Tremor in Hyperthyroidism

TREMOR IN HYPERTHYROIDISM

ITS VALUE IN THE DIAGNOSIS AND ASSESSMENT OF THE CONDITION.

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THE work described in this paper was undertaken in order to determine whether a quantitative examination of the rate and amplitude of tremor was of any diagnostic value in cases of hyperthyroidism, and whether a relationship existed between the tremor and the clinical severity of hyperthyroidism in an individual. It was thought that, if such a relationship did in fact exist, it would prove of value in the treatment of these cases.

Tremor is a cardinal sign of hyperthyroidism, and is usually observed in the fingers of the outstretched hand of the patient. In a typical case the tremor is said to be fine, *i.e.* of small amplitude, and rapid in rate. A review of the literature reveals that the subject received more attention towards the end of last century than in recent years. Charcot (1856) stated that tremor might be one of the first signs of hyperthyroidism to develop, that it was of great diagnostic importance and with Marie (1883) gave the rate of tremor as 8 to 10 per second. Byrom Bramwell (1889) also recorded tremor in hyperthyroidism, using a Dudgeon's sphygmograph placed over the centre of the wrist, and gave its rate as 8 to 10 per second. These with other early observations on the rate of tremor in hyperthyroidism are given in Table 1. Whilst the values are gathered together into one table, they were measured by different methods, and sometimes in different parts of the body, and are thus not strictly comparable. These authors did not comment on the amplitude of the tremor, and did not enquire into the possible relationship of the tremor to the clinical severity of their cases.

TABLE 1.

Pierre Marie (1883)	8 to 9 per second
Wolfenden & Williams (1888)	10·8 to 11·5 per second
Bramwell (1889)	8 to 9 per second
Peterson (1890)	8·7 to 12 per second
Dutil (1891)	8 to 9·5 per second
Dana (1892)	8 to 9·5 per second
Eshner (1897)	7·2 per second

More recently the occurrence of tremor in normal individuals under various circumstances has attracted some attention. The present position has been well summarised by Sollenberger (1937). It is recognised that tremor occurs during normal postural contraction, and that the individual tremor waves are often irregular as regards both rate and amplitude. The majority of investigators find that the rate lies between 5 and 15 per second, and that the degree of tension in the muscles of the fingers influences the results. A statement on an inverse relationship between rate and amplitude was first made by Eshner (1897), and included as one of the laws of tremor by Binet (1920). Sollenberger (1937) carried out detailed observations on two cases, and found that the rates were 9 to 11·9 per second in one individual, and 12·6 to 15·1 per second in another; the amplitude varied between 0·05 and 1·5 mm.; the articulations of the second and third phalanges of the right index finger were investigated.

METHOD.

Most observers have found it convenient to record the tremor of the outstretched finger, usually the index. The older workers recorded tremor by attaching a lever to the finger, or by allowing the finger to rest lightly on the surface of a tambour, and allowing another tambour, connected to the first, to write on a kymograph. These methods are open to objections. It is difficult to get the natural frequency of such systems sufficiently high to record faithfully the abrupt changes in direction which occur in the course of tremor. Further, the fact that the finger is attached to, or is touching, the apparatus introduces cutaneous sensations, which are difficult to standardise, and which may, in conjunction with proprioceptive sensations, modify the tremor considerably.

The method we used is essentially the same as that used by Sollenberger (1937), and Mehrtens and Pouppirt (1928). The patient was seated at a steady table, and the right forearm and hand were rested on a Carr splint attached at a comfortable angle to a heavy stand. A thimble bearing a fine steel wire was placed on the outstretched index finger. The finger was not supported beyond the metacarpo-phalangeal joint, so that movements could occur at the three distal joints. The wire was about 2 cm. long, and 0.25 mm. in diameter (33 s.w.g.). The temper was taken out of the wire by heating. A white screen about 8.5 cm. in diameter, with a target hole 3.5 mm. in diameter, was clamped on the stand carrying the splint; it was adjusted to a convenient distance, and the subject was instructed to keep the tip of the wire on the index finger at the centre of the target hole. The steel wire was illuminated by the usual lamp (75 watt exciter lamp) and condenser system; an image of the wire was formed on the cylindrical lens of the recording camera by a camera lens of 5 cm. focal length and aperture f/8. The distance between the lens and the camera was 100 cm., and the magnification of the movement of the wire was therefore 19 times. Intervals of one-fifth of a second were recorded by a lever attached to the escapement wheel of a calibrated clock. Any electrocardiographic camera could be used. The tremor was recorded on bromide paper (Kodak B.G.1). The heavy stand carrying the splint was provided with vertical and horizontal screw adjustments so that the image of the wire could be brought into focus on the recording camera without disturbing the patient. When the patient was comfortably adjusted, the operator started the camera, and the photograph was taken without the patient's knowledge. Three separate records, each lasting 2 to 3 seconds, were taken at each session. The recordings were carried out in a dimly lighted side-room attached to the wards in the hospital; if the patients were confined to bed, they were wheeled into the side-room on a chair. It was possible to carry out the observations on in-patients suffering from hyperthyroidism without upsetting them.

RESULTS AND DISCUSSION.

Examples of the tracings obtained are given in Figs. 1 and 2, which are sufficiently explained in the legends. In the analysis of the tracings certain conventions were observed. A complete reversal in the direction of the wave was regarded as indicating a tremor (Fig. 1A); an interruption of the movement without a reversal was not counted as a tremor (Fig. 1B). The total number of tremors on the three tracings obtained at the one session was counted, and the rate expressed as tremors per second. Rates, calculated from each tracing taken during one session, were found to approximate closely to each other, and the average of these rates could be used as the final tremor rate. As the amplitude of the tremors varies considerably in a tracing the following practical scheme of estimation was adopted. Five grades of amplitude were used as shown in Table 2.

TABLE 2.

AMPLITUDE GRADE	DESCRIPTION OF PHOTOGRAPHIC RECORD.
—	Almost no perceptible tremor.
+	Majority of Waves about ¼ in.
+ +	,, ,, ,, ½ in.
+ + +	,, ,, ,, 1 in.
+ + + +	,, ,, ,, 1½ in.

It is possible, of course, to measure the amplitude of each tremor wave in a tracing, and to determine the mean values, but it was not considered that such a degree of accuracy was necessary for the present work where relatively large numbers of cases were examined.

Tremor was recorded in a group of 41 normal individuals; the average rate of tremor was 7·03 per second, with a standard deviation of 1·57; the extreme values were 4·1 and 9·8; 22 per cent of these cases had tremor amplitude of Grade — and 59 per cent Grade + (Table 3). The majority of these cases were between 20 and 40 years of age, but there

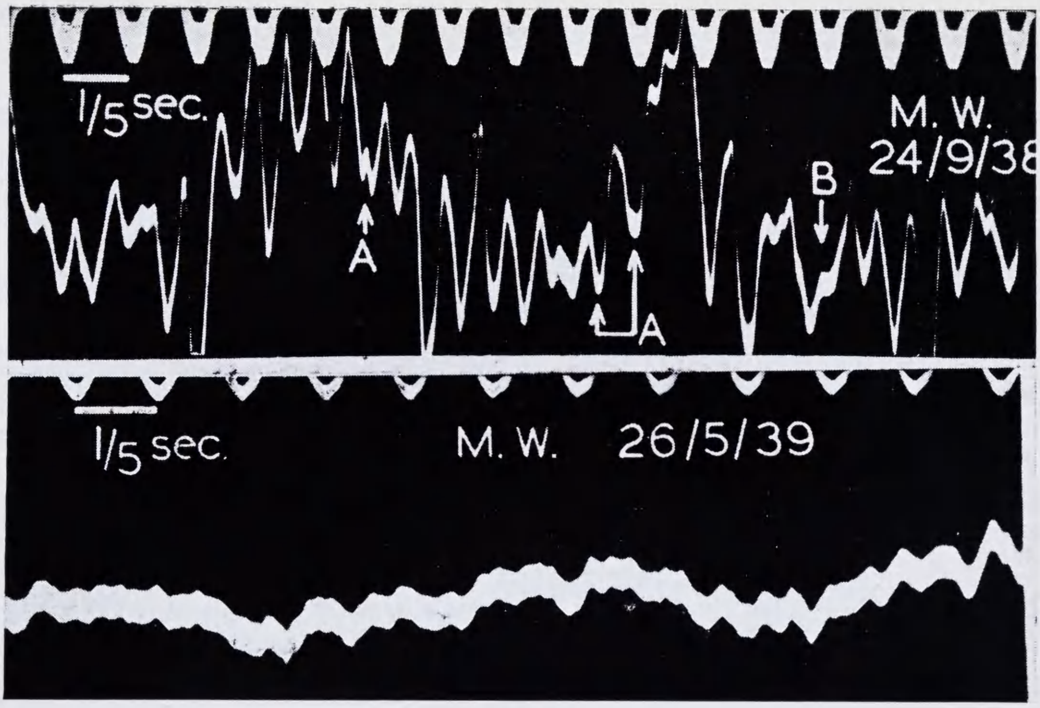

Fig. 1.

M. W. Aet. 42. Deep *X*-ray therapy to thyroid gland given during April 1938.
Upper tracing, 24-9-38. Tremor rate 10.5 per sec.
Amplitude, grade + + +. Clinical severity, + + grade.
Weight, 6st. 9lb.

Lower tracing, eight months later. Tremor rate, 8.5 per sec.
Amplitude grade +. Clinical severity, + grade.
Weight, 7st. 11 lbs.

A : Changes in direction counted as tremors.

B : A change in slope not counted as a tremor.

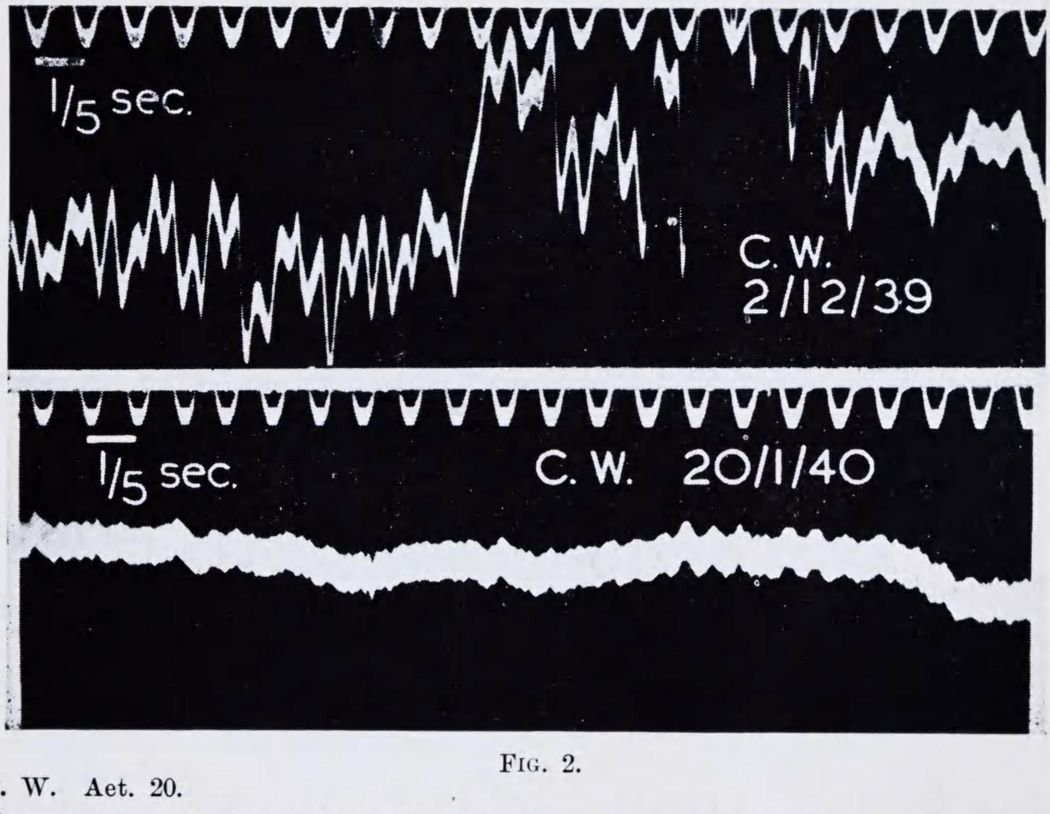

Fig. 2.

C. W. Aet. 20.

Upper tracing, six days before operation. Tremor rate, 10.9 per sec.
Amplitude, grade + + +. Clinical severity, + + grade

Lower Tracing, 45 days after thyroidectomy (Mr Mill Renton).
Tremor rate, 5.4 per sec. Amplitude, grade —. Clinical severity, — grade.

was no correlation between age and tremor rate. These 41 subjects served as our control group, and we have taken their average tremor rate and distribution to be that of the normal under the conditions of recording specified. It was necessary to examine a control group because there are no recorded figures giving the tremor rate in a group of normal individuals using this method.

TABLE 3.

	Normal controls	Clinical severity of hyperthyroid cases				All hyperthyroid cases
		— grade	+ grade	+ + grade	+ + + grade	
Number of observations	41	53	55	49	24	181
Mean rate of tremor	7·03	7·13	8·96	9·33	9·75	8·63
Standard deviation	1·57	1·90	1·61	1·03	1·35	1·83
Mean amplitude of tremor in mm.	0·34	0·21	0·48	0·64	0·88	0·53
P.c. of cases showing tremor of amplitude + +	17	13·2	32·7	45	37·4	31
amplitude + + +	2·4	1·9	5·5	14·6	37·4	11
Mean pulse rate	—	82·4	93·4	98.4	112·9	93·5

Our observations on tremor in hyperthyroidism were made on a group of 93 cases, and extended over four years. The majority of these cases received deep X-ray therapy. It was necessary to classify the cases according to the severity of the disease. In doing this, no rigid criteria are available at present—the whole condition of the patient has to be taken into account. The following features were specially considered: (a) the patients' symptoms; (b) their functional efficiency, *i.e.*, whether ambulant or not, and, if ambulant, what proportion of their normal activity they were able to undertake ; (c) the degree of goitre, exophthalmos, tachycardia and loss of body weight. The classification can be described as follows: —grade means that the patient had had hyperthyroidism, but was apparently cured at the time of examination, and was able to carry out normal activity ; + grade means that a mild degree of hyperthyroidism existed, but the patient was able to carry out restricted activities ; + + grade means hyperthyroidism of moderate severity ; + + + grade indicates severe hyperthyroidism ; in extremely severe cases the test was not carried out, as these patients were confined rigidly to bed. One of us (S.L.) had the opportunity of observing the in-patients during their stay in hospital.

The results are summarised in Table 3. It will be seen that there is a progressive increase of the tremor rate with increasing severity of the hyperthyroidism. There is a statistically significant difference between the mean tremor rates of the normal group and of those suffering from hyperthyroidism, even of a mild degree, *i.e.*, + grade (difference of means 1.93, standard error 0.327). The rates of those cases which were regarded as being cured (— grade) were not significantly different from those of the normal controls (difference of means 0.096, standard error 0.358), but were significantly different from those of + grade (difference of means 1.83, standard error 0.334). Table 3 also shows that there is progressive increase in the amplitude of the tremor with increasing clinical severity, and the same tendency is seen in the case of the pulse rate. The rate, amplitude of tremor and pulse rate in — grade cases, *i.e.*, those successfully treated, were all restored to the normal range.

We next proceeded to examine whether a correlation existed between the amplitude, the rate of tremor and the severity of hyperthyroidism. Pearson's co-efficient of mean square contingency, C, and Tschuprow's co-efficient of contingency, T, both of which are applicable to categorical data, were calculated. It will be seen, from Table 4, that there is a significantly high correlation between the degree of severity of the cases of hyperthyroidism, and both the amplitude and the frequency of tremor (Table 4, A and B). It is of interest to note that the correlation between the amplitude of tremor and the severity of hyperthyroidism (Table 4 A) is the highest obtained in the course of the present analysis.

TABLE 4.

	Correlation.	N	n	χ^2	C.	T	χ^2 for P =0.01.
A.	Clinical severity and amplitude of tremor	181	12	509.933	0.859	0.902	26.217
B.	Clinical severity and frequency of tremor	180	9	59.291	0.50	0.332	21.666
C.	Clinical severity and pulse rate	144	18	61.261	0.546	0.317	34.805
D.	Amplitude and frequency of tremor	183	12	104.009	0.602	0.405	26.217
E.	Pulse rate and frequency of tremor	139	18	34.638	0.446	0.242	34.805
F.	Pulse rate and amplitude of tremor	139	24	43.507	0.488	0.253	42.980

N is the total number of observations.

n is the degrees of freedom.

If the calculated value of χ^2 is greater than that given in the last column, then there is a significant correlation between the two variables.

C and T are defined in the text.

The pulse rate has long been recognised as a valuable index to the severity of a case of hyperthyroidism. We counted the pulse rate at the time of recording the tremor, and were thus able to determine the correlation between pulse rate and clinical severity in our group of cases (Table 4 C). As was to be expected, a significant correlation between these two variables was present. However, we were surprised to find that this correlation was of the same order as that between tremor rate and clinical severity (Table 4 B), and was actually lower than that which existed between clinical severity and amplitude of tremor (Table 4 A). If a single sign were to be used as an index of severity of hyperthyroidism, then it would appear that the amplitude of tremor is superior to the pulse rate. The correlations between the pulse rate and the tremor (Table 4 E & F) are relatively poor; this suggests that the tremor and the pulse rate are objective signs of different aspects of hyperthyroidism.

There is a fairly good correlation between the amplitude and the frequency of tremor in hyperthyroidism (Table 4 D); that is to say that on the whole the amplitude increases with the tremor rate (see also Table 3). The same thing has also been noted in the tremor of fatigue (Bousfield, 1932), which is thus another exception to Binet's law of tremor.

It is of interest, in view of the definite significant inter-relationship between all four factors considered, to obtain an idea of the relationship of each with severity of the disease, independent of variations in the remaining ones. For this purpose, utilising the values of T as sufficient approximation to the co-efficient of correlation and, in the absence of anything to the contrary, assuming that the regression in each case is linear, we have calculated partial correlations with the following results:

Variable	Constants	Partial Correlation
Severity and amplitude	Frequency and pulse rate	·888
Severity and frequency	Amplitude and pulse rate	—·122
Severity and pulse rate	Amplitude and frequency	·230

It would appear again that the variable of outstanding importance in assessing severity of the disease is amplitude of tremor. The remaining two values are of a very much lower order of importance, and of doubtful significance statistically. Pulse rate shows a small, probably significant, positive correlation, but frequently the tremor rate has little association with severity, when variations in the remaining two variables are eliminated.

It is of interest to note the association between the three physical signs themselves when one or other is constant.

The results are these:—

Variable	Constants	Correlation
Amplitude and frequency	Pulse rate	·366
Amplitude and pulse rate	Frequency	·175
Frequency and pulse rate	Amplitude	·158

There is a significant residual correlation between amplitude and frequency of tremor, but the correlation between heart rate and either amplitude or frequency, when one or other of these is held constant, is extremely small and of little prognostic import.

Conclusions.

The rate of tremor, even in mild cases of hyperthyroidism, is significantly greater than that in a normal control group. Analysis has shown that the amplitude of tremor is much more closely related to the severity of hyperthyroidism than either the tremor rate or the pulse rate. This leads us to stress the importance of the amplitude of tremor as a guide to the severity of a known case of hyperthyroidism.

It is possible that the analysis of photographic records of tremor will be found to be of value in differentiating hyperthyroidism from hysteria, neurocirculatory psychasthenia and similar conditions.

Summary.

A method of recording tremor in the outstretched index finger is described. Using this method the mean tremor rate in a group of 41 normal individuals was found to be 7.034 per second, with a mean amplitude of 0.34 mm.

181 observations on 93 cases of hyperthyroidism were made. The mean tremor rate varied from 7.13 to 9.75 per second, and the amplitude from 0.21 to 0.88 mm. according to the severity of the cases. Analysis revealed that (a) the tremor rate in hyperthyroidism, even of mild severity, is significantly greater than that of normal people; (b) a high degree of correlation exists between the amplitude of the tremor and the severity of the hyperthyroidism; (c) whilst the correlation between tremor rate and clinical severity was low, it was significant, and of the same order as that between pulse rate and clinical severity; (d) the tremor rate and amplitude in hyperthyroidism can be restored to the normal range by successful treatment.

The variable of outstanding importance in assessing severity of hyperthyroidism is amplitude of tremor.

It is suggested that the quantitative examination of tremor may be found to be of value in the differential diagnosis of hyperthyroidism.

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