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RESEARCHES ON THE CONTRACTURE OF SKELETAL MUSCLE.

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I. INTRODUCTION.

THE literature of contracture of skeletal muscle is extensive. Gasser [1930] has recently devoted to it a critical review. Points of importance which emerge are that (1) contractures seemingly quite diverse have yet features in common; (2) many reversible contractures in their essential chemistry resemble normal contraction. All alike show formation of lactic acid [see Gasser, 1930], splitting of phosphagen and production of ammonia. Iodoacetic acid prevents formation of lactic acid in contracture just as in contraction [Bethe, Norpoth and Huf, 1931]. The chemistry of contracture seems thus not to differ qualitatively from that of contraction.

Further, the researches of Hartree and Hill [1922] on veratrine contracture have shown quantitative similarity between the energetics of contracture and contraction. "The efficiency—measured by the ratio H/Tl—with which prolonged contraction is maintained is almost exactly the same in veratrine contraction and in normal tetanus." The same conclusion is reached by the myothermic researches of Hartree and Hill [1924, 1928], and of Furusawa and Hartree [1926] on caffein contracture and the contracture provoked by direct stimuli of greatly supramaximal intensity; also for this latter contracture by the analyses of Meyerhof and Lohmann [1925]. We seem to have before us here a broadly applicable fact.

Its theoretical importance is great. It shows that the reversible contracture of skeletal muscle is neither extreme slowing of the process of relaxation nor the operation of a special contractile apparatus, myofibrillar, or—on Bottazzi's [1897, 1926] hypothesis—sarcoplasmic.

Since reversible contractures neither in chemical process nor in mode of energy turn-over depart essentially from ordinary tetanus the differences between the two must precede the final mechanical and thermal steps. One is led thus to approach contracture by the path of muscular excitability, especially the reversible contractures which are reactions of the muscle fibre to a stimulus, electrical or chemical.

Reversible contracture of skeletal muscle might be the result of a muscular excitation whose characteristic was slowness of development and subsidence, with absence of wave propagation. This hypothesis is borne out by the facts obtaining for direct and indirect electrical excitation of contracture, as also by the electromyogram of the "neuro-muscular" contracture of the anural Amphibia.

II. MATERIAL AND GENERAL METHOD.

The experiments have been mostly on various Anura and the cat. In the former the tendency of any given muscle, especially gastrocnemius, to respond to excitation by contracture is variable. Two factors of influence are species and nutrition. *R. temporaria* especially tends to contracture, a tendency favoured by vigorous condition of the muscle and by resistance to fatigue, therefore probably by richness in reserve nutriment. The tendency decreases under captivity.

My experiments have been on the muscles *in situ* with circulation intact (decerebrate). The contractions have been recorded, either isotonically on the kymograph with light levers (5–10 g.), or isometrically and optically with the torsion-wire type of myograph of Sherrington of rapid natural frequency, and photographed along with the electromyogram given by the string galvanometer (Cambridge new model).

III. GALVANIC CONTRACTURE.

If the reversible contractures of skeletal muscle connote an excitability of extreme slowness, that slowness should reveal itself (1) by high chronaxie, (2) by possibility to evoke contracture by "addition latente," *e.g.* summation of direct electrical stimuli too brief to be singly adequate, (3) also by summation of successive motor nerve impulses.

It is well known that closing or opening a galvanic circuit in series with frog muscle can excite a response which, owing to greater or less contracture, exceeds in duration the twitches excited by stimuli, indirect or direct, which are quite brief. Biedermann [1895] studied this galvanic contracture particularly in relation to the direction of the stimulating current. I have tested the influence of the duration of the electrical stimulus upon the contracture. I have excited the gastrocnemius of *R. temporaria* lengthwise by two AgCl electrodes, at tendon and proximal pole of the muscle respectively, the contractions being registered isotonically. Under these conditions muscles tending even strongly to galvanic contracture respond by twitches free from all contracture to brief single stimuli—break shocks or feeble condenser discharges—adjusted to give contractions of comparable "height." In general the contracturing action of the galvanic current is more marked, or present only, for the "ascending" current. Fig. 1 A shows the contracture from an ascending current (cathode proximal), while a descending current of the same strength (Fig. 1 B) excites only a twitch without contracture at closure, at opening a smaller twitch but clearly prolonged by contracture. When the current is ascending the greater part of the muscle is submitted to the contracturing action of the virtual cathode, near the proximal pole of the muscle; with the opposite direction of current (cathode at tendon) the main bulk of the muscle is under the inhibiting (relaxing) influence of the anode. In Fig. 1 C, with a strong descending current, the twitch at opening has quite the appearance of "post-inhibitory rebound." This relaxatory inhibition appears more clearly still in Fig. 1 D. First an ascending current is sent into the muscle and provokes a twitch followed by strong contracture which persists after cessation of the current. Some seconds later a descending current is sent into the muscle: its commencement causes a weak twitch

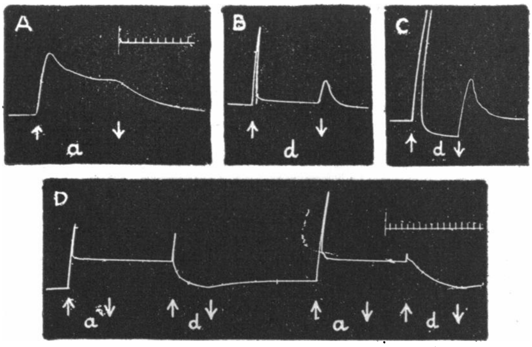

Fig. 1. Galvanic contracture of the gastrocnemius of *R. temporaria* "longitudinally" excited. Isotonic lever with a load of 5 g. Make and break of current marked by arrows pointing upwards or downwards respectively. Reduced by ½. A. Ascending current (*a*) of 1·5 volts. B. Descending current (*d*) of 1·5 volts. C. Descending current of 2·5 volts. D. An experiment (performed on another preparation) showing the contracture producing action of the cathode and the inhibitory action of the anode. Explanation in the text.

closely followed by relaxation of the contracture. This last recurs directly the inhibitory current stops. The figure shows a further example. This inhibitory effect of the anode on galvanic contracture proves the active character of this contracture. A similar anodal inhibition was shown by Biedermann for veratrine contracture.

In experiments on gastrocnemius of *R. temporaria* in the cold (11–14° C.) I have found it possible to separate to some extent contracture from contraction, and to measure the chronaxie of the former. Exciting the muscle with currents of increasing voltage, contracture can appear regularly before any trace of the ordinary contraction (Fig. 2 A). This latter does not occur until considerably higher current intensities are reached. Hence one can measure the threshold for contracture and determine approximately its chronaxie by the well-known rapid method of Lapicque, namely, to double the rheobasic voltage and to find the shortest duration which the stimulus of doubled intensity must have in order to excite. Fig. 2 B gives a determination, at 11·5° C. The chronaxie of the contracture is 70–75σ; that of the twitch contraction about 0·7σ. The chronaxie of the contracture is about a hundredfold that of the ordinary contraction.

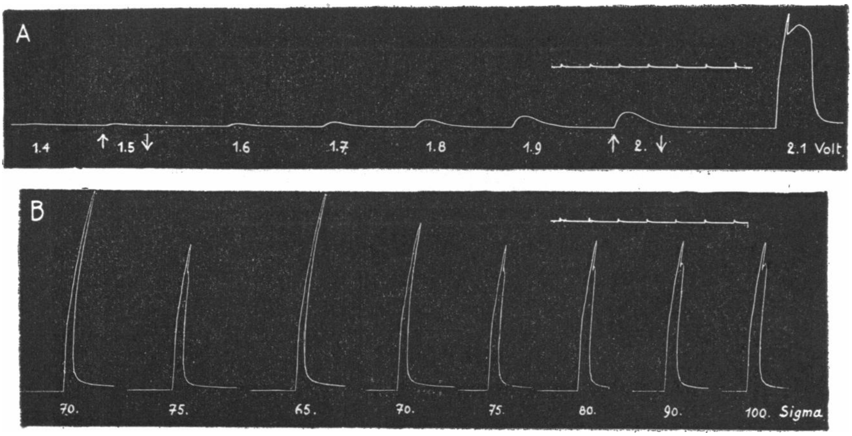

Fig. 2. Galvanic contracture of the gastrocnemius of *R. temporaria*. Isotonic lever. Load 5 g. Temp. 11·5°. Time in seconds. Reduced by ½. A. Determination of the threshold (rheobase) of contracture. B. Determination of the chronaxie of contracture. For explanation see text. Notice the diminished height of the twitches associated with contracture. This phenomenon, which is constant, is apparently explained by a very early increase in the viscosity of the muscle, which decreases its speed of shortening and diminishes the inertia of the lever.

The galvanic contracture of mammalian skeletal muscle in the course of Wallerian degeneration of the motor nerve is absolutely similar to that of normal amphibian muscle (Fig. 3 B). The influence of duration of the stimulus is just as clear. It is seen in the different form of the twitch tension curves evoked respectively by the break and make shock of the inductorium. The make shock, which is slower than the break shock, evokes a twitch of sounder summit (Fig. 3 C). The twitches of the normal muscle reveal no trace of such a difference.

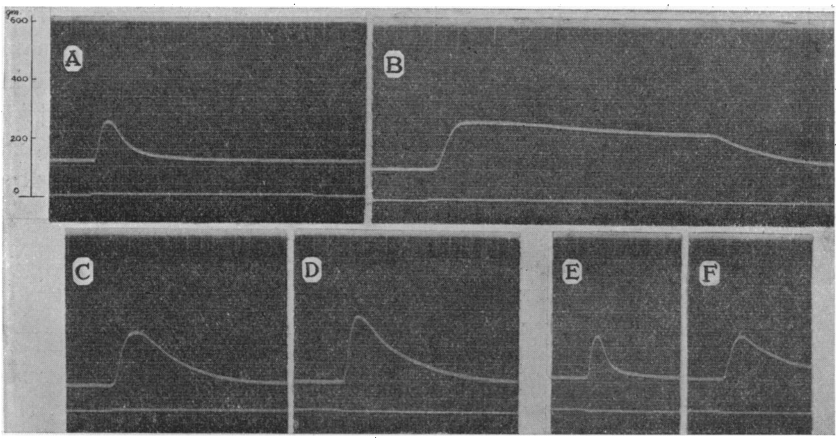

Fig. 3. Galvanic contracture of degenerated mammalian muscle (tibialis anticus of the cat, denervated 20 days previously). Longitudinal excitation. Sherrington isometric lever. Optical registration. Time in $\frac{1}{25}$ of a sec. Reduced by $\frac{1}{2}$. A. Galvanic excitation (ascending current of 2 volts) of the normal tibialis anticus. B. Similar excitation of degenerated tibialis anticus. C. Make-shock twitch, degenerated muscle (coil at 8 cm.). D. Break-shock twitch, degenerated muscle (coil at 8 cm.). E. Break-shock twitch, normal muscle (coil at 10 cm.). F. Break-shock twitch, degenerated muscle (coil at 10 cm.). Twitches in response to make shocks of the same height were identical in all respects.

This galvanic contracture of degenerating muscle is evidently the main cause of the seeming "slowness" of the galvanic twitch of the muscle under direct inspection, a "slowness" of diagnostic value to the clinician. Apart from this slow relaxation traceable to contracture, there exists certainly a slowness of the true twitch; this latter slowness attaches notably to the ascending phase of the isometric myograms given by degenerate muscles (cf. Fig. 3 A and E with B and F). This slowing of the twitch contraction of degenerate muscle is presumably related to the increase of chronaxie.

Discussion.

These experiments, confirming and extending older ones, show galvanic contracture as an outcome in the muscular fibre of a certain state of excitation capable of being inhibited by the anode. They define further the duration required for the stimulating electric current to give contracture. It is as though contracture attached to an excitable substance with a chronaxie much higher (× 100) than that of the excitable substance attaching to the ordinary "twitch"; in saying which I do not intend to imply the existence of two morphological entities coexistent in the muscle fibre to provide for two excitabilities. This approximate ratio 1 : 100 of the chronaxies of contraction and galvanic contracture in normal *temporaria* is just that found by Bourguignon [1923, 1931] for the two chronaxies of "myotonic" muscles of man, and by Kodera and Brücke [1928] for the chronaxies of contraction and contracture of initial stage of veratrinization in frog's muscle.

IV. CONTRACTURE EXCITED BY DIRECT ELECTRICAL STIMULI GIVING "ADDITION LATENTE."

An electrical stimulus of given intensity though failing singly, because of its brevity, to excite contraction of a slow muscle (or, generally, the reaction, of a protoplasm of high chronaxie), can yet by repetition, of above a certain frequency or length of series, be effective, in virtue of "addition latente." This summation has been the subject of researches by Keith Lucas [1907] and of Lapicque [1925, 1926]. If galvanic contracture has for its immediate antecedent a slow excitation with a very high chronaxie, one should find "addition latente," and evoke contracture by summation of brief stimuli, for example by induction shocks applied directly to curarized muscle. Previous curarization is required of course to preclude participation by nerve.

This expectation is confirmed. Gastrocnemius (*temporaria*) was employed with its marked tendency to contracture enhanced by previous short tetanization. Complete curarization an hour beforehand, 0·001 mg. per g. frog.

Electrodes at the muscle poles, cathode proximal. Break shocks from two (or three) coils, of like construction, coreless and placed so as to avoid mutual induction. The openings of the primary circuit were adjustable to $0{\cdot}1\sigma$ approximately by a Lapicque rheotome modified by replacing the closure cam by an opening cam, and adding a third opening cam. The graduation was verified by means of the string galvanometer. The stimuli were slightly supramaximal for the muscle.

Under these conditions a curarized gastrocnemius, exhibiting strong tendency to contracture with two or three break shocks given directly at variable intervals, never responds to one of the shocks given singly by other than a twitch entirely like the maximal twitch to an indirect stimulus (Fig. 4 C). So also with two similar shocks separated by an interval less than the absolute refractory period of the muscle measured by the least interval for tetanic summation. But, once beyond a minimal interval corresponding approximately with the least interval for tetanic summation (2σ), the isotonic twitch, now heightened because a tetanic fusion of two, is immediately followed by a secondary slow contraction (Fig. 4 B and C). The height of this secondary contraction increases at

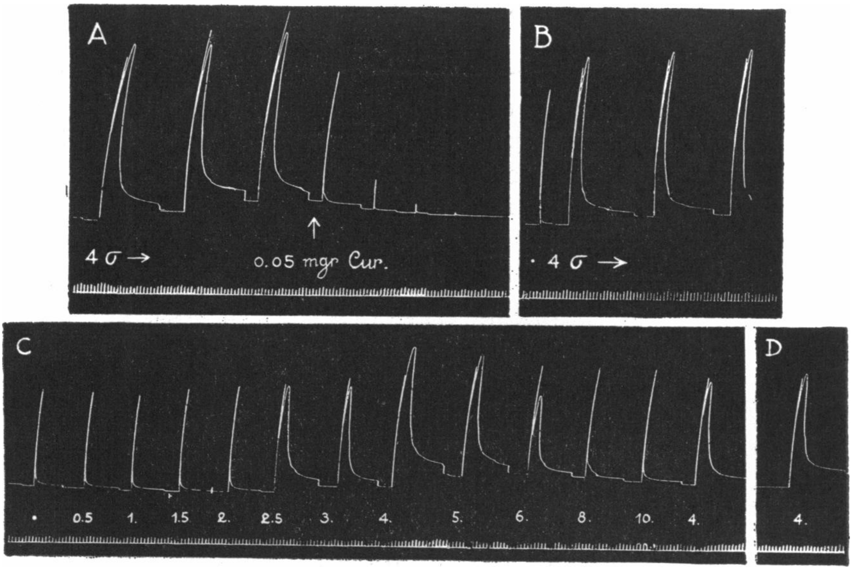

Fig. 4. Isotonic twitches of the gastrocnemius of *R. temporaria*, provoked every 2 min. Temp. 19° C. Time in seconds. Reduced by ⅓. A. Twitches showing a strong neuro-muscular contracture provoked by the summation of two volleys of motor impulses at the optimum interval of 4σ. 0·05 mg. of curare was injected intravenously after the third twitch. B. Same muscle completely curarized. Contracture provoked by summation of two direct stimuli (break shocks of maximal intensity). C. Series of twitches of the same muscle showing the relation of the height of contracture with the interval between direct stimuli. D. Resistance of this same contracture to atropinization. An intravenous injection of 6 mg. of atropine sulphate between C and D.

On this figure and on the subsequent figures, single stimuli are designated by a point, and double stimuli by their interval in sigmata, under each contraction.

first with increase of the interval between two stimuli up to an optimum interval of about 4σ (at 18° C.), then diminishes, first rapidly, then more and more slowly. With a greater interval than 10σ all trace of the phenomenon usually disappears (Fig. 4 C). The height of the secondary contraction can exceed that of the twitch to which it is appended. Its duration, apart from the contraction residue which prolongs it, is usually about 10 sec., but may be longer (Fig. 4 B, C, D). This secondary contraction excited by direct stimuli of appropriate interval completely resembles myographically the secondary contraction excited by indirect stimuli (*v. infra*) which is certainly a contracture.

When two successive stimuli fail to cause the contracture, for instance because too far apart, the addition of a third stimulus following the second at a similar, or even greater, interval, can evoke the contracture. If three do not suffice a greater number may. As is usual with "addition latente" an insufficient frequency of the stimuli can be met by increase in serial number.

Discussion.

It was not foreseen that two successive direct stimuli should, in order to be effective, require to be separated by an interval not less than the absolute refractory period of the muscle fibres as measured by the usual method for tetanic summation. It is as though the contracture and the contraction, though very different in their speed of excitation, were yet linked by a refractory period common to both. During the absolute refractory period the muscle, although it retains the effect of the first stimulus in the form of "excitation latente," appears insensitive to the second stimulus. The functioning of the muscle fibre is thus singularly complex.

The ineffectiveness of the single break shock for producing contracture in the above experiments seems to contradict the well-known fact that it is possible to evoke contracture of the veratrine type by single induction shocks of high intensity, or by brief rectangular currents of high voltage [Lapicque and Weill, 1912]. The contradiction is merely in appearance. The contracturing power of these brief currents is due to their intensity being such as to do damage [Suranyi, 1926]. In my experiments the short currents (induction shock, condenser discharge) were of physiological intensity and just supramaximal; they never gave contracture. I cannot then agree with Lapicque [1929, p. 105] who regards brevity of electrical stimulus as efficacious for causing contracture.

The observations of M. Lapicque and J. Weill [1912] are capable of another interpretation. In their experiments stimuli of extreme brevity, rectangular currents of 0·1σ

for the rectus anterior of *Rana*, gave contracture; the explanation lies in the considerable intensity required to be used in order to obtain twitches of appreciable height. The contracture was certainly a Tiegel contracture, as Gasser [1930] has suggested. The rectangular currents of longer duration (1–2 σ), but yet far below the chronaxie of contracture, did not give contracture because their intensity was no longer harmful, and their duration insufficient to reach (physiologically) the threshold of contracture.

V. NEURO-MUSCULAR CONTRACTURE.

Of all suggestions offered to account for neuro-muscular transmission the simplest is that which likens the motor impulse in its excitation of the muscle fibre to a brief electric current. Accepting this provisionally, and admitting that the motor nerve impulse acts with a brevity comparable to that of break shock in a coreless coil, such nervous impulses, taken singly, will be as devoid of contracturing effect as are such break shocks taken singly. But when suitably repeated they will prove effective, by "addition latente."

Tiegel [1876], and after him many observers, notably Langley [1905, 1909], were struck by the impossibility of evoking a contracture by the single indirect stimulus, even of supramaximal intensity. Beritoff [1923] claims to have sometimes excited a veratrine-like contracture by a single-shock indirect stimulus to gastrocnemius (*esculenta*), the frogs having been at 22° C. for several days. I have never, myself, in hundreds of experiments, obtained a contracture in gastrocnemius from one single-shock indirect stimulus alone.

Of course, "contraction remainder," such as occurs after any shortening, active or passive, in muscles lightly weighted under fatigue, or even fresh as in the case of ileofibrilaris and coraco-brachialis of frog [Sommerkamp, 1927] is not counted as contracture. These residual shortenings, due to muscular viscosity, can, it is true, vary in the same sense as tendency to contracture; but they are not themselves true contracture, *i.e.* an active reaction. I have to insist on this distinction, since Wachholder [1931] has recently adduced as evidence of a contracture excited by a single indirect stimulus a myogram typically that of contraction remainder in coraco-brachialis. This pseudocontracture from single indirect excitation differs from the neuro-muscular contracture just described, not only myographically, but has none of its typical features, notably not the characteristic fatigability.

I find, however, perfectly possible the regular excitation of contracture in the frog by summation ("addition latente") of nerve impulses. The conditions are those given above in the previous section, with the one difference that the stimuli are applied to the sciatic nerve of the normal frog instead of to curarized muscle. The sciatic is cut at the level of the plexus and armed with Lapicque electrodes (Ag—$AgCl_2$) half up the thigh, cathode distal.

The slow "secondary contraction" provoked by two successive indirect stimuli at appropriate intervals is just like that provoked by two direct stimuli. The height of the isotonic myogram is similarly a function of the interval between the stimuli (Figs. 5, 6, 7 and 11). The slow contraction as a rule appears (Fig. 5 C) so soon as the interval exceeds the absolute refractory period of the motor nerve fibres (± 1·5σ at 18° C.). Its height increases rapidly with increase of the interval up to 3–4σ, then gradually declines. Usually all trace is lost at intervals above 10σ (Figs. 5 A and D, 7 and 11). The rise to the optimum (Fig. 6) recalls that of the curves of impulse summation (*addition latente périphérique et*

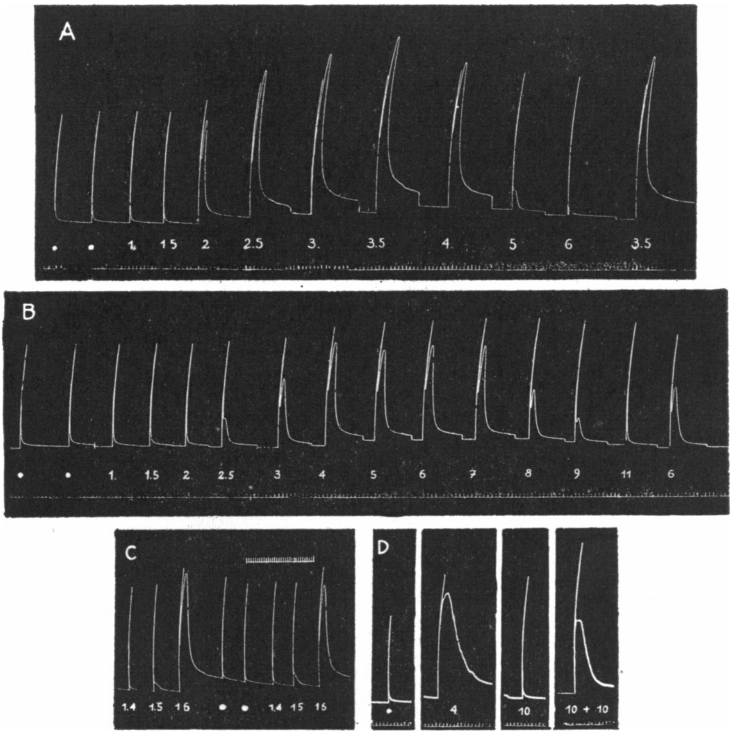

Fig. 5. Neuro-muscular contraction (isotonic) of the gastrocnemius of *R. temporaria.* Time in seconds. Reduced by ½. A. Nerve and muscle at 18° C. B. Nerve at 18°, muscle cooled to about 10° C. C. Another preparation showing the coincidence at about one ten-thousandth of a second, of the minimum interval for summation of contracture with the minimum interval for tetanic summation. D. Another preparation showing the contracturant efficacity of three successive stimuli, when two are ineffective because of too great an interval (10σ).

centrale), which I have described and analysed elsewhere [Bremer, 1927, 1929 *a*; Bremer and Homès, 1932].

The position of the optimal interval depends on the temperature of the muscle (and neuro-muscular junctions) and is independent of the temperature of the nerve at the seat of stimulation (Figs. 5 A and B, and 6). Conversely, the minimal interval for summation depends, *ceteris paribus*, on the temperature of the nerve. As usual with "addition latente" it is possible to compensate excessive separation of the stimuli by adding to the serial repetitions (Fig. 5 D).

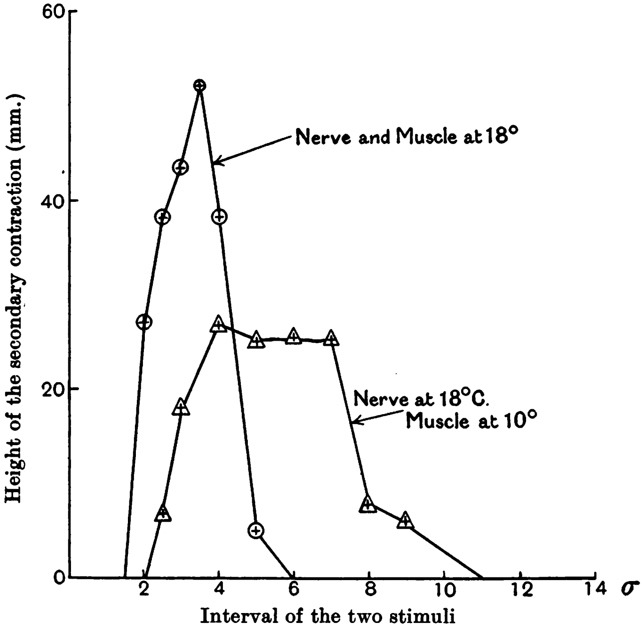

Fig. 6. Summation curves for neuro-muscular contracture constructed from the series of twitches A and B of Fig. 5. Notice the displacement toward the right of the optimum interval for summation, resulting from cooling the muscle (curve with triangles).

Myographic characters of neuro-muscular contracture.

The features of the slow "secondary contraction" prove it a contracture and not a contraction of special muscle fibres. Thus, it can be added to the residual contractions of fatigue or to acetylcholine contracture. In some instances I have succeeded in exciting strong contracture in a perfectly fresh muscle. There (Fig. 7) the line of the myogram joined the abscissa in some seconds without trace of permanent residual contraction. Conversely, when excited in a muscle which has previously for a short time been tetanized, it revives somewhat the residual contracture (of fatigue), and there occurs a progressive rise of the abscissa when a succession of twitches followed by secondary contraction are evoked (Fig. 11 A). It is the secondary contraction which revives the residual

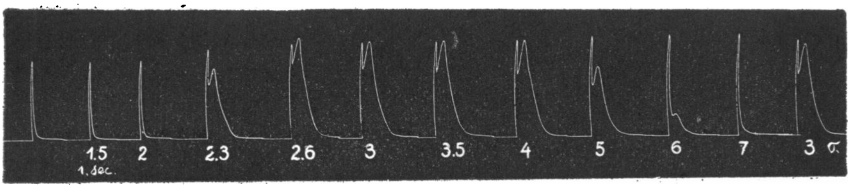

Fig. 7. Neuro-muscular contracture (isotonic) of a fresh gastrocnemius of *R. temporaria*, without any preliminary tetanization. Temp. 17° C. Reduced by ½.

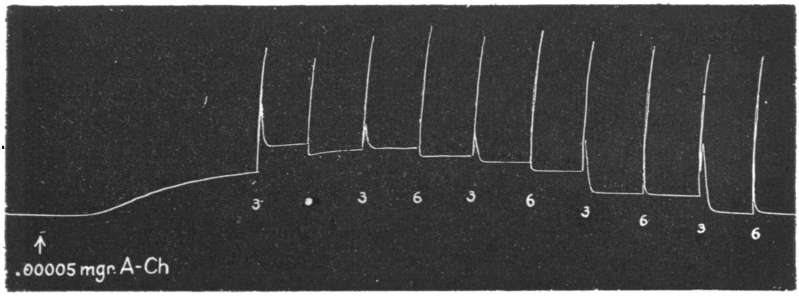

Fig. 8. Acetylcholine contracture and neuro-muscular contracture. (Gastrocnemius of *R. temporaria in situ*, acetylcholine injected intravenously.) Neuro-muscular contracture accentuates acetylcholine contracture when the latter is in the ascending phase, while it accelerates the annulment of alcaloidal contracture in the regressive phase even more than do ordinary twitches. Reduced by ⅓.

contracture because simple twitches and tetani not followed by secondary contraction do not do so (Figs. 5 and 11). In the same way as intercurrent neuro-muscular contracture hastens the onset or increases the intensity of acetylcholine contracture (Fig. 8).

The height and shape of the isotonic myogram of the secondary contraction vary from preparation to preparation, but for the same experiment are constant. The height of the secondary contraction in a muscle lightly weighted (5 g.) can much exceed the height of a brief tetanus (Figs. 5 A, 9 A and 10 C). Again, the secondary contraction can graft itself so early upon the twitch that it appears merely as an increase of height and duration of this latter. In general its form is that of a slow smooth twitch lasting several seconds (Figs. 4 A, 5, 6 and 7). At times the relaxation is late and irregular (Fig. 9 A); in such cases inspection finds the muscle bunched up towards its proximal (neural) pole and fibrillating more or less markedly.

The tension of the secondary contraction is always less than that of the twitch which precedes it, even when the shortening of the contracture (isotonically registered) exceeds that of the twitch (Fig. 9). The strongest secondary contraction I have registered has not exceeded $\frac{1}{5}$ tension of the corresponding double twitch. This disparity between shortening and tension is often met with in contracture both of skeletal and of smooth muscle. It is important to bear this in mind in relation to the metabolism of contractures such as acetylcholine contracture. A contracture which is strong to judge by the isotonic record of a lightly weighted muscle may develop little contraction tension, and give correspondingly little lactic acid or heat. This has to be remembered of the recent experiments of Miura [1931] and of the interpretation he gives.

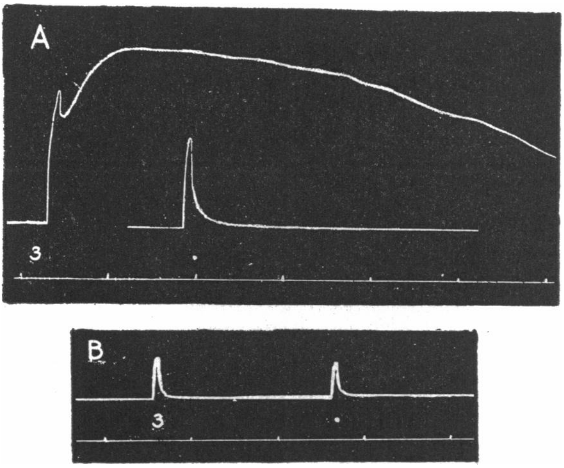

Fig. 9. Twitches followed by a secondary contraction and single maximal contractions isotonically recorded (A), and isometrically recorded (B), at an interval of a few minutes. An extreme example of the contrast existing in neuro-muscular contracture between the degree of shortening of the muscle and the feebleness of the tension developed by the contracture. Time in seconds. Reduced by $\frac{1}{3}$.

Fatigue and temperature on neuro-muscular contracture.

Neuro-muscular contracture is incomparably more sensitive to fatigue than is the neuro-muscular twitch. A rapid succession of twitches, each with its appended secondary contraction, soon tires out the latter (Fig. 10 A). Some minutes of rest restores the contracture fully. The fatigue seems mainly seated at the neuro-muscular junction, for contracture by summation of direct stimuli (Fig. 10 B) is more resistant. Besides fatigue of neuro-muscular contracture ensues quicker from twitches followed by contracture than from twitches not so followed. The mechanism of neuro-muscular contracture is therefore fatigable through the action of rapid contraction but still more so through its own action.

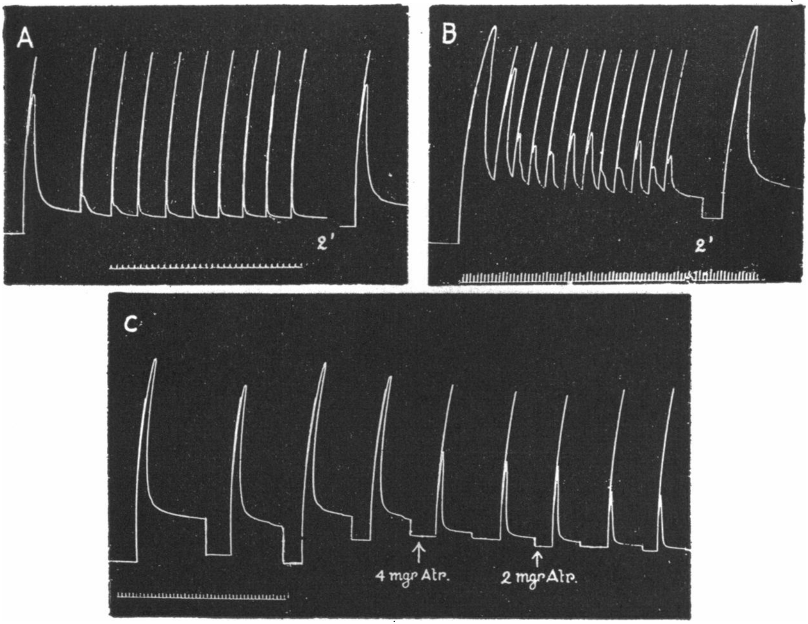

Fig. 10. A. Fatigability and very rapid restoration of neuro-muscular contracture. Having disappeared completely after a rapid series of 10 contractions (double tetani at an optimum interval of 4σ), it reappeared with the same intensity after a rest of 2 min. B. Lesser fatigability of contracture provoked by the summation of two direct stimuli on a curarized muscle. C. Selective sensitivity of neuro-muscular contracture to atropine. Double tetanic contractions (optimum interval $3{\cdot}5\sigma$) elicited every 2 min. Two successive intravenous injections of 4 and 2 mg. Atropine sulphate considerably weakened the secondary contraction without diminishing the height of the twitch. On the three records, time in seconds. Reduced by $\frac{1}{3}$.

Warming of the muscle to 25° C. or higher annuls at once its tendency to neuro-muscular contracture (Fig. 11 A, B), but the contracture response to direct galvanic stimulation persists. Cooling the muscle restores ability for neuro-muscular contraction (Fig. 11 C).

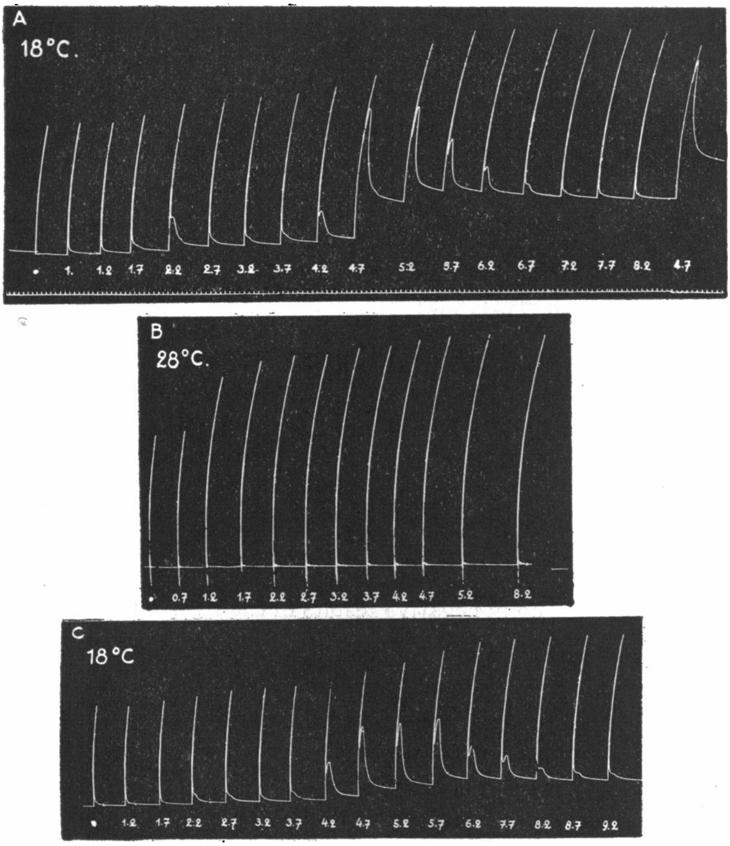

Fig. 11. Reversible disappearance of neuro-muscular contracture by warming the muscle to 28° C. The three series of twitches were successively recorded in the course of half an hour. Time in seconds. Reduced by ½.

Pharmacology of neuro-muscular contracture.

Contracture is somewhat selectively affected by curare. Under incomplete curarization the elicitation *via* the nerve of the rapid twitch is always less impaired than is that of the "secondary contracture" (Fig. 4 A). This is intelligible, since the production of the contracture, involving a summation of impulses, is more complex and thence more vulnerable than that of the neuro-muscular twitch. At the stage in which contracture is abolished the twitch is however much reduced (Fig. 4 A).

The atropine group has a markedly selective action on neuro-muscular contracture, even in doses which do not touch the twitch (Fig. 10 C). The atropinized muscle still responds by contracture to suitable direct stimuli (Fig. 4 D). There seems in fact a true "curarization" of the contracture, a point of interest for its explanation. The dose of atropine abolishing neuro-muscular contracture is much higher than that suppressing the parasympathetic effects. This action of atropine is probably unrelated to its parasympathetic affinity. Suffice it here to cite the identity of refractory period of the "motor" fibres of contracture and of ordinary motor fibres (Fig. 5 C). Further, the lack of proof, anatomical and pharmacological [Dale and Gasser, 1926], of any parasympathetic innervation of the skeletal muscular fibre.

As already stated the neuro-muscular and acetylcholine contractures sum one with another (Fig. 8). It is, however, little likely that acetylcholine plays a part in the production of neuro-muscular contracture, which exhibits only exceptionally the "resolution" [Riesser, 1921, 1925; Hess and Neergaard, 1924] so characteristic of choline contracture (Fig. 8). Further, acetylcholine in the perfusion fluid (oxygenated Ringer) for the gastrocnemii when they are giving strong neuro-muscular contractures gives me wholly negative results in the five experiments I have performed. Hearts of *R. temporaria* used as reagents for the alkaloid were sensitive to dilutions of acetylcholine of 10^{-7} to 10^{-9}.

Adrenaline, even in toxic doses (0·01 mg. per g. intravenously injected), is without effect on neuro-muscular contracture. I have performed no experiments using ergotamine.

Discussion.

To obtain a contracture of skeletal muscle by indirect excitation, it is thus necessary to make use of the mechanism of summation of nervous impulses by repetitive stimuli. This neuro-muscular contracture furnishes a myogram exactly similar to that of the summation of two or more brief stimuli applied to the same muscle after curarization. These facts are in perfect accord with the hypothesis that reversible contracture of skeletal muscle is the reactional expression of a very slow, specific excitability of the muscle fibre.

The remarkable pharmacological properties of neuro-muscular contracture seem to me to furnish a new argument in favour of this conception.

As we have seen, there is a manifest difference between the action of curare and of atropine on slow secondary contraction, in respect of their selectivity: when applied to the gastrocnemius of *R. temporaria*, atropine and scopolamine paralyse selectively neuro-muscular contracture, while the action of curare is on the contrary but very imperfectly selective.

In the theory of Lapicque [1926], taken in its most general form, curarization of a neuro-muscular apparatus is considered to result from the rupture of the minimum accord necessary for neuro-muscular transmission between the respective speeds of excitability (chronaxies) of the muscle and the nerve. This theory of curarization could be further enlarged by attaching it to the general hypothesis of Herman-Cremer-Lillie, and expressing it thus: The abolition of nervous command over a muscle results from all alterations of the excitability of the muscle fibre which render it inexcitable by those particular stimuli constituted by the action currents of the nerve. This alteration of excitability may be either a modification of the chronaxie, or a simple rise in the threshold of the muscle fibre.

It is well known [Lapicque, 1926] that atropine and the alkaloids of its group are much more toxic for slow muscles than they are for rapid muscles, while exactly the opposite is found in the case of curare. This explains why atropine, which has but an imperfect effect on rapid muscles, has in sufficient doses an effective curarizing effect on slow muscles. Its selective curarizing action on neuro-muscular contracture is thus well explained by the hypothesis that this contracture is the manifestation of a very slow excitability which is as such very susceptible to atropine. The possibility of this selective curarization of contracture may be considered a proof of its long chronaxie. The reality of a specific toxic action of atropine on the excitable substance of contracture is further demonstrated by the fact that this alkaloid, when in a much higher concentration than that necessary for paralysing neuro-muscular contracture, also causes the disappearance of galvanic contracture in the muscles of Anura, without nevertheless abolishing the ordinary rapid contractility [Rückert, 1930 *b*].

VI. ELECTROMYOGRAM OF NEURO-MUSCULAR CONTRACTURE.

The electromyographic study of neuro-muscular contracture is of particular interest. The experiments that have just been described tend to show that reversible contracture of skeletal muscle is the expression of a specific type of excitation of the muscle fibre. At present it seems well established that the electrical manifestations of muscular contraction are, in part at least, determined by the state of excitation of the muscle fibre, independently of the mechanical phenomenon of contraction. Bishop and Gilson [1927], confirming the older observations of Lee [1887], have shown, in fact, that the monophasic electrogram of the isometric twitch of the frog's sartorius is the expression of an electrical negativity lasting during the entire period of contraction, but that this electrogram might be dissociated to a certain extent into two successive phases: (1) a brief initial negative phase of great amplitude; (2) a second negative phase, normally more or less fused with the first, the shape of which corresponds to that of the isometric myogram. According to Bishop and Gilson, the first phase is the electrical expression of the wave of excitation passing over the fibres, while the second corresponds to the electrochemical reaction which is supposed to be the basis of the process of contraction. As Gasser [1930] suggested, one can equally well account for this division of the electromyogram into two successive elements by assuming that the muscle fibre in a simple contraction passes successively through two distinct, although causally linked, stages of excitation: (1) the wave of excitation and of negativity which is translated into the initial sharp deflection, and (2) the state of excitation which is the immediate cause of the contraction, and which is shown by the delayed phase of negativity.

If this dualistic interpretation of the electromyogram is correct, then reversible contractures, which are characterized by the absence of propagation of the contractile process along the fibre, should present as their sole electrical manifestation only that negativity which is in immediate causal relationship with the contractile process and the intensity and duration of which vary proportionally as the intensity and duration of the latter. This functional negativity ought to evince itself, in the monophasic electromyogram, in a curve devoid of oscillations, whose shape corresponds more or less to that of the isometric myogram of the contraction, but which may be initiated before the appearance of tension.

This is essentially what has been observed in the case of many reversible contractures. But these potentials have been very differently interpreted: in some cases as the electrical manifestation of an authentic state of excitation, in others as a current of deformation, and in still others as a current of alteration resulting from the harmful action of the chemical agent producing contracture [see literature in the review of Gasser, 1930].

Further, the presence of rapid oscillations complicating a continuous deviation in the electrogram of various contractures, notably of veratrine contracture, has often been interpreted, recently by Wachholder [1930 *a*], as the proof of the fundamentally tetanic nature of these contractures. To these conclusions Dittler and Freudenberg [1923] and Gasser [1930] have raised serious objections.

All these electrographic studies were made, besides, on chemical contractures, capable of causing changes in the muscle which in themselves might generate differences of potential. Thus it was particularly interesting to make an electromyographic study of a contracture provoked by electrical stimuli, especially indirect stimuli, which joins to the advantage of being the most physiological method, that of eliminating all possibility of an electrical artefact due to the stimulus.

Beritoff and Woronzow [1926] have already studied the electrical manifestations of the post-tetanic contracture of the gastrocnemius of the frog indirectly faradized. They demonstrated the existence of a non-oscillatory negativity concomitant with the contracture, which is gradually dissipated in the same time as the latter. But it is probable, because of the conditions (prolonged tetanus) and the object (*R. esculenta*) of their experiments, that the contracture was one of fatigue and not the contracture by excitation in which we are interested.

The neuro-muscular contracture of *temporaria* lends itself well to electromyographic registration because of its constancy of reaction, which permits the successive registration, in a few minutes, of twitches followed by a secondary contraction, and of ordinary single twitches.

These researches were performed by means of a Cambridge string galvanometer. Because of the small size of the electromotive forces involved the tension of the string was in general reduced to a displacement of 30–40 mm. per millivolt, which, considering the optical amplification and the resistance of the string according to the formula of Forbes and Ray [1923], represented a sensitivity of 330–450 metres per ampere. The leading electrodes were two fine silver chloride pins, one of which was inserted into the belly of the gastrocnemius muscle, and the other into the tendon of Achilles, which was itself attached to a Sherrington isometric myograph arranged for optical registration. The resting current, generally feeble (several millivolts), was always compensated.

My own observations of the electromyogram (Pl. I) of twitches free of contracture registered under these strictly isometric conditions, with approximately monophasic derivation, and with a high string sensitivity, find that it is composed of two successive and clearly distinct phases, fully confirming the results of Bishop and Gilson [1927] mentioned above. In the case of double tetanic contractions, provoked by two stimuli at a sufficiently long interval, the positive appendage of the initial negative deflection is double (Pl. I C), while the delayed negative deflection remains simple corresponding to the myogram of the two fused contractions.

This duality of the monophasic electromyogram of a twitch, recorded with a galvanometer having a very sensitive string, corresponding to that which Bishop and Gilson [1927] obtained with the cathode-ray oscillograph in their study of the monophasic myograph of the isometric twitch of the frog's sartorius is, seemingly, as these authors suggested, the expression of a duality of origin of the potentials. The brief initial phase represents, according to this hypothesis, the potential of the muscular "impulse" which precedes the contraction; the second phase, of lower potential, and which is synchronous with the development of tension, would be intimately associated with the process of contraction. Control experiments permitted the exclusion both of the phenomenon of De Meyer (current of deformation), and of an artefact resulting from displacement of the electrodes. Pl. I D shows that passive variations in the tension of the muscle, although greater than the active variations corresponding to contractions A, B, and C, cause but insignificant variation in potential when compared with those of the delayed phase of the electromyogram of these twitches.

The fundamental experiment destined to demonstrate the electrical sign of neuro-muscular contraction consisted in recording, in a rapid series, the isometric myogram and electrogram of four twitches, some (the 1st and 4th, Pls. II and III A and D) followed by the slow secondary contraction because they were promoted by two indirect stimuli of adequate interval ($\pm 3{\cdot}5\sigma$), and others (the 2nd and 3rd, Pls. II and III B and C) free of contractures because they were provoked by a single stimulus, or by two stimuli at a sufficiently great interval (in general 10σ). As in my preceding experiments, the tendency of the muscle toward neuro-muscular contracture was augmented by a short tetanization preliminary to the rest of the experiment.

The neuro-muscular contracture is represented on the isometric myogram (Pls. II and III A and D) by a renewal of the contraction which interrupts at various points the phase of relaxation of the double tetanic contraction, and which lasts, although progressively decreasing, for 1–2 sec.

Electrographically (Pls. II and III A and D) the contracture is characterized (1) before any mechanical manifestations by the augmentation of the amplitude of the delayed negative wave of the electrogram of the twitch; (2) by the prolongation of the decreasing phase of this wave in a curve which slowly approaches the line of isoelectricity at the same time as the line of the myogram approaches the position of initial tension of the quiescent muscle. The parallel between the two curves is striking. Sometimes the line of the electrogram of the contracture is irregularly scalloped (Pl. III A and D). These waves may pass the line of isoelectricity, especially near the end of the contracture, and give the appearance of a diphasic electrogram. In general, with the exception of these apparently secondary waves corresponding to the waves in the myogram, the curve is simple. But from time to time one can distinguish very fine rapid oscillations which are hardly visible. The appearance of the electromyogram of contracture is somewhat variable from one experiment to another, but is remarkably constant for the same muscle and for the same position of the leads.

The negative potential associated with neuro-muscular contracture is slight, as is the tension developed by the contracture, and is at all times proportional to this tension. The highest electromotive force that I have recorded is of about 3 millivolts; it corresponded, in this experiment, with a tension of 40 g., while the tension of the contraction which it followed was 300 g.

Discussion.

From these observations it seems that the monophasic (from muscle-tendon leads) electromyogram of neuro-muscular contracture of the gastrocnemius of *R. temporaria* consists essentially of a non-oscillatory negativity of the active lead. This negativity, being neither current of deformation, as demonstrated by control experiments, nor a result of alteration of the muscle substance, because the contracture was provoked by indirect stimuli, can be legitimately considered as the electrical expression of the specialized type of muscular activity represented by contracture. This potential is feeble, as is the tension developed by the contracture itself, is proportional to this tension and is slowly dissipated in the same as this latter.

The small rapid oscillations sometimes present in the electromyograms are seemingly the electrical sign of fibrillations which are visible to the naked eye in the muscle in contracture.

These observations and these interpretations are in complete accord with electrographic observations which have been recently made on other reversible contractures in skeletal muscle, especially with those of Schäffer and Licht [1926*a*, *b*] on acetylcholine contracture and the Vulpian-Heidenhain phenomenon, and of Bishop and Kendall [1929] on aldehyde contracture of the frog's sartorius. Shäffer and Licht demonstrated the complete parallel between the electrogenic activity of acetylcholine and its contracture producing action (experiments on the mammalian muscle, in a normal state or in a state of Wallerian degeneration), while Bishop and Kendall discussed, and rejected categorically, the opinion of Verzâr and Peter [1925], which attributes the potential changes in aldehyde contracture (which is of the veratrine type), to alterations contingent on the form and electrical resistance of the muscle in contracture.

My experiments, performed under strictly isometric conditions which in themselves exclude the above interpretation, reveal an additional fact, irreconcilable with that interpretation, namely, that the negativity associated with the contracture commences several hundredths of a second before the appearance of the tension on the simultaneously recorded isometric myogram. One sees in Pls. II and III that the amplitude of the negative phase corresponding to the period of relaxation of the twitch is clearly greater in the record of twitches A and D, which are followed by a contracture, than in twitches (single or double) in which contracture is absent. This increase of negativity does not correspond to any increase in contractile tension, for the tension developed by neuro-muscular contracture never determines an increase in the height of the isometric twitch. Yet it is probable (see Fig. 2 B) that the period which immediately precedes the appearance of the contracture is already characterized by an increase in the muscular viscosity.

GENERAL DISCUSSION AND CONCLUSIONS.

The aim of these researches was to verify the hypothesis, already deduced by a critical examination of known facts, that reversible contracture of skeletal muscle is the expression of a particular type of excitation of the muscle, which is characterized by the slowness of its development, and especially of its dissipation.

In favour of this conception I may claim to have brought forward new arguments, some indirect, and others more direct. I have been able to show: (1) that conformable to the well-known law relating the duration of the process of excitation in a tissue to the speed of excitation of the same object, to elicit a reversible contracture requires either a single stimulus of a considerable duration, or the "addition latente" of two or more stimuli which are singly too short to be effective; (2) that by using particularly sensitive muscles, such as the gastrocnemius of *R. temporaria*, one can obtain a true contracture by indirect stimulation if one takes advantage of the phenomenon of the "addition latente" of nervous impulses. I have indicated that the similarity between this "addition latente" of nervous impulses, and the "addition latente" of direct electrical stimuli of very short duration, results evidently from the fact that the bioelectric currents of the nerve impulse have the same effect on the muscle as very brief electrical stimuli; (3) a third and direct argument was furnished by a study of the electromyographic properties of neuro-muscular contracture. This contracture, provoked by truly physiological stimuli, independently of any pharmacological action, is shown to be characterized by a non-oscillatory negativity, the curve of which follows closely that of the contractile tension developed.

This particular form of excitation of the muscle may be supposed to set into action the same contractile mechanism as is employed in ordinary contraction. The identity of the metabolism of contracture and contraction demonstrated by Hartree and Hill obliges us to acknowledge the unity of the contractile mechanism. There is thus a duality of excitation but not a true duality of contraction. Contracture and contraction then, seem only to differ in the nature and duration of intermediate processes constituting the protoplasmic excitation, which form a link in the chain of phenomena leading from the stimulus to the liberation of muscular energy.

This conception of the mechanism of contracture approaches in detail that which was more or less explicitly developed by Jensen [1914], and by A. V. Hill [1926, p. 76]. That of Jensen in particular postulated, as Gasser [1930] also emphasized, "two modes of approach to the same metabolism or mechanism."

All the evidence indicates that the "excitable substance" of contracture co-exists in each individual muscle fibre with the excitable substance of rapid contraction, and is not provided for by special fibres. I have shown, in fact, that the nerve fibres responsible for the transmission of the "motor" impulses of neuro-muscular contracture are in all probability the ordinary motor fibres. On the other hand, if it is true that different muscles of the same vertebrate can be differentiated on the basis of their unequal aptitude for contracture, and that one can even distinguish in certain muscles, as in the ileofibularis of the frog studied by Sommerkamp [1927], two groups of fibres, both on the basis of their contractile properties and their macroscopic appearance, it is also true that these fibres with particular aptitude for contracture have by no means lost their aptitude for ordinary tetanic contraction.

In a muscle capable of contracture the very same fibre can thus react according to the qualities[1] of the direct or indirect stimulus, either by a twitch or tetanus free of all contracture, or by a contraction followed by a contracture.

What is the biological significance of this dual excitability? Has it an important functional significance? *A priori* this seems hardly probable by reason of: (*a*) the extreme variability of the tendency toward contracture in the same muscle, as the gastrocnemius of Anura, according to the species, and even the individuals of the same species; (*b*) the fact that contracture of skeletal muscle does not represent a more economical mode of activity than normal contraction; (*c*) the feeble contractile tension developed by neuro-muscular contracture. No one any longer defends the hypothesis of a direct relationship of contracture with postural tonus of vertebrates.

Nevertheless, the idea of a functional rôle for this type of muscular reaction has reappeared in several recent publications. Thus Hess and Büsch [1927] have suggested its adjuvant rôle in tetanic fusion.

To this hypothesis there is the objection resulting from my own researches that at a frequency necessary for neuro-muscular contracture tetanic fusion is already complete. Besides, A. V. Hill and his collaborators have demonstrated that completion of tetanic fusion is economically provided for by the effective mechanism, common to all Vertebrata, of the prolongation of the phase of relaxation of a contraction by fatigue and by initial extension of the muscle.

Wachholder [1930 *b*, *c*, 1931], demonstrating the parallel existing between the sensitivity of skeletal muscles to contracture by acetylcholine and their degree of postural activity, attributes to this fact a fundamental biological importance.

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[1] I call attention here to the fact that that which determines the appropriateness of a stimulus for a "slow" excitable substance is its relative duration, and not, as Bethe, Fraenkel and Wilmers [1922] mistakenly supposed, the progressiveness of its establishment. The rapidity of establishment of a stimulus always favours its efficacity, but slow tissues tolerate a more gradual establishment of a stimulus than do rapid tissues [Lapicque, 1926].

Since mechanical, thermal, and chemical stimuli are always of considerable duration in comparison with the duration of an induction shock, their efficacity in provoking contracture can readily be explained.

But the recent researches of Freund and Rückert [1930] and Rückert [1930 *a*, *b*] lead to a different interpretation of these "tonic" properties of skeletal muscle. They have shown that the aptitude of a muscle to electrical or alcaloidal contracture varies inversely as the ontogenetic and phylogenetic evolution of the muscle, other conditions being equal. One can discover in the adult the stages of this evolution, either in comparing in the same animal muscles of different phylogenetic antiquity, or in following the same muscle through the vertebrate series. This evolution may be accelerated because of functional causes, as in the case of the wing musculature of birds, and of some of the muscles of the posterior limbs of Anura [Freund and Rückert, 1930]. The same cause, participation in rapidly alternating movement of which the execution would be hampered by contracture, seems to me to explain the striking difference in aptitude for contracture between the gastrocnemius of *R. temporaria* and *Bufo* which are terrestrial Anura whose locomotion is chiefly by walking, and the same muscle of *R. esculenta* which is a swimming and jumping animal (Fig. 12). In this sense was taken the statement of Freund and Rückert, contrary to the interpretation of Wachholder, that "only the loss of the tonic properties seems to be dependent on the functional specialization of the muscle."

Aptitude for contracture would thus characterize a primitive evolutionary state of the muscle fibre, a condition which has been passed by some muscles but not yet by others, either because despite their phylogenetic antiquity they have retained primitive function (ocular muscles of mammals, Duke-Elder [1930]), or because, by reason of a too recent appearance in phylogeny, they have not yet had time to accomplish their evolution (diaphragm of mammals).

This evolutionary stage is also reproduced by all mammalian muscles in the course of their ontogeny [Rückert, 1930 *a*]. Normal muscles of adult mammals have practically lost these "tonic" properties, but not entirely, as is demonstrated by the greater duration of galvanic contractions compared with contractions of the same height provoked by short stimuli or indirect stimuli (compare A and F in Fig. 3), and by the possibility of provoking galvanotonic contracture by very intense stimuli. The tonic properties reappear in various pathological conditions: Thomsen's disease, myotonic myopathies, and Wallerian degeneration, which are characterized by a regression to an embryonic structural type. I have elsewhere called attention to the analogies between myotonic contracture in human pathology and neuro-muscular contracture in the Anura. This comparative study has led me to the conclusion that the myotonic rigidity which prolongs contraction in Thomsen's disease and myotonic myopathies (Fig. 13) is a neuro-muscular contracture of abnormal muscles, provoked by a summation of normal nerve impulses [Bremer, 1929 *b*; Bremer and Mage, 1929].

This relationship of contracture to the evolutionary stage attained by the muscle fibre is well in accord with the facility with which smooth muscle responds to various stimuli by contractures, which in certain cases at least [Bozler, 1930 *a*, *b*] entail a notable expenditure of energy and thus cannot be interpreted simply as a manifestation of extreme muscular viscosity.

It fits in well also with the characteristic properties of the process of excitation which is the basis of contracture: slowness of development

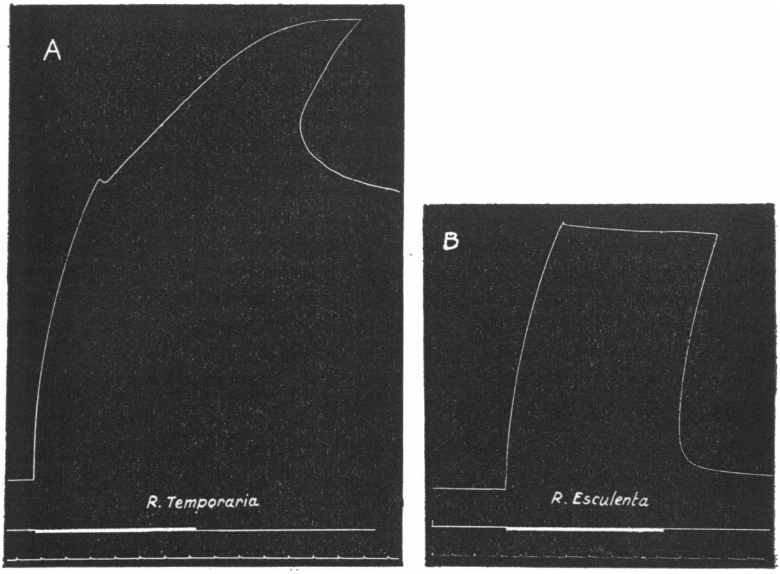

Fig. 12. A. Isotonic neuro-muscular tetanus (5 g. load) of a brown frog (*R. temporaria*) showing strong neuro-muscular contracture. Note the normal start of the plateau of the tetanus (latent period of contracture) and the dome which the contracture then produces. B. Neuro-muscular tetanus identically registered and provoked—at the same frequence of about 60 break shocks per second—of the gastrocnemius of a green frog (*R. esculenta*) of the same weight and the same state of nutrition, at the same temperature, 18° C. Time in seconds. Reduced by ½.

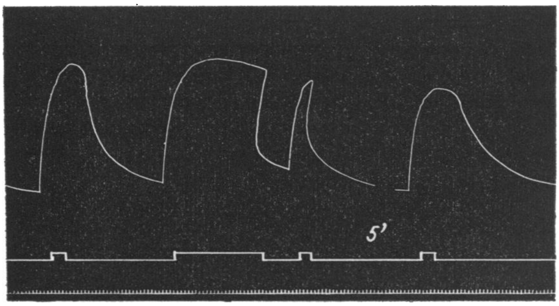

Fig. 13. Myotonic rigidity in man. Patient, 39 years, showing an accentuated myotonic myopathy. Myograms of the superficial flexors of the fingers. Registration by means of a "cardiographic" pneumograph applied over the muscle. Faradization of the motor point at a frequence of 40 break shocks per second. Note the prolonged contracture which follows the first tetanus, its disappearance after a more prolonged faradization, and its complete reappearance after a rest of 5 min. Time in seconds. Reduced by ½.

and dissipation, absence of propagation along the fibres, polar localization (cathodal), and absence or feeble development of the phenomenon of adaptation. These characteristics of the process of excitation in contracture present an analogy, already noticed by Biedermann [1895], with those of the visible reactions to galvanic stimuli by the undifferentiated protoplasm of numerous Protozoa.

Reversible contractures of the skeletal musculature of vertebrates which might be provoked by electrical, alkaloidal, or nervous stimuli, seem thus to be a primitive form of reaction of the muscle fibre. Tendency to contracture is the expression of a vestigial property, seemingly without any functional rôle, and of variable intensity according to the evolutionary stage of the muscle, its state of nutrition, and its functional specialization.

SUMMARY.

1. The gastrocnemius of *R. temporaria* presents a particular tendency to contracture by direct or indirect electrical and alkaloidal stimuli. The better the state of nutrition of the muscle, the stronger is this tendency.
2. The chronaxie of contracture of the gastrocnemius of *R. temporaria*, measured by means of metallic electrodes and "longitudinal" excitation, is about a hundred times that of ordinary contraction.
3. Very brief direct electrical stimuli (for example break shocks), of physiological intensity, although maximal as far as the twitch is concerned, do not cause contractures of the curarized gastrocnemius when applied singly, but become effective only when repeated often enough and at an adequate interval, because of summation of stimuli. Two successive stimuli can suffice. In order to be effective at the ordinary temperature the interval ought to be between $\pm 2\sigma$ and $\pm 8\sigma$, with an optimum of $\pm 4\sigma$.
4. A single stimulus is equally ineffective in the case of indirect stimulation of the gastrocnemius of *R. temporaria*. In order to provoke a contracture of this muscle it is necessary to obtain a summation of nerve impulses. Neuro-muscular contraction provoked by two stimuli of adequate interval ($1{\cdot}5$–8σ, with an optimum of $\pm 4\sigma$) presents complete myographic analogy with the contracture elicited by summation of two direct stimuli on the curarized muscle.
5. Neuro-muscular contracture is selectively sensitive to (*a*) fatigue, (*b*) heat, (*c*) atropine and related alkaloids. The "curarization" of neuromuscular contracture by atropine may be explained by the particular toxicity of this alkaloid for substances of long chronaxie.

6. The monophasic electromyogram of neuro-muscular contracture consists in a non-oscillatory negativity of the active electrode. The potential developed, which is very feeble, is proportional to the tension developed by the contracture. Its appearance seems to precede on the electromyogram the first manifestation of tension of the contracture.

7. Myotonic rigidity of human pathology presents striking analogies in properties and mechanism with neuro-muscular contracture in Anura.

8. Contracture by excitation of skeletal muscle seems to be a primitive form of reaction of the muscle fibre, connected with an "excitable substance" of long chronaxie, and characterized by the slowness of development and dissipation of its excitatory process, its absence of wave-like propagation, and its persistence throughout the duration of a galvanic stimulus (absence of adaptation).

9. A comparative study of the same muscle, such as the gastrocnemius, in various Anura, suggests that the tendency of a muscle to contracture depends on its functional specialization, in the sense that habitual participation of the muscle in a rapid alternating movement (swimming and jumping) accelerates its evolution towards a stage characterized by no, or only a feeble, aptitude for contracture by excitation (confirmation of the hypothesis of Freund and Rückert).

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EXPLANATION OF PLATES.

PLATE I.

Isometric myogram and electromyograms of the gastrocnemius of a frog showing no neuro-muscular contracture. Decerebrate animal. Tendon-muscle leads; proximal negativity (muscular) indicated by a downward displacement of the string. String tension: 50 mm. per millivolt; sensitivity reduced to 5 mm. per millivolt after the muscle was connected. From top to bottom; time in seconds, electromyogram, myogram. Temp. 20° C. Reduced by $\frac{1}{2}$. A. Single maximal twitch (indirect excitation). B and C. Double tetanic contractions elicited by two break shocks at intervals of $3{\cdot}5\sigma$ and 10σ respectively. D. Passive variations in tension of the same muscle.

N.B. On these records, as on those of Pls. II and III, the large initial phase of the monophasic electrogram is not seen, because of the amplitude and very great rapidity of movement of the string. One can only see the positive deflection which succeeds it. The small regular oscillations in the string record are due to induction of the alternating current of the building on the very loose string.

PLATES II AND III.

Isometric myogram and electromyogram of the gastrocnemius of two brown frogs showing a strong neuro-muscular contracture. Same experimental conditions as for Fig. 1. Tension of the string: 40 mm. per millivolt; sensitivity reduced to 3 mm. per millivolt after the preparation was connected. Reduced by $\frac{1}{2}$. A and D. Double tetanic contractions elicited by two break shocks of just supramaximal intensity applied to the sciatic at the optimum interval of $3{\cdot}5\sigma$. Neuro-muscular contracture. B. Double tetanic contraction provoked by two stimuli at an interval of 10σ. Absence of contracture. C. Single maximal twitch. No contracture.

N.B. Contractions A, B, C, and D, were elicited in rapid succession, in this order. Explanation in text.

Plate I

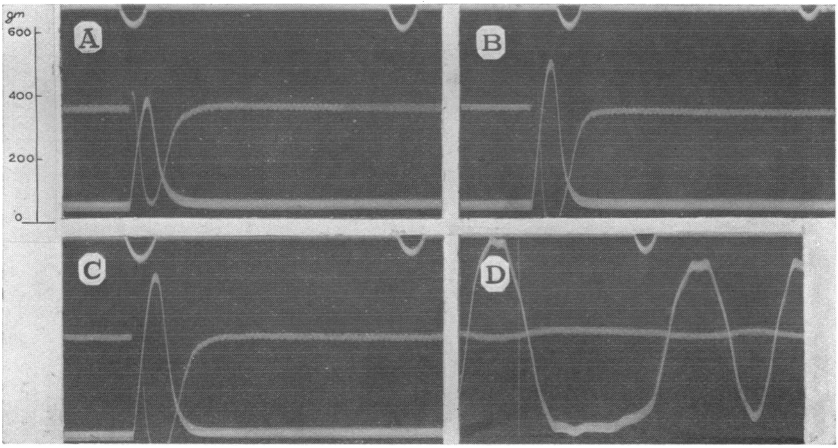

Plate II

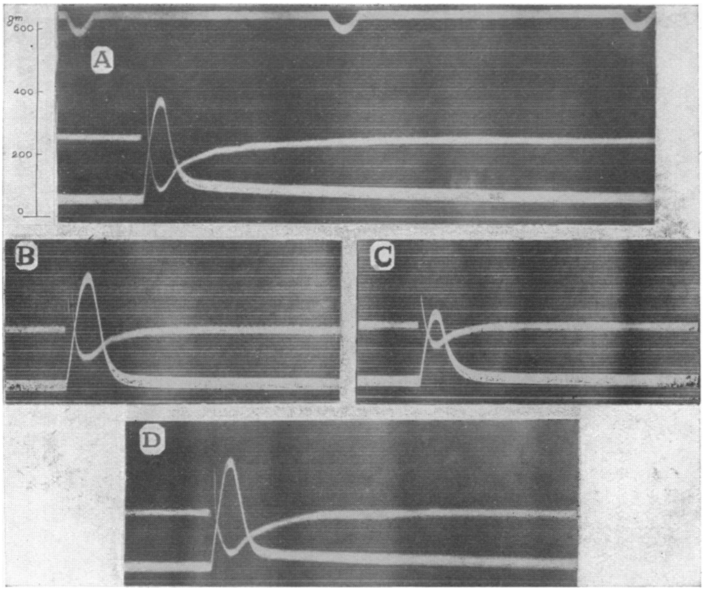

Plate III