroid function.

Evaluation of the patient's thyroid status was made before measurement of the ankle reflex time and was based on a variety of parameters described elsewhere (Hobbs, Bayliss & Maclagan, 1963; Bayliss, 1967a, b) including protein-bound iodine, uptake of ^{132}I, the tri-iodothyronine suppression test, the thyrotropin stimulation test, changes in the serum cholesterol and ECG in response to thyroxine treatment, prolonged clinical assessment and the response to treatment.

Tracings were recorded from 232 consecutive patients who were referred for assessment of thyroid function. Some were already being treated with thyroid extract or thyroxine; others were receiving antithyroid drugs or had been treated by thyroidectomy or radioiodine in the past. Assessment of thyroid function by chemical or isotopic methods was made in close temporal proximity to recording the photomotogram. Twelve patients were discarded because a certain assessment of thyroidal function could not be made due to incomplete or equivocal results.

Results

The final assessment of thyroid status without reference to the photomotogram, the sex and ages of the 220 patients are shown in Table 1.

TABLE 1
Final assessment of thyroid function in 220 patients

Thyroid status	Total	Male	Female	Mean age (yr) and range
Euthyroid	116	24	92	43 (10–71)
Hyperthyroid	62	9	53	43 (14–77)
Hypothyroid	42	1	41	48 (19–74)

The half-relaxation time and half-contraction-to-half-relaxation time were measured in all subjects. The distribution curve of the half-relaxation time (HRT) in these patients is shown in Fig. 2. Plotted on a linear arithmetic scale the curve is skewed to the right (above), but when plotted on a logarithmic scale it assumes a more 'normal' distribution (below).

The mean values, standard deviations, 95% confidence limits and coefficients of variation in the euthyroid, hyperthyroid and hypothyroid groups are shown in Table 2. The antilogarithms

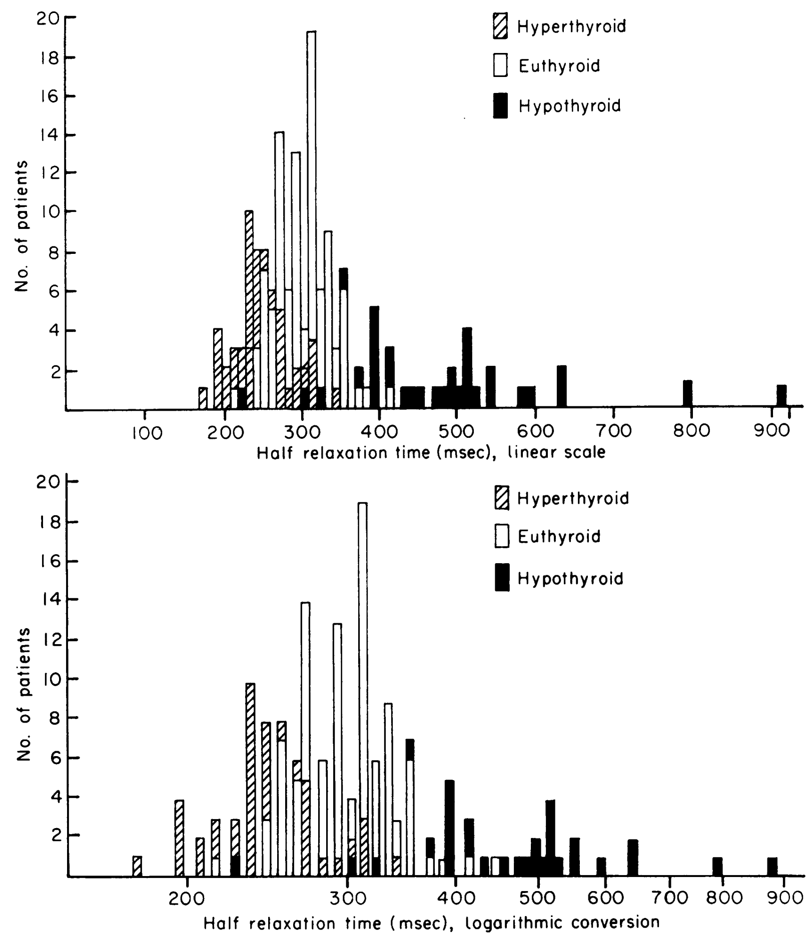

FIG. 2. The distribution of the 'half-relaxation time' in hyperthyroid, euthyroid and hypothyroid patients on a linear scale (above), and on a logarithmic scale (below).

of the results derived from the logarithmic scale are tabulated for convenience of comparison. The half-contraction-to-half-relaxation time gives a poorer discrimination between each group than does the half-relaxation time, and the latter gives a significantly better discrimination when plotted on a logarithmic scale. For this reason the half-relaxation time derived from the logarithmic scale is only considered further.

Euthyroid patients

No attempt was made to establish normal values of HRT in healthy controls unsuspected of thyroid disease. Our normal range was derived from the 116 patients finally judged to be euthyroid by other criteria than the ankle reflex time. The mean HRT for the whole group was 310 msec (range 250–380) (Table 2). The results are influenced in slight degree by the patient's sex and age. Thus the mean HRT for the twenty-four euthyroid males was 310 msec (SD 40) as compared with a mean of 290 msec (SD 40) in the ninety-two euthyroid females, a statistically significant difference ($0{\cdot}025<P<0{\cdot}05$). The mean HRT for the thirty euthyroid patients aged 11–30 years was 300 msec (SD 25); 310 msec (SD 45) for the forty-three subjects aged 31–50; and 330 msec (SD 45) for the thirty-two older subjects aged 51–70. The difference between the oldest and the other two age groups is significant ($P<0{\cdot}0025$).

The results for the patients with hypo- or hyper-thyroidism are given in Table 2 and shown graphically in Fig. 3. Table 3 is an analysis of the numbers and percentages falling into each diagnostic category when judged by the HRT.

TABLE 2

Comparative results of ankle reflex times

	Half-relaxation time (msec) Log scale	Half-relaxation time (msec) Linear scale	Half-contraction to half-relaxation time (msec)
Euthyroid (116 cases)			
Mean	310	320	210
Standard deviation	30–35	40	40
Normal range*	250–380	240–400	130–290
Coefficient of variation	11%	12·5%	19%
Hypothyroid (42 cases)			
Mean	440	470	350
Standard deviation	60–70	120	105
Normal range	300–660	230–710	140–560
Coefficient of variation	16%	25%	30%
Hyperthyroid (62 cases)			
Mean	250	320	160
Standard deviation	20–30	30	30
Normal range	210–310	190–310	100–230
Coefficient of variation	12%	12%	19%

* Normal range = ±2 SD.

TABLE 3

Analysis of the distribution of patients according to half-relaxation time

	Half-relaxation time			
	Log scale		Linear scale	
	No. patients	Percentage	No. patients	Percentage
Euthyroid patients	116	100	116	100
Euthyroid range	107	92	113	97
Hypothyroid range	8	7	2	2
Hyperthyroid range	1	1	1	1
Hypothyroid patients	42	100	42	100
Euthyroid range	12	27	16	38
Hypothyroid range	29	71	25	60
Hyperthyroid range	1	2	1	2
Hyperthyroid patients	62	100	62	100
Euthyroid range	35	62	47	76
Hypothyroid range	—	—	—	—
Hyperthyroid range	24	38	15	24

Hypothyroid patients

The mean HRT for the hypothyroid patients was 440 msec (range 300–660) and this is significantly different from the mean of 310 msec for the euthyroid group ($P<0{\cdot}0005$). However 27% of the hypothyroid patients had a HRT in the euthyroid range and one patient overlapped into the hyperthyroid range (Fig. 3 and Table 3).

Hyperthyroid patients

The mean HRT in the hyperthyroid patients was 250 msec (range 210–310) and this was significantly shorter than the mean of 310 msec for the euthyroid patients ($P<0{\cdot}0005$). However, in 62% of the hyperthyroid patients the HRT fell within the euthyroid range (Fig. 3 and Table 3).

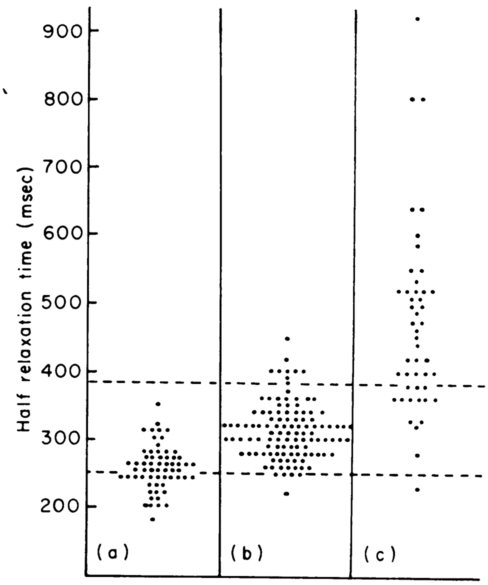

FIG. 3. The half-relaxation times in (a) sixty-two hyperthyroid, (b) 116 euthyroid and (c) forty-two hypothyroid patients. The dotted lines show two standard deviations of the mean for the euthyroid patients.

Discussion

Some workers have noted that the tendon reflex time may be longer in euthyroid women than men (Nuttall & Doe, 1964; Reinfrank *et al.*, 1967) although others have observed no such difference (Lambert *et al.*, 1951; Robson, Hall & Smart, 1965; Abraham, Atkinson & Roscoe, 1966). We have found a small but significant increase in relaxation time in men matched for age with women. Most workers have found no correlation between age and the tendon reflex time (Lambert *et al.*, 1951; Nuttall & Doe, 1964; Abraham *et al.*, 1966) but our results show a statistically significant lengthening of the relaxation time in those aged 50 or over, and this has been observed by others (Reinfrank *et al.*, 1967).

These factors, however, are too small to effect materially the results obtained or to decide whether the tendon reflex time is a useful index of thyroidal function. The claims on this point are indeed conflicting (Lambert *et al.*, 1951;

Fogel *et al.*, 1962; Nuttall & Doe, 1964; Mann, 1963; Sherman *et al.*, 1963; Miles & Surveyor, 1965; Robson *et al.*, 1965; Rives, Furth & Becker, 1965; Abraham *et al.*, 1966; Reinfrank *et al.*, 1967). Some find that as many as 78% of their hyperthyroid and 38% of their hypothyroid patients have tendon reflex times within the normal euthyroid range (Rives *et al.*, 1965) whereas others claim complete differentiation between hypothyroid patients and euthyroids and find that only 10% of hyperthyroid patients have normal reflex times (Abraham *et al.*, 1966). Some workers believe that better discrimination is achieved with the kinemometer (Abraham *et al.*, 1966), and measuring 'valley-to-peak' time (Fig. 1) by this technique does avoid inclusion of the nerve conduction time (Nuttall & Doe, 1964). However the 'valley-to-peak' time in the kinemometer method approximates closely to the 'half-contraction-to-half-relaxation' time in the photomotogram (Fig. 1) which we have found even less reliable than the half-relaxation time (Table 2). Others have compared the results with the kinemometer and photomotogram methods directly and found no difference (Rives *et al.*, 1965).

It seems probable that the wide variation in opinion as to the diagnostic value of the ankle reflex time is due to bias in the selection of cases rather than to differences in technique. In some series the patients have been selected because the diagnosis was beyond doubt and those with borderline abnormalities have deliberately been excluded (Lawson, 1958; Sherman *et al.*, 1963; Mann, 1963). In one series many of the hypothyroid patients were selected for the test because their reflexes were thought to be clinically prolonged by the referring physician (Robson *et al.*, 1965).

In the largest reported series Rives *et al.* (1965) used, like us, a number of parameters upon which final assessment of the thyroid function was based. They excluded from final analysis 20% of their patients, as opposed to our exclusion of 5%, on grounds of uncertainty of dianosis. Even so their results show the poorest discrimination in the diagnosis of both hyper- and hypo-thyroidism of all the published reports, although they are only slightly worse than ours (Table 4). These workers used a method of probit analysis, finding a normal distribution of their study population whereas we have found the distribution markedly skewed to the right; and this has been found by others (Robson *et al.*, 1965). Analysis of results after logarithmic conversion gives significantly better diagnostic discrimination in our series but it is of interest to note that the figures for the HRT derived from the simple linear scale (Table 3) are almost identical to those of Rives *et al.* (Table 4): 76% compared with 78% of the hyperthyroid patients and 38% of the hypothyroid patients from both series falling into the euthyroid range. In the clinical situation involving assessment of an individual patient little is gained by these mathematical manoeuvres which cannot basically improve a relatively imprecise test, and in practice we use the linear arithmetic scale.

TABLE 4

Percentage of patients with normal relaxation time

	Hypo-thyroid	Hyper-thyroid	Method
Rives *et al.* (1965)	38	78	K and P
Young (1964)	60	60	P
Lambert *et al.* (1951)	23	75	S
Robson *et al.* (1965)	12	69	E
Nuki & Bayliss (this study)	27	62	P
Sherman *et al.* (1963)	6	23	P
Reinfrank *et al.* (1967)	28	8	P
Abraham *et al.* (1966)	0	10	K
Mann (1963)	0	10	K

P = photomotogram, K = kinemometer, S = strain gauge transducer, E = electronic recorder.

The value of the Achilles tendon test is further limited by a number of conditions which may prolong the reflex time such as oedema (Harrell & Daniel, 1941; Abraham *et al.*, 1966), diabetes mellitus (Beardwood & Schumacher, 1964), sarcoidosis (Richards, 1962), neurosyphilis (Simpson, Blair & Nartowicz, 1963a), myasthenia gravis and schizophrenia (Simpson *et al.*, 1963b), hypokalaemia (Carr *et al.*, 1963), peripheral vascular disease (Galpin & O'Brien, 1964), normal puerperium (Reinfrank *et al.*, 1967), sprue (von Binswanger, Studer & Wyss, 1961) and pernicious anaemia (Nuttall & Doe, 1964). Some drugs may shorten the reflex time, namely amphetamine, ACTH, cortisone, oestrogens and salicylates (Lawson, 1958), adrenaline (Goldberg, 1962; Avera & Overholt, 1962) as well as thyroid hormones. Bromides and antithyroid drugs may lengthen the time (Lawson, 1958).

The fact that the ankle reflex time gives some indication of the peripheral end-organ action of thyroid hormone, coupled with its simplicity, cheapness and immediate availability, makes it a useful adjunct to the clinical assessment of thyroid status provided its limitations are appreciated. The test is of value in following the response of the hypo- and hyper-thyroid patient to treatment.

Acknowledgment

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Recent trends in acute viral hepatitis

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ACUTE hepatitis is one of the most important infectious diseases to which man is prone. There is good evidence that a virus is the infective agent; but the offending virus or viruses continue to be elusive despite intensive efforts at isolation, both *in vivo* and in tissue culture (Rightsel, 1967). It is clear that the vital problems are the failure to propagate the infective agent in any host except man, and the consequent absence of any specific diagnostic serological test.

Post-transfusion hepatitis

While infective hepatitis is usually spread by ingestion, there has been increasing interest in viral hepatitis known to follow injections or similar manoeuvres, and the transfusion of blood,