TREMOR IN GRAVES' DISEASE.

BY A. MAUDE.

THIS important symptom was first discovered by Charcot in 1856,¹ in the earliest French record of a case of this disease: Trousseau also noted excessive tremor in one instance. It did not escape the observation of Sir Morell Mackenzie in 1868,² while Dr. Hector Mackenzie³ finds it noted in the records of St. Thomas' Hospital more than a dozen years ago.⁴

But on the whole this important factor in the recognition of the disease seems to have attracted little attention in England. Dr. Gowers' book is the only English text-book which mentions it, and in the discussion at the Ophthalmological Society in 1886, Dr. S. West, alone alluded to it.

Unquestionably it is a very constant symptom in Graves' disease, for I found it present in a typical form in six patients of a series of nine taken at random;⁵ only two years ago, however, a patient was shown at a provincial medical society, and the tremors were ascribed to alcoholism.

The symptom has been very fully studied in France, chiefly by Charcot⁶ and Marie, and the important monograph⁷ of the latter embodies most of our knowledge on the subject.

¹ *Gaz. Méd. de Paris*, No. 38.

² *Trans. Clin. Soc.*, 1868.

³ *Lancet*, ii., 1890, 545.

⁴ Russell. *Med. Times & Gaz.*, 1876, p., 250.

⁵ A number of references in French literature are given by Marie. The more important are:—Chvostek, *Weiner Med. Presse*, 1870, Nos. 38, 39, 40, 42; Féréol, *Soc. Méd. des Hôp.*, Nov. 13, 1874; Delasiauve, *Soc. Méd. des Hôp.*, Nov. 27, 1874; Raynaud, *Thèse de Paris*, 1875; Rey., *Thèse de Paris*, 1877; Teissier, *Congrès de Clermont pour l'avancement des sciences*, 1876; Douglas, *New York Med. Journal*, 1879; Russell, *Med. Times & Gazette*, p. 250, 1876; Wynne Foot, *Dublin Journ. of Med. Sc.*, Nov., 1880; Nothnagel, *Wiener Allgemeine Zeit.*, p. 501, 1882.

St. Bartholomew's Reports, xxvii., 1891. Cases of Grave's disease, by A. Maude.

⁶ See *Leçons du Mardi*, 1888-9, p. 231 (et sequit.).

⁷ *Contributions à l'étude et au diagnostic des formes frustes de la Maladie de Basedow*, Paris, 8vo.

I think it would not be too much to say that tremor is always present at some time or other in the course of the disease; even when we fail to find it on examination we shall learn that it occurs on excitement, or on any sustained muscular movement. In cases that begin rather suddenly, and settle down into an ill-marked condition, it has generally existed early, and does not last very long; but as a rule tremor is a late symptom. One patient of mine who had had goitre and exophthalmos for twenty years, had never noticed the tremor till a year before she came under my charge; and in all my cases except two it has been long after the establishment of other cardinal signs that it appeared. In one instance the patient, after some years of futile treatment by drugs, has improved very greatly under the continued use of a Leiters tube to the epigastrium; tremor has been present in a slight degree for a year or two, but since the general symptoms have improved the tremor has become far more persistent and marked.

The degree varies so much that in many cases the patient is quite unaware of it, and the condition is generally only noticed at first by the subjects of it because it interferes with delicate movements of the fingers, such as writing or sewing; but it may become so severe as to cause her to drop cups and plates, as in my patient's case, or even to prevent walking,¹ or preclude the physician from feeling the pulse.²

My experience confirms the observation that the movements are as a rule very small in amplitude, strikingly regular, and are not dependent on voluntary motion.

The vibration is most marked in the hands, and may in very slightly marked cases be confined to them. The other muscles most affected are the pectorals, the serratus magnus and the erector spinæ. But if the tremor is well marked in any group of muscles it is sure to be general, over the whole body, to some degree. I have seen one lady who had never noticed it in her hands, where it was slight, but had noticed it in the muscles of the back; it was confined to these two muscular groups.

Tremor is usually symmetrical, but not necessarily; and

¹ Charcot.

² Russell.

has been known to be unilateral, when the goitre or exophthalmos are also unilateral.¹ In cases where it is well marked, the patient is in a state of perpetual vibration, sitting or standing. It is then much marked in repose, and only slightly exaggerated during movement.² But though muscular repose does not necessarily free the patient from tremor, mental repose does so to a great extent. It is always increased by agitation or "nervousness": it is produced or increased by hurried muscular action, or by any attempt to perform a movement carefully or accurately, especially if the patient is aware of her tremulous condition.

It is easy to ascertain the existence of even slight tremor by placing the hands on the patient's shoulders when she stands up. In this position the vibrations are, in well-marked cases, best felt in the vertical direction, but even in slight cases, where no vertical movement is felt, a small lateral oscillation can often be seen, if not felt.

On stripping the subject we may perceive that the muscles of the extremities and trunk are in a state of continual fibrillary movement, "that the whole surface of the body is the seat of a kind of general palpitation of a most curious character." (Marie.)

The tremor may be so exaggerated as to affect the respiratory muscles, producing a jerking laryngeal sound audible at some distance.³ To study this condition carefully, make the patient stretch out her arms, stripped, with the hands lightly extended. The whole limb is then seen to be affected by rapid contractions of the muscles, the amplitude of which varies in different subjects. The movement is usually fine, and is always quite regular and constant. The oscillations are most easily visible in the hands, and they affect the hand as a whole, being produced in the flexor and extensor groups of the forearm. The fingers have little individual movement, and the interossei especially have no share in it. The wrist is the joint most affected by the oscillations, and probably the fact that the flexion and extension movements are more marked than the supination

¹ Gowers.

² Féréol.

³ Charcot, *loc. cit.*

and pronation is due to the greater ease with which the wrist moves in the former plane, than to any election of groups of muscles in the forearm on the part of the tremor. The oscillations are more visible in the hands, not because the hands are farther from the point of support of the limb, but because the muscles of the forearm are affected most.

This "flexor tremor" is also characteristic of alcoholism, but at the same time in alcoholism there is distinctly more contraction of the interossei and consequent lateral deviation of the fingers.

In the same way the movements of the lower limbs may be studied. Let the patient stand with the foot extended, just pressing the floor with the toes; the vibrations are then usually marked. Then let her sit with the knees at a right angle, and the toes touching the floor, and we shall find in a well-marked instance, the same sort of vibration as in "ankle-clonus" (Fuss phenomenon). In this connection I examined the patellar reflexes in five cases, and found them absent in four, and feeble in the fifth. Tremor is usually constant in any one patient for a long period, but it has terms of exacerbation, just as have all the other symptoms; so that in many cases the habitual or constant tremor passes unnoticed by the patient, but the exacerbations are observed.

I have not succeeded in finding any direct relation between the increase of tremor and increase of other symptoms.

Marie has obtained mechanical tracings of this tremor, and gives us an excellent account of them in his monograph; and to his work I am entirely indebted for knowledge on this part of the subject.

Registration of the vibrations was obtained by two methods. First, by a modification of Marey's tambour, applied to the dorsal aspect of the metacarpus; secondly, by means of an india-rubber ball or "pear" grasped in the patient's fist (like an enema syringe) not tightly enough to compress it. Of course, in both cases the tambour and "pear" are connected with an ordinary recording apparatus, furnished with a tuning fork to record the rate.

Marie and Boudet also tried to obtain tracings by means of Rosapelly's apparatus; but the instrument only gave the frequency of the vibrations, without any record of their amplitude.

In all comparative experiments of course the same mechanism, pressure and tuning fork must be used.

From the tracings we learn, first as to the *rapidity* of the oscillations, that they are strikingly regular in rhythm; the interval between the crests of the successive waves varies very little; in fact the tracings are almost as regular as those of a tuning fork.

In eleven cases, in which tracings were taken by Marie, the rate of movement was almost the same in all, varying only from $9\frac{1}{2}$ to 8 oscillations per second, with a mean for all cases of $8\frac{1}{2}$. As to amplitude, in the vertical direction the oscillations present anything but regularity. If we examine tracing 1 of Marie, (p. 20), we see that the waves increase gradually for a certain number and decrease again. The tracing presents a series of roughly fusiform enlargements, described as nodes (nœuds) by M. Fernet in his monograph.

These variations in amplitude are very irregular, and no explanation has yet been offered as to their causation, but they certainly have no correlation with the movements of respiration or circulation. A distinct correlation is however found to exist between the increased waves and the occurrence of cough; an attack of cough produces a greater amplitude of vibration without disturbing the rate. This change is probably merely due to the shock of the chest wall, produced by the cough, being transmitted through the shoulders and arm to the hands.

In reply to the question whether there is any direct relation between the degree of tremor and the intensity of other symptoms, my own impression is strong that there is none. Not only, as I have said above, may it become most pronounced as other symptoms are improving, but it is more constant, in individuals who present it, than any of the other (notoriously inconstant) symptoms of the disease.

It has also no relation to a general emotional (or "nervous") state, as hysterical tremor often has.

When we compare the tracings produced in Graves' disease with those produced by other forms of tremor, the difference is instructive. Such other forms are senile tremor, paralysis agitans, general paralysis, disseminated sclerosis, hysteria, and poisoning by alcohol, mercury, lead or arsenic.

The tracings obtained in Graves' disease are exactly

similar in time and form to those produced in animals after excision of the thyroid gland.¹

Mr. Horsley also drew attention to the fact that the tremor wave in paralysis agitans is a compound wave, a summation of two separate waves, as the larger convulsive tremor waves in myxœdema are summations of smaller ones.

The correspondence of the tremors in myxœdema and exophthalmic goitre afford some evidence of the seat of production of the tremor; for Schiff had shown that the tremor in cachexia strumipriva was of central origin, and Horsley confirmed the observation, while he carried the investigation further, for he removed in one case the centre in the cortex for the upper limb; the result was complete brachiooplegia, but no interruption of the tremors; thus proving that the tremor originated not in the cortex but in some lower centre, either in the basal ganglia, the bulb, or the spinal cord; and support is given to this assumption by the fact that at first voluntary effort abolishes the tremor, that the inhalation of ether increases it, and that it disappears on reflex irritation.

Moreover the rate of vibration is 8 to 10 per second at first, and later some multiple of these numbers, which is the rate determined by Loven for the spinal cord in frogs, and probably also the rate for the spinal cord in man (Horsley).

Mr. Horsley, however, admits that none of these experiments disprove the possibility of the tremors being idiomuscular.

In the disease we are studying we have seen the rate of vibration is very constant, 8 or 9 per second; in senile tremor it is much more slow, $4\frac{1}{2}$ to $5\frac{1}{2}$ (Marie); in no case above 6 per second. In paralysis agitans the rate varies considerably in different cases; it may simulate disseminated sclerosis in its slow rate and its irregularity. Charcot gives an average of 3 to 6 oscillations per second, and Marie an average of 5. On the other hand it is quite exceptional for the movements of insular sclerosis to be as fine and regular as in Graves' disease.

The movement in Graves' disease and mercurial poisoning are shown by Charcot² to differ only in rate, and in the fact that in the former affection they are much more continuous and regular, and are not increased, as a rule, by intentional muscular action.

In general paralysis and alcoholism the rate of vibration may be much the same as in Graves' disease, but tracings

¹ Brown Lectures, 1885.

² *Leçons du Mardi*, 1, p. 878.

show that while the general line in the latter is regular and straight, that produced in the other two affections is much more wavy and jerky. Moreover in Graves' disease the intrinsic muscles of the hand and tongue escape, while they are particularly affected by alcohol poisoning.

Tremor in lead poisoning is so rare and varies so much in character that it is impossible, as yet, to draw distinctions on this head.

An important feature which separates that of Graves' disease from tremor due to metallic poisoning is the entire escape of the muscles of the head, neck, lips and tongue.

I have not sought to press the diagnosis of this form of tremor from others, but merely by indicating what I believe to be its salient features, to leave to the cultivated neurologist its differentiation from other forms better known.

The affinities of this tremor are rather to purely "asthenic" trembling, such as follows in many subjects an acute illness, or to the tremor of old age.

From hysterical it is separated broadly by its great regularity in rhythm, but, of course, so-called hysterical trembling may resemble that of Graves' disease, as it will occasionally imitate that of any other neurosis.

The points on which I would lay stress, are :—

(a) The great frequency of it in cases of exophthalmic goitre.

(b) Its constancy when it does exist.

(c) Its constant character.

It may be observed that I make no mention of chorea in this neurosis. The condition has been noted by observers fully capable of differentiating true choreic movements, but there is no evidence as to whether it exists or not side by side with the ordinary trembling.

We ought not to lay too much stress, except for diagnostic purposes, on differences in tremor in various diseases. We know nothing about the pathogeny of tremor, or of the seat of the lesion, and it may well be that what appear to be distinct forms of trembling owe their difference to the fact that certain muscles are affected rather than to the fact of different causation.