AUGUSTUS D. WALLER.

PRECIS OF

PHYSIOLOGICAL PAPERS,

1878—1899.

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By AUGUSTUS D. WALLER, M.D., F.R.S. (1878-1899.)

I.—Die Spannung in den Vorhöfen des Herzens während der Reizung des Halsmarkes. *Du Bois-Reymond's Archiv*, 1878, p. 525.

Work done at Leipzig, forming part of the investigation of vascular and cardiac nerves, carried out by various observers under the guidance of Professor Ludwig.

Chief results and conclusions.—Tetanisation of the spinal cord causes a distension and arrest of the left auricle; this is a mechanical effect of increased pressure, by vaso-constriction, not a nerve-inhibition, for it can be produced by mechanical constriction of the aorta. It is not due to regurgitation from the left ventricle, for ventricular pressure may be 10 cm. Hg, while auricular pressure is *in maximo* 2 to 3 cm. No such effect is produced in the right auricle, *i.e.* there is no vaso-constriction in the lung comparable with systemic vaso-constriction produced by tetanisation of the cord. Reasons given why medullary excitation need not be expected to produce pulmonary vaso-constriction.

Cf. Openchowsky, "Ueber die Druckverhältnisse im kleinen Kreislaufe," xxvii., p. 233. 1882.

II.—Note of Observations on the Rate of Propagation of the Arterial Pulse-wave. *Journal of Physiology*, Vol. iii., p. 37. 1880.

Simultaneous records on man of (*a*) the cardiac impulse and (*b*) the arterial pulse at points accessible to exploration. From such records the following measurements were taken.

Cardiac impulse and carotid pulse	=	0·10 second.
,, ,, radial ,, ...	=	0·17 ,,
,, ,, fermoral ,, ...	=	0·17 ,,
,, ,, anterior tibial pulse	=	0·22 ,,
,, ,, volume of foot (plethysmograph)	=	0·25 ,,
Carotid pulse and radial pulse	=	0·07 ,,
Fermoral ,, ant. tibial pulse	=	0·05 ,,

NOTE.—I have recently devised a simple sphygmograph to be applied to a finger-nail (after the plan of Herz and Laulanié) which gives immediate indications of the state of the precapillary arterioles. There is no appreciable delay between the pulse in the radial artery and the pulse of a finger nail. The pressure is in the latter case = about 2 cm. Hg.

III.—Recurrent Pulsation in the Radial Artery. *Practitioner*, 1880, p. 412.

On account of free palmar anastomosis it is necessary to compress the ulnar as well as the radial artery in feeling the pulse for tension. A more or less marked "recurrent" pulse felt in the radial artery below a point of compression indicates a more or less relaxed state of the peripheral arterioles.

NOTE.—At the time of publication, no previous observations of this point were known to me. It is, however, alluded to in Jaccoud's "Clinique Médicale." The term "recurrent pulse" and the precautions to be observed are now matters of common knowledge. (Cf. Ringer's "Therapeutics," 9th edition, 1882, p. 18.) The fact itself, as well as the method of feeling the pulse there recommended, is described at length in Ewart's "How to Feel the Pulse," London, 1892, pp. 70, 71, 75.

IV.—Sur la Durée de la Systole Cardiaque. *Progrès Médical*, 1882, May 6.

The duration of systole varies with varying frequency of the heart's beat. From measurements obtained by the graphic method, the following averages were obtained:—

Pulse-frequency per minute	Duration of systole in hundredths of a second	Duration of diastole in hundredths of a second	Ratio of systole to cardiac cycle	Hours of work per diem
50	37	83	·31	7·5
60	34	66	·34	8·2
70	32	54	·37	8·9
80	30	45	·40	9·6
90	28	38	·42	10·2
100	27	33	·45	10·8

V.—On Muscular Spasms known as Tendon-Reflex. *Brain*, 1880, p. 179.

Evidence by time-measurements that the phenomenon is not (as was then generally believed) a reflex action, but a direct muscular response of which a necessary condition is the reflex tonus of the spinal cord. (Cf. also "Lancet," 1881, vol. ii., p. 83.) The average rhythm of tremor and clonus is 8 to 10 per second.

VI.—Nouvelles Expériences sur les Phénomènes nommés Réflexes Tendineux (with Dr. J. L. Prévost). *Revue Médicale de la Suisse Romande*, 1881.

Four experiments on rabbits made conjointly with Dr. Prévost to test the objection that *crossed* reflex proves the phenomenon not to be a direct reponse. Percussion of the knee of a limb of which all nerves are cut causes contraction of the opposite limb, *i.e.* direct excitation of the opposite limb by vibrations transmitted along the bones.

VII.—Sur le Temps perdu de la Contraction d'ouverture. *Archives de Physiologie*, 1882, p. 383.

The anodic break contraction (upon man) has a latent period 0·04 longer than that of the kathodic make contraction. An anelectrotonic depression of excitability may last for 0·05 second after cessation of the polarising current.

VIII.—On the Influence of the Galvanic Current on the Excitability of the Motor Nerves of Man (with Dr. de Watteville). *Philosophical Transactions of the Royal Society*, 1882, p. 961.

The main outcome of these observations may be most briefly summarised by quoting two passages from "An Introduction to Human Physiology," 1st edition, 1891.[1]

"*The formula of contraction on man.*—The above statements are based upon experiments with the nerves of frogs; experiments on man give results of which the principle is the same, but with differences which are owing to differences in the conditions of experiment. In the case of a frog's nerve cut out of the body, the points of entrance and of exit of the exciting current are usually chosen some distance apart, so that the kathode and anode are distinct, the current entering the nerve at one electrode and leaving it at the other. In the case of human nerve the conditions are different, for the nerve is imbedded in the tissues below the skin. A pair of electrodes cannot be applied to a nerve so as to send a current in at one point, out at another point; so that it is incorrect to speak of 'ascending' and 'descending' currents under such circumstances, and it is useless to attempt to study the effects when both electrodes are applied along the course of one and the same nerve. We must apply one electrode only to the nerve, and attend to its effects alone, completing the circuit through a second electrode which is applied according to convenience to some other part of the body. Confining our attention to the first electrode, let us see what will happen according as it is *anode* or *kathode* of a galvanic current. If this electrode be the anode of a current, the latter enters the nerve by a series of points, and leaves it by a second series of points; the former or proximal series of points collectively constitutes the *polar* zone or region, the latter or distal series of points collectively constitutes the *peripolar* zone or region. In such case the polar region is the seat of entrance of current into the nerve, *i.e.*, is *anodic*; the peripolar region is the seat of exit of current from the nerve, *i.e.* is *kathodic*. If on the contrary, the electrode under observation be the kathode of a current, the latter enters the nerve by a series of points which collectively constitute a 'peripolar' region, and it leaves the nerve by a series of points which collectively constitute a 'polar' region. The current at its entrance into the body diffuses widely, and at its exit it concentrates; its 'density' is greatest close to the electrode, and the greater the distance of any point from the electrode, the less the current density at that point; hence it is obvious that the current density is greater in the polar than in the peripolar region.

[1] The principle here stated was derived from a suggestion made by Helmholtz at the Nat. Med. Verein, Heidelberg, 1867.

"These conditions having been recognised, we may apply to them the principles learned by study of frogs' nerve under simpler conditions. Seeing that with either pole of the battery, whether anode or kathode, the nerve has in each case points of entrance (constituting a collective anode), and points of exit to the current (constituting a collective kathode), and admitting as proved that make excitation is kathodic, break excitation anodic, we may with a sufficiently strong current expect to obtain a contraction at make and at break with either anode or kathode applied to the nerve. And we do so in fact. When the kathode is applied, and the current is made and broken, we obtain a *kathodic make contraction* and a *kathodic break contraction;* when the anode is applied, and the current is made and broken, we obtain an *anodic make contraction* and an *anodic break contraction.* These four contractions are, however, of very different strengths; the kathodic make contraction is by far the strongest; the kathodic break contraction is by far the weakest; the kathodic make contraction is stronger than the anodic make contraction; the anodic break contraction is stronger than the kathodic break contraction. Or otherwise regarded, if, instead of comparing the contractions obtained with a 'sufficiently strong' current, we observe the order of their appearance with currents gradually increased from weak to strong, we shall find that the kathodic make contraction appears first, that the kathodic break contraction appears last, and the formula of contraction for man reads as follows:—

Weak current	K.C.C.	—	—	—
Medium current	K.C.C.	A.C.C.	A.O.C.	—
Strong current	K.C.C.	A.C.C.	A.O.C.	K.O.C.

"That such should be the normal order of appearance is fully accounted for by the following considerations:—

In the	The nature of the stimulus is	The situation of stimulus is	Conditions of excitation
K.C.C.	Kathodic	Polar	= best stimulus in best region
A.C.C.	Kathodic	Peripolar	= best stimulus in worst region
A.O.C.	Anodic	Polar	= worst stimulus in best region
K.O.C.	Anodic	Peripolar	= worst stimulus in worst region

which also account for an apparent anomaly, viz., that sometimes the anodic closure contraction precedes the anodic opening contraction, while sometimes this order is reversed; this difference depends upon relative current densities in the two regions, which are determined by the nature of the tissues by which the nerve is surrounded. In testing this point we shall hardly fail to notice a very evident token of the fact that polar and peripolar excitation is differently localised in the nerve; the muscles that contract to anodic make are not the same as those that contract to anodic break, if, *e.g.*, the exploring electrode is applied to the median nerve. This point need not, however, be further discussed here.

"The latent period of the break contraction on man is exceedingly and constantly long (·05″); on the frog its duration is very variable, sometimes very short, sometimes very long. With strong currents, it is usual on man to obtain tonic contraction during the passage of the current—*galvanotonus*—as well as single twitches at make and at break.

. . . .

"*Electrotonus on Man.*—The above conclusions are based upon experiments made upon frogs' nerves. Experiments on man give similar results with minor differences, owing to differences in the conditions of experiments. As regards frogs' nerve, it is isolated, and the test is applied separately from the polarising current, induction currents being most convenient for testing the extrapolar region, while mechanical stimuli are best adapted for testing the intrapolar region. As regards human nerve imbedded in the tissues, such a mode of testing is not possible, and it is necessary to adopt some means for insuring that the test shall coincide with the polarised region of the nerve. This can be effected by conjoining in one circuit the testing with the polarising current, or in the case of mechanical stimuli by applying the latter through the electrode of the polarising current.

"The effect of an induction shock alone is compared with its effect in the presence of a polarising current; the difference observed is owing to the modification of excitability which the polarising current produces. The polar effects under the conditions of application of electricity to the human body, and the distinction between polar and peripolar excitation must be borne in mind in this connection. Remembering that a current entering or leaving the body through an electrode applied over a nerve, has in that nerve a polar and a peripolar region—polar of the same sign as the electrode, peripolar of the opposite sign; remembering further that make excitation is kathodic, break excitation anodic, it is easy to understand the effects of various possible combinations between testing and polarising currents. If the induction current is used as the test, the combinations which it is possible to form at the exploratory electrode, with a polarising current in the same circuit, are as follows:—

1. Kathode of testing current, and of polarising current.
2. Anode of testing current, and of polarising current.
3. Kathode of testing current, and anode of polarising current.
4. Anode of testing current, and kathode of polarising current.

"Putting these four cases to the test, it will be found that excitability is *increased* in the polar region when it is *kathodic*, *diminished* when it is *anodic*, and that similarly, but in smaller degree, excitability is increased in a peripolar kathodic region, diminished in a peripolar anodic region.

"Similar results follow the application of other tests—make and break of a constant current, alone, and in the presence of a polarising current in the same circuit—mechanical stimulation alone and during the passage of a polaring current—viz., increased excitability in a kathodic region, diminished excitability in an anodic region."

IX.—On the Influence of the Galvanic Current on the Excitability of the Sensory Nerves of Man (with Dr. de Watteville). *Proceedings of the Royal Society*, 1882, p. 366.

A verification on *sensory* nerves of the phenomena described in the previous paper relating to motor nerves. Experiments of this nature on man, as compared with analogous experiments on animals, present the advantage that alterations of sensory excitation can be better appreciated by the subjective evidence of sensibility than by the objective signs from which inferences are drawn.

X.—Experiments and Observations relating to the process of Fatigue a Recovery. *First Report, British Medical Journal*, July 1885. *Second Report, British Medical Journal*, July, 1886.

The general tenor of these two papers will be most briefly presented by quotations of the following account in the *British Medical Journal*, to which may be added the remarks (1) that the first report contains a description of a new application of photography to the recording of galvanometric deflections, (2) that the second report was a brief preliminary communication of facts more fully set forth in Paper XI.

THE PROCESS OF FATIGUE AND RECOVERY.

"The conclusions reached by Dr. Waller concerning the part played by the motor end-plates in the process of fatigue, and in the allied process of degeneration, are of special interest and importance, and justify our acceptance of the generalisation that the junction of nerve and muscle is a weak link in the chain, and is the first to suffer in its transmitting-function by poison, by excessive action, and by disorderly nutrition. We have, in short, under these last two conditions, an effect precisely similar to that which is brought about by the action of curare; and we see that an identical result—namely, the establishment of a block between nerve and muscle—can be produced by curare, by fatigue, and by degeneration; that is to say, by agents in the toxicological, in the physiological, and in the pathological domains: a generalisation which is still further extended to include the changes which naturally occur at death. Dr. Waller's experiments on this last point are not advanced as being entirely conclusive. The problem here is to examine whether, in the dying organism, the excitability of nerve outlasts the excitability of muscle by stimuli applied to its nerve; and the only method by which this could be accomplished was by the observation of the 'negative variation' as the index of excitation occurring in the nerve when it had ceased to have action on muscle. This method was followed, and instruments were devised for the purpose of recording the results. A complication, however, arises, owing to the development of electrotonic currents which might mask or be mistaken for the negative variation; and Dr. Waller promises to repeat these experiments with additional precautions. These experiments, relating to the motor end-plate, also go far to prove that it is an organ that can be fatigued; and, therefore, when called into action, a force-producing organ, and not merely a passive conductor, like nerve, as was held by Tschiriew. The last-named observer stated that fatigue by excitation of nerve runs a parallel course with fatigue by direct excitation. The present report contains, however, curves in which the fatigue-decline is more rapid for indirect than for direct excitation.

"Another question of practical importance which is broached in these experiments is that of the principal site of fatigue, when normal voluntary action is sustained or repeated for long periods. It clearly results, from the experiments made by Dr. Waller on this point, that, when central nerve-cell, nerve-fibre, and muscle are together called into play in the accomplishment of repeated voluntary efforts, it is the central cell that is the weakest link in the chain; and that voluntary action grows weaker as fatigue increases—not because either muscle or nerve are becoming exhausted, but because the central motor is expending its power. Dynamometric observations show diminished voluntary power at a time when the excitation of nerve or muscle gives none of the ordinary signs of fatigue at the periphery; evidence of peripheral fatigue appears, indeed, to be obtainable with a difficulty which contrasts strongly with the ease and rapidity of the occurrence of voluntary fatigue. The bearing of these observations upon some of our guiding notions in medical practice is obvious, and appears at first sight to be out of harmony with the recent experiments of Zabludowski and others, and the undoubtedly good effects of 'massage,' which can only be understood on the supposition that fatigue is, in part, peripheral. This is, however, not excluded by the above observations; an instance of peripheral fatigue by excessive central action is given in the case of strychnia acting on the spinal cord; and the conclusion appears to be that the process of fatigue expresses itself at both ends of the nerve—more, however, at its central than at its peripheral end. Data are still wanting, however, before we may assign to each constituent of the nervous arc its share in the depression of function that results from expended activity. We know already, from the older experiments of Du Bois-Reymond, and the more recent experiments of Wedenski and of Bowditch, that the nerve proper has little or no share in the depression; that it does not expend force, but is merely a passive conductor; that it is, therefore, practically unsusceptible of fatigue. Bernstein's older experiments, on the course of fatigue and recovery in nerve, have been entirely supplanted by these modern experiments; and we now require a comparison of the process in the nerve-centre with that at the periphery, and not the comparison of muscle with nerve in this respect, seeing that the last-named organ is practically independent of functional fatigue and recovery.

"Dr. Waller's report contains further an account of experiments showing that the effect of a poison, when it has added itself to the normal effect of which an organ is capable in response to excitation, can itself be dissipated in consequence of a series of excitations, and reaccumulated during an interval of repose, even if the organ be completely isolated from any fresh supply of the poison. Such phenomena are shown to occur in the case of the action of veratria upon muscle, and in that of strychnia upon the spinal cord; the veratria character disappears from muscle in consequence of repeated action, and returns during subsequent repose; the strychnia character disappears from the spinal cord in consequence of repeated action, and returns during repose. The analogy of these phenomena with each other and with the normal process of fatigue and recovery is complete; they differ only in the rapidity with which they are developed. The process in the cord is evidently of the same causation as the changes in excitability recently observed by Walton upon animals poisoned by strychnia, to the effect that the cord, after repeated excitation, regains its property of summating stimuli, and loses this property during subsequent repose.

"The course of an intoxication has many points of resemblance with the course of fatigue; both are usually characterised by an initial increase and subsequent decline of excitability; but the case of the action of strychnia upon the cord appears to be exceptional; the excitability is increased, even in advanced intoxication, in the presence of signs of muscular exhaustion. Under such conditions, however, a sign of fatigue is present in the form of the well-known delay of reflex action, which increases as the toxic effects deepen, and is an index of a gradually increasing block of transmission in the cord. Dr. Waller reports experiments made in order to test the point of the nervous arc at which this block of transmission occurs, and has found that it does so at first exclusively, and later chiefly, at the junction of the afferent nerve with the spinal cord, for at first the time of reaction is prolonged in the absence of any retardation in the transmission of nervous impulses within the cord; and later, when such retardation does take place, it is small in comparison with the prolongation of the time of reaction.

"The report concludes with some important observations upon the alteration of resistance which is caused in the human body during the passage of the galvanic current. But it is not our intention, nor have we attempted, to summarise the entire report, which is itself a concise summary of observations, and a preface to further study of an important borderland province between physiology and pathology."

Cf. Mosso, "Die Gesetze der Ermüdung," Du Bois-Reymond's "Archiv," 1890, p. 89.

XI.—On the Action of the Excised Mammalian Heart (with Professor E. Waymouth Reid). *Philosophical Transactions of the Royal Society*, 1887, p. 215.

The purport of this paper is given in an abstract sent to the Académie des Sciences.[1]

It was reported upon by the "Commission d'examen" (MM. Marey, Charcot, Lappey, Ranvier, and Brown-Séquard) in the following terms:[2]

"Ce travail contient nombre de faits nouveaux et très intéressants à l'égard des phénomènes électriques du cœur, de la durée de l'action rhythmique des quatre parties de cet organe après l'excision, et de la lenteur que peut acquérir l'onde de contraction cardiaque dans certaines circonstances. Nous pourrions nous borner, pour légitimer notre conclusion à l'égard de la récompense que nous proposons d'accorder à ces physiologistes, à renvoyer à l'analyse qu'ils ont publiée de leur Mémoire dans les Comptes rendus (séance du 31 Mai dernier, p. 1547). Mais nous croyons devoir rappeler quelques-uns des points établis par ces auteurs.

"Ils ont fait voir que le cœur excisé des mammifères se comporte comme celui des batraciens, quant au passage de l'onde de contraction, mais avec quelques différences. Dans le cœur des mammifères, la variation n'est pas toujours diphasique. Elle ne l'est pas aussitôt après l'excision, mais le devient plus tard, d'ordinaire après quelques minutes. Les mouvements du galvanomètre et de l'électromètre indiquent, dans les variations monophasiques, une négativité prédominant soit à la pointe, soit à la base; dans la variation diphasique, une négativité à la pointe, puis à la base, ou vice versa. Une autre différence á été trouvée entre le cœur des mammifères et celui de la grenouille; c'est que le mouvement de la pointe s'est montré presque toujours avant celui de la base, tandis que chez la grenouille c'est toujours l'inverse qui a lieu.

"Les expériences de ce physiologistes ont été excessivement multipliées et leur Mémoire donne un nombre très considérable de graphiques établissant l'exactitude de leurs conclusions.

[1] *Comptes Rendus de l'Académie des Sciences*, 1887, p. 1547. [2] *Ibid.* 26 Décembre' 1887, p. 1370.

XII.—Note sur la force électromotrice d'un animal à sang chaud (chat) après la mort. *Archives de Physiologie*, 1888, p. 457.

Observations of the great length of time after death during which the electromotive action persists in the muscles of warm-blooded animals.

XIII.—A Demonstration on Man of Electromotive Changes accompanying the Heart's Beat. *Journal of Physiology*, 1887, p. 229.

XIV.—On the Electromotive Changes connected with the Beat of the Mammalian Heart and of the Human Heart in Particular. *Philosophical Transactions of the Royal Society*, 1889, p. 169.

XV.—Détermination de l'action électromotrice du cœur de l'homme. *Archives de Physiologie*, 1890, p. 146

Of the above three papers, the first contains the description of a "demonstration" and the third a summary account of more complete "determination," of the electrical action accompanying the beat of the human heart.

The Apex and Base of the human heart lie in an oblique axis A B passing through the left side and the right shoulder. With each beat of the heart differences of potential arise between A and B, and currents are established in and around an axis A B. At each such event equipotential surfaces are formed round A and B respectively on each side of an equator lying in an oblique axis at right angles to A B passing through the right side and the left shoulder, so that the body is divided into two asymmetrical electrical fields, viz., a portion *b*, *b*, *b*, comprising the head and right upper extremity, and a portion *a*, *a*, *a*, comprising the trunk and three other extremities.

Any two points *a* and *b* on opposite sides of the equator (*e.g.*, the mouth and the left hand) are "effective" upon the capillary electrometer, and the column of mercury is seen to pulsate with each beat of the heart.

Any two points *a* and *a*, or *b* and *b*, on the same side of the equator (*e.g.*, the mouth and the right hand) are ineffective; and the column of mercury exhibits no pulsatile movement. The left hand and either foot are ineffective; the right hand and either foot are effective.

In persons the subjects of *situs viscerum inversus* the mouth and the right hand form an effective lead-off, whereas the mouth and left hand are ineffective. In such cases the left hand and either foot are effective, the right hand and either foot are effective.

Cf. Bayliss and Starling. Internat. Monatschr. f. Anat. u. Physiol., 1892.

XVI.—On the Physiological Mechanism of the Phenomenon termed Tendon-Reflex. *Journal of Physiology*, 1890, p. 383.

Repetition on the rabbit of time-measurements previously made on man, with conclusions similar to those stated in Paper V.

XVII.—A new Colour-contrast Experiment (*Proceedings of the Physiological Society*). *Journal of Physiology*, 1891.

Modification of Meyer's colour-contrast experiment. Argument that the modified experiment is more consonant with the psychological theory of Helmholtz than with the physiological theory of Hering.

XVIII.—A possible Use of the Membrana Tectoria (*Proceedings of the Physiological Society*). *Journal of Physiology*, 1891.

Exposition of a theory to the effect that auditory stimulation may be produced by "pressure-patterns" of the hair-cells against the membrana tectoria.

Papers XIX. (on the sense of effort) and XXIV. (on the functional attributes of the cerebral cortex) deal with matters of mainly psychological interest, from a physiological stand-point. The nature of the arguments, which of necessity deal with much sub-positive matter, renders it difficult to give a short abstract of their contents. Experimental points presenting themselves in connection with psychological considerations involved in these two papers, and susceptible of actual demonstration, are dealt with in papers XX., XXI., XXII. and XXIII.

XIX.—The Sense of Effort: an Objective Study. *Brain*, 1891, pp. 179—249.

The main argument in this paper has been summarised as follows in "An Introduction to Human Physiology" (2nd ed., p. 550).

"Muscular sense, sense of movement, sense of effort, are terms used to denote the sensation that accompanies all voluntary muscular contractions. The factors of this composite sensation are:— (1) *peripheral*, arising from variations of tension and of pressure in the moved organs, *i.e.* in tendons, ligaments, cartilages, possibly in the muscle itself, certainly in the skin of the part; (2) *central*, arising from material changes accompanying the elaboration and emission of motor impulses.

"Whether a central as well as a peripheral factor contributes to the sensation of movement or effort has been much debated, and is still denied by some authorities, who regard it as of exclusively peripheral origin. The view that the central state is implicated in the formation of the sensation is materially supported by the objective signs of fatigue. Admitting that material changes *after action* occur in the same parts as material changes *with action*, we may learn the incidence of the effect by studying the incidence of the after-effect. Now the after-effect of muscular action, subjectively felt as fatigue, is demonstrable by objective signs at the centre as well as at the periphery; from which we infer that the motor effect, which is subjectively felt as the sensation of movement or of effort, is associated with material changes at the centre as well as at the periphery. This is to say, that the sensation called 'muscular sense,' 'sense of movement,' 'sense of effort,' is associated with changes *at the centre and at the periphery*; we have no right to say that it is caused by changes in either of these situations to the exclusion of the other."

The same paper contains a description of the "Dynamograph," employed in the observations described in Paper XX. for the study of voluntary and of electrically excited fatigue.

"The value of the dynamometer is much increased if it is converted into a *dynamograph;* the manner of maintenance of a prolonged maximum effort for regular periods, or the character of a series of maximum efforts for regular periods, may then be recorded on a slowly travelling surface, *e.g.* a cylinder on the hour axis of an ordinary clock; and from such records an estimate may be formed of the muscular strength, of its rate of decline in a succession of efforts, and of its rate of recovery from such decline.[1]"

[1] *Intr. H. Physiol.*, p. 339.

XX.—A peculiar Fatigue-effect on Human Muscle. *(Proceedings of the Physiological Society.)* *Journal of Physiology*. 1891, p. lv.

A simultaneous record of the longitudinal and lateral effects of muscular contraction taken from the muscles of the forearm exhibits practically simultaneous beginning and end of effects in the normal state, but in the state of fatigue the lateral effect commences to cease nearly one-tenth of a second later than the longitudinal effect. The change is characteristic of voluntary fatigue and is not produced by direct electrical tetanisation.

XXI.—The Muscular Sound during Galvanotonic Contraction (*Proceedings of the Physiological Society*). *Journal of Physiology*, 1891, p. 56.

Demonstration of a muscular sound during "galvanotonus" identical in pitch with that heard during voluntary tetanus.

XXII.—Experiments on Weight-discrimination (*Proceedings of the Physiological Society*, January 30, 1892.

The discrimination between different weights is more delicate: (1) by voluntary than by electrically excited contraction; (2) by galvanisation than by faradisation; (3) by muscle electrically excited than by nerve electrically excited.

XXIII.—On the Inhibition of Voluntary and of Electrically Excited Muscular Contraction. *Brain*, 1892, p. 35.

Experimental and critical study regarding the question of peripheral inhibition of voluntary muscle.

Conclusions:—(1) "Anodic inhibition" and "kathodic excitation" are normal phenomena of human, as of all animal muscle and nerve. (2) There is no proof of the passage of inhibitory impulses to voluntary muscle, either by the ordinary motor channels or by any special inhibitory fibres.

XXIV.—On the Functional Attributes of the Cerebral Cortex. *Brain*, 1892, pp. 329-396.

Historical and critical study of experimental data relating to the cerebral cortex, and of their psychological significance.

XXV.—Expériences myothermiques sur l'homme. *Proceedings of the Physiological Congress of Liège.*, 1892.

On Calorimetry by Surface Thermometry and Hygrometry. *Proceedings of the Physiological Society*, November, 1893.

Preliminary communications embodying thermometric and hygrometric observations on man and calorimetric deductions therefrom. New methods of recording temperature variations: (1) by the galvanograph described in paper X.; (2) by an air thermograph. Loss of heat by evaporation is separately calculated from chloride of calcium vessels weighed before and after application to the skin during a given period. Local increase of surface temperature consequent upon muscular contraction—*e.g.*, of a limb—is in major part due to increased blood-supply, in minor part to muscular thermogenesis.

XXVI.—Points relating to the Weber-Fechner Law. Retina, Nerve, Muscle. *Brain*, p. 200. 1895.

XXVII.—The Quantitative Relation between Stimulation and Negative Variation of Nerve. *Proceedings of the Physiological Society*, June, 1895.

The Weber-Fechner law, expressing the relation between stimulation and sensation is considered from a more general standpoint, in so far as it is an instance of the universal relation between physical cause (stimulus) and physical effect (mechanical and electrical changes) in the excitation of living matter.

The effects submitted to experimental investigation are :—

The electrical response of the retina to the stimulus of light.

The electrical response of medullated nerve to electrical stimulation.

The mechanical response of muscle to electrical stimulation.

Conclusions.

In the case of the retina the magnitudes of effect as ordinates corresponding to an arithmetical increase of stimulation as abscissa, form a curve concave to the abscissa—*i.e.*, equal increments of cause give diminishing increments of effect—(confirmatory of Dewar & McKendrick).

In the case of muscle the magnitudes of contraction as ordinates corresponding to arithmetical increase of stimulation as abscissa, form a curve which is at first convex, then concave to the abscissa—S-shaped—viz., equal increments of cause give at first increasing, subsequently diminishing increments of effect.

In the case of nerve within the physiological working range the relation between cause (excitation) and effect (negative variation) is arithmetical.

An entire curve expressing the relation between cause and effect within the nerve itself (excitation along the X axis) is S-shaped, consisting of :—

(*a*) A short subminimal portion, convex to the abscissa, with effects increasing by increasing increments.

(*b*) A long middle portion, inclusive of the functional range from minimal to maximal muscular effects, with effects increasing by equal increments, *i.e.*, in a straight line.

(*c*) A long ultra-maximal portion, concave to the abscissa, increasing by diminishing increments.

There is a disproportion between stimulus and sensation such that equal increments of stimulation produce diminishing increments of sensation. Is this disproportion physiological, *i.e.* between the external stimulus and the internal sensificatory change, or psychological, *i.e.* between the sensificatory change and the sensation? Answer: It is probably the former.*

The foregoing experiments involved an examination of the electrical response of nerve under the influence of anæsthetics, and led to the systematic employment of nerve to gauge activity of a large number of reagents.

Portions of this wide field of research have been entered upon during the ensuing four years, and reported upon in the following papers :—

* Intr. Human Physiology. 3rd edition. p. 557.

XXVIII.—The Action of Anæsthetics upon Isolated Nerve.—*Proceedings of the Physiological Society*, November, 1895.

Experimental demonstration of the comparative anæsthetic power of carbon dioxide, of ether and of chloroform, and summary account of the action of chloromethanes and of chloroethanes.

XXIX.—Action of Carbon Dioxide on Nerve, and Production of Carbon Dioxide by Nerve.—*Proceedings Physiological Society*, January, 1896.

XXX.—Action of Carbon Dioxide and of Ether on Electrotonic Currents. *Proceedings Physiological Society*, February, 1896.

XXXI.—Action of Reageants on Isolated Nerve. Anæsthetics.. *Brain*, p. 43, 1896.

XXXII.—Action of Reagents on Isolated Nerve. Bromides, &c. *Brain*, p. 277, 1896.

XXXIII.—Action of Reagents on Isolated Nerve. Alkaloids.—*Brain*, 1897.

XXXIV.—Observations upon Isolated Nerve.—*Croonian Lecture Royal Society*, March 12, 1896. *Phil. Trans. Roy. Soc.*, 1897.

XXIX., XXX., and XXXIV. contain the full description of the action of carbon dioxide upon the electrical phenomena of nerve, and the cumulative evidence in favour of the conclusion that carbon dioxide is produced in tetanised nerve. The first two of these papers give summary reports of communications to the Physiological Society, the third was the Croonian Lecture to the Royal Society for 1896.

The inexhaustibility of nerve-fibres urged in paper X., is now presented in a new light. "Medullated nerve-fibres are experimentally inexhaustible, not because their tetanisation effects little or no chemical change, but because such change is extremely rapid and rapidly effaced by a change in an opposite direction. The materials of which normal medullated nerve is composed (grey neuroplasm and white trophoplasm) are in a state of great chemical lability, so that whatever is done is done easily, and as easily undone (Croonian, p. 65).

XXXI., XXXII., and XXXIII. are three laboratory lectures embodying data relating to the action upon nerve of anæsthetics, of salts, and of alkaloids.

The first lecture gives a general account of the scope of the method, and the results of a preliminary survey of the action of gases and vapours.

The second lecture embodies results relating to the action of reagents in solution—salts and alkaloids. From an examination of the comparative effects of a large number of neutral salts—more especially the chlorides, bromides, and iodides of ammonium, sodium, and potassium—the general conclusion is drawn that in the action any salt AB, B (the basic moiety) is predominant. Comparative anæsthetic effects of chloride, bromide, and iodide of ethyl. Comparative toxic effects of several analgesic and other alkaloids.

Aconitine, veratrine, cocaine, physostigmine, chloral hydrate, butyl chloral hydrate, gelseminine, digitaline, convallamarine and curarine † are active upon nerve. Muscarine, atropine, aconine hyoscine and morphine have little or no action under the conditions of experiment.

The third lecture is in substance a communication to the Neurological Society, including the actual demonstration of three representative experiments—(*a*) the comparative anæsthetic effects of ether and chloroform, (*b*) the comparative sedative effects of bromide of sodium and of bromide of potassium, (*c*) the inertness of morphine as compared with the toxicity of aconitine.

The subject entered upon in the above papers, XXIX. to XXXIV., is further pursued in several directions in subsequent publications.

Papers XXXV., XXXVI. and XXXVIII. give account of a study of elementary phenomena in nerve associated with its electrical activity.

Papers XXXIX. and XL. deal with practical bearings of a comparative study of the action of anæsthetics upon the nerves and upon the heart.

XXXV.—Action of Temperature on Electrotonic Currents. *Proceedings Royal Society*, p. 384, vol. 60, 1896.

The principal conclusions stated are that both Anodic and Kathodic electrotonic currents are temporarily abolished at about 40°, returning with fall of temperature to a state in which the normal superiority of the Anodic over the Kathodic current is diminished or reversed. This change is briefly designated as a decrease of the electrotonic quotient A/K.

XXXVI.—Action of Acids and Alkalies on Electrotonic Currents. *Proceedings Royal Society*, p. 80, vol. 60, 1897.

It is stated (1) that the electrotonic quotient A/K is diminished by acidification, increased by basification and (2) that the characteristic change common to the three presumably dissociative agencies (*a*) rise of temperature (*b*) acidification, (*c*) tetanisation, is a diminution of the electrotonic quotient.

XXXVII.—Action of Carbon Dioxide on Muscle (with Miss S. C. M. Sowton). *Proceedings Physiological Society*, 1896.

The "Staircase" effect in voluntary muscle, as in nerve, is probably due to an evolution of carbon dioxide.

† The curarine here referred to was the ordinary curarine of commerce, which, according to Boehm, is a mixture consisting of curine and tubo-curarine. From recent experiments, I have learned that both the last-named substances act upon nerve, whereas true curarine is quite inert.

The influence of carbon dioxide upon muscle, curarised and uncurarised, is similar to that witnessed at the outset of fatigue, viz., augmented height of contraction, and diminished rapidity of relaxation.

The beat (spontaneous and excited) of an excited heart (frog) is gradually but temporarily abolished by carbon dioxide.

XXXVIII.—Comparative Effect of Reagents upon the Negative Variation, and upon Electrotonic Currents. *Proceedings of the Physiological Society*, 1897.

The negative variation is more easily influenced by reagents than are the electrotonic currents.

All these kinds of currents are in varying degree subject to physiological modification by reagents.

XXXIX.—Action of Anæsthetics on Nerve: Ether and Chloroform. *Presidential Address to the Section of Physiology, British Medical Association*, Montreal. *British Medical Journal*, November 20, 1897.

Measured by their effects upon isolated nerve, the physiological power of chloroform and ether is in the relation of 7 or 8 to 1. Chloroform is physiologically seven times as powerful as ether.

The anæsthetic power of a mixture of chloroform and ether is the sum of the powers of the two constituents. Chloroform at 2 per cent. = ether at 15 per cent. = chloroform at 1 per cent. + ether at 7·5 per cent. In the A.C.E. mixture anæsthesia is principally ($\frac{5}{6}$) effected by chloroform.

XL.—The Dosage of Chloroform. *British Medical Journal*, 1898.

Chloroform vapour is in itself a certain and uncapricious agent, producing effects more or less pronounced in gravity, according as it acts in greater and smaller quantity.

Quantity administered is the all-important factor in anæsthesia by chloroform, and in death by chloroform.

Anæsthesia requires the continuous administration of a mixture of chloroform and air at an average percentage of 1·5—not below 1 per 100 and not above 2 per 100.

XLI.—Histological Changes in Medullated Nerve after treatment with the Vapours of Ether and Chloroform (with Mr. F. S. Lloyd). *British Association Reports*, p. 520, Toronto, 1897.

Changes are visible in the appearance of nerve fibres after prolonged anæsthesia, viz.:—the Medullary sheath becomes faintly granular, incisures become more distinct, nodes of Ranvier become less distinct. The effects are more marked after chloroform vapour than after ether and carbonic acid, and cannot be detected after brief anæsthesia which has sufficed to abolish electromobility of the nerve.

XLII.—On the Action of Anæsthetics on Vegetable and Animal Protoplasm (with Professor Farmer). *Proceedings of the Royal Society*, vol. 63, 1898.

Simultaneous and comparative observations of the effects of certain anæsthetics upon (*a*) the movements of chlorophyl bodies, and (*b*) the electromobility of frog's nerve. The effects in such case are of similar order, viz., slight initial augmentation, followed by temporary arrest in the case of carbon dioxide, more prolonged arrest in the case of ether, permanent and final arrest in the case of chloroform.

XLIII.—Influence of Polarisation on the Electrical Resistance of Nerve. *Proceedings of the Physiological Society*, November, 1898.

The electrical resistance of nerve is higher to make the induced current than to the corresponding break current. The polarisation counter-current of the make current is greater than that of the break.

The electrical conductivity of chloroformed nerve is increased 10 to 20 per 100 by reason of its diminished polarisability.

XLIV.—The Characteristic of Nerve. *Proceedings of the Physiological Society*, February, 1899.

The characteristic of nerve is defined to be the numerical value indicating the rate of decline of the energy curve of a true minimal stimulus. A true minimal stimulus is not merely the smallest stimulus of any kind or shape evoking a smallest visible contraction, but the smallest amount of visibly effective *energy* at an optimum *rate* of impact, as delivered by a condenser of varying capacity charged at varying pressure.

The characteristic of nerve is raised and lowered by rise and fall of temperature.

XLV.—Comparative Action of Veratrine Alkaloids upon Nerve and Muscle. *Physiological Society*, July, 1899.

Veratrine acts principally upon muscle. Protoveratrine acts principally upon nerve.

XLVI.—Excitation of Muscle by Condenser Discharges (with Mr. St. John). *Physiological Society*, July, 1899.

The minimal energy of a direct stimulus of uncurarised muscle is 0·5 erg., and of curarised muscle 1·5 erg. With rising temperature this minimal is at first diminshed, subsequently increased.