"THE ELECTRICAL DIAGNOSIS OF PERIPHERAL NERVE INJURY, AND SOME APPLICATIONS OF ELECTRONICS TO PHYSIOLOGY AND CLINICAL MEDICINE."

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INTRODUCTION.

In the summer of 1941 the Scottish E. M. S. Hospitals organization established a special Unit for the reception and treatment of patients suffering from peripheral nerve injury at Gogarburn Hospital on the outskirts of Edinburgh. In connection with this specialized type of injury, relatively rare in peace-time but assuming considerable importance in War, invitations were issued to various persons specializing in ancillary branches of Medicine and Surgery to attend the clinical meetings of the Peripheral Nerve Unit, to consider applications of their work to this particular problem, and to have access to the patients for the assessment of their methods.

Peripheral nerve injury diagnosis and treatment involves a considerable field of application for methods which have been primarily developed as physiological techniques, particularly in the use of modern electrical apparatus, and the Director of the Unit, Professor J. R. Learmonth, invited me to attend the clinical meetings, and to make a study on the patients of modern methods of electrical diagnosis, and this opportunity, gladly accepted, has furnished me with a wealth of problems and of material ever since.

This thesis accordingly presents such of

these /

these problems as have at present been worked out to the extent of being of clinical or laboratory use.

The wide field of work afforded, and the fact that a completely free hand was given in the nature of the research undertaken, has resulted in the work gradually spreading over wider and wider fields in several branches of applied science, in an attempt to collect from all sources methods and ideas which could assist in the immediate practical problem - that of developing and establishing clinical methods of assessing peripheral nerve injury.

The first part of this thesis deals, therefore, with the approach to, and the results achieved from, the _ad hoc_ problem of peripheral nerve injury diagnosis. We have been concerned with the testing and establishment of diagnostic techniques which can be used at the bedside in a routine manner, as far as possible by non-technical operators. This first part of the thesis is entitled "The Electrical Diagnosis of Peripheral Nerve Injury".

But the establishment and development of new methods, or of refinements of older ones, goes beyond the clinic, and in this type of work depends on laboratory research in the first place. There is no lack of information in the literature on

electro-diagnosis /

electro-diagnosis of peripheral nerve injury, as various methods were largely used during the 1914-18 War. But, although the principles of peripheral nerve injury have not changed since 1920 - though they have been neglected, as is natural, in peace-time - the whole aspect of that great new science, Electrical Engineering, has changed since then; the development of the thermionic valve in its various forms, and the refinement of measurement and of appreciation of electrical phenomena have made it necessary to review the whole subject again at the present time.

Neuro-physiology has always depended on engineering technique for the increasingly refined methods by which nerve function and activity is revealed. Many instruments devised by engineers and physicists have gradually been translated from laboratory curiosities to physiological adjuncts, and then to the clinical commonplaces; the X-ray tube, the electrocardiogram and the cathode-ray tube are three obvious examples. At the same time, this transition is not an easy one to achieve. The field covered by physicists and engineers is a vast and strange one to the clinician, and the urgency and difficulty of Medicine and Surgery is foreign to the research laboratory. The innumerable devices described in the literature /

literature of physics are not, as a rule, directly applicable to biological work, and the general attitude of physics research is not one which can be adopted in a physiological laboratory. The biological worker has not got at his disposal the complex and costly equipment which is referred to as standard apparatus in the applied physicist's armament, and must adapt and contrive one or two instruments to give him the information which he requires.

We have accordingly entitled the second part of this thesis "<u>Applications of Electronics to Physiology and Clinical Medicine</u>", and attempted in some measure to discuss and demonstrate how recent advances in electro-physical engineering technique can be adapted for biological work. A great deal of the described work is not original, and its repetition here is only justified on two grounds. Firstly, there is no single source of information on electrophysiology in its practical applications, and any worker entering this field has a long course of reading and of practice to go through before emerging on original ground. In the second place, I have already pointed out that a physiologist necessarily works with a restricted number of physical instruments, and must make the most of them. In war-time, this has been /

been a very important consideration, and adaptations have had to be made continually to overcome the shortage of materials and accessories. Despite the repetition of a considerable amount of work which has been collected from widely-spread sources, tested out, and criticised, we have developed and established certain new techniques which are of value in biological work, and these are described in relation to their forerunners.

In general, two considerations have been borne in mind in the account to be given of technical applications; they have all, as far as possible, been tested not only in the laboratory but under clinical conditions - they can, in fact, be guaranteed to work in practice; and they are all within the grasp of biological workers who possess a fair working knowledge of modern electronic physics. None of them requires the elaborate resources of a physics research institution, and all have been developed and tested with the relatively simple equipment to be expected in a physiology and bio-physical laboratory.

There is a further justification at the present time of an intensive study of the applications of modern physical science to biology. During the war years the development of scientific technique has proceeded /

proceeded under very great pressure, and devices which were unheard of, or mere laboratory toys at the commencement of war have been shaped and adapted to routine purposes in unskilled hands. Electronic science in particular has developed all the refinements of radiolocation and of the beam reflection bomb-sight and many other practical applications still secret. These advances cannot fail to have a profound influence on research of all kinds - and particularly neuro-physiological research - within a few years of their published descriptions. Secrecy regarding the construction and operation of innumerable devices has been essential to the country's security, and at the termination of the need for silence a flood of new inventions and equipment will come about; and some of these will be of the greatest value in applied biology and medicine.

Therefore, although we are bound to realise that much of the material here presented may be already obsolete by reason of advances as yet undisclosed, we can yet claim to be ready to appreciate and accept the new information, and welcome any help that it can give us towards examination of the problems of the laboratory and hospital clinic.

I have a great number of acknowledgements

to /

to make in connection with this work, which I most gladly do. In the first place, my thanks are due personally to Professor Learmonth for advice and help whenever sought, and for the completely free hand which I have been allowed. Secondly, my gratitude is due to the Wilkie Surgical Research Fund for financial assistance in respect of apparatus which has been essential to the work. Professor I. de B. Daly, Professor of Physiology, has encouraged and supported the work throughout, and I am grateful to him for a great deal of acute and interested criticism.
Dr R. L. Richards, Gogarburn Hospital, as a personal friend of some years' standing, will expect no thanks, but on him has fallen the task of sorting out for me the various patients for clinical examination, which he has faithfully done.

To the staff of Gogarburn Hospital in general I express thanks for many kindnesses, and to individuals in the other Peripheral Nerve Units throughout the country with whom I have exchanged views.

When the work was well under way, and becoming known, I have had most gratifying and valuable help from authorities in the field of electrical engineering and research. Information received, and apparatus /

apparatus loaned have in the last few months extended the scope of the research very greatly; I am indebted particularly to Mr Bergin, H.M. Office of Works Technical Staff, Mr C. Horne, of Marconi's Ltd., Mr A. Poliakoff of Multitone Electric Coy., Dr James Greig of the Northampton Polytechnic and Dr MacDonald of the Birmingham Sound Reproducers, Ltd.

P A R T I

"THE ELECTRICAL DIAGNOSIS OF PERIPHERAL NERVE INJURY".

1. THE PHYSIOLOGY OF PERIPHERAL NERVE INJURY.

The diagnosis of peripheral nerve injury is primarily anatomical, and must be made in the clinic on a knowledge of the distribution of the motor and sensory components of the nerve involved. As the definitive treatment of nerve injury is in the first instance surgical, precise information as to the site of the lesion is of great importance; in closed injuries, or those involving large or lacerated wounds, this information can be obtained only by detailed examination of the motor and sensory loss from the anatomical point of view.

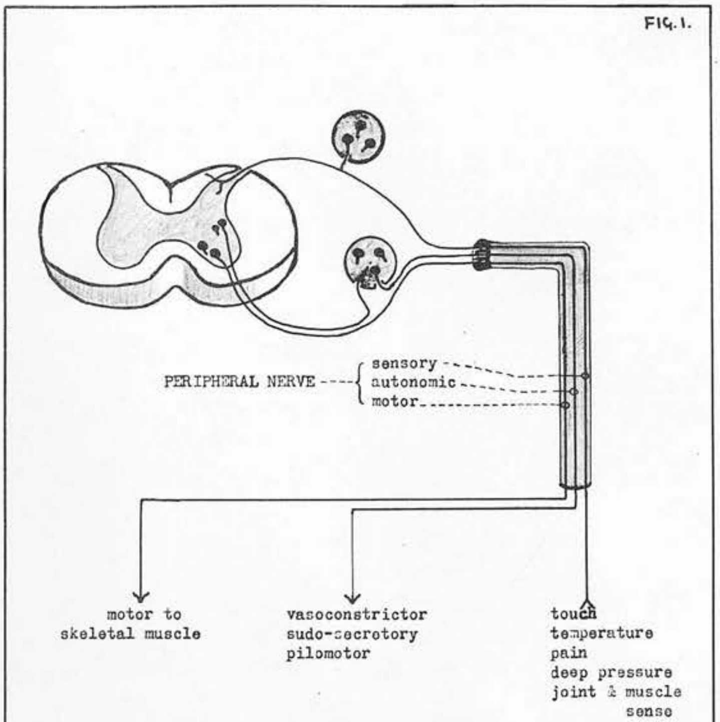
But in addition to the anatomical description of the defect, a physiological study of the functional alteration described as "paralysis" or "sensory loss" can often supply valuable information, especially as regards assessment of recovery. From the point of view of function, we distinguish three main components in the mixed peripheral nerve, damage to any or all of which produces characteristic changes in the operation of the tissues supplied thereby. The lower motor neurone, originating in the cell body in the anterior horn of the spinal cord, transmits the nerve impulses controlling voluntary muscle movement and maintaining reflex postural tone. The sensory fibres convey the various modalities of sensation from /

from the appropriate end-organ to the spinal cord and central nervous system; these fibres vary in size, structure, and vulnerability to injury. Thirdly, the autonomic component is distributed to the plain muscle of peripheral blood vessels and hair follicles, and is secretory to the sweat glands in the skin; the autonomic fibres proceed outwards from the spinal cord in two stages, a preganglionic neurone originating in the spinal grey matter and terminating in the autonomic ganglion, whence the second neurone arises to be distributed with the peripheral nerve to the end-organ concerned. A diagrammatic presentation of these components is given in Fig. 1.

Anatomical observation of the regions and muscles altered in activity gives a fairly exact definition to the level at which damage to the mixed nerve has occurred, and if nerve injury in practice had only two aspects - complete normality or complete division - would give an adequate account of the injury. But nerve damage varies in nature and in degree, and it is in dealing with types of injury intermediate between the extremes mentioned that physiological assessment has an important part to play.

Seddon (1943) has reviewed and discussed the types of nerve injury which are encountered in war /

Fig.1.



The main physiological components of peripheral nerve.

war surgery, and he divides them into three main groups, each presenting different problems of diagnosis, treatment, and prognosis. In the first place we have a relatively mild degree of axon injury which abolishes or impairs impulse propagation over a varying length of nerve, but leaves the fibre intact distal to the site of damage, and the end-organ normal and attached to this intact distal portion. This type of injury, named "Neurapraxia" by Seddon, is familiar to most people in the mild form of paresis that results from nerve pressure in an awkward posture, in the "Saturday night" or crutch palsies of axillary pressure, and in various occupational palsies that arise from chronic localized pressure. Local and temporary abolition of nerve conduction, without structural damage, is also produced by local anaesthetic administration, application of cold, or certain types of electric current. In that this type of injury produces no gross changes, and does not require axon regeneration for restoration of function, it recovers spontaneously after a relatively short interval from the time of removal or disappearance of the cause.

Secondly, Seddon names "Axonotmesis" the axon injury which is sufficiently prolonged or severe as /

as to produce Wallerian degeneration in the distal portion; such lesions occur in general after severe pressure, contusion, or toxic applications, and leave the neurilemma tube and supporting connective tissue intact and in continuity, so that the regenerating axon tip is automatically guided to the end-organ with which it was originally connected. When such a "lesion in continuity" occurs to a mixed nerve, it bears an excellent prognosis, because although the end-organs are denervated, and must await regeneration of axons, they remain connected as it were by "guides" to their original cell-bodies.

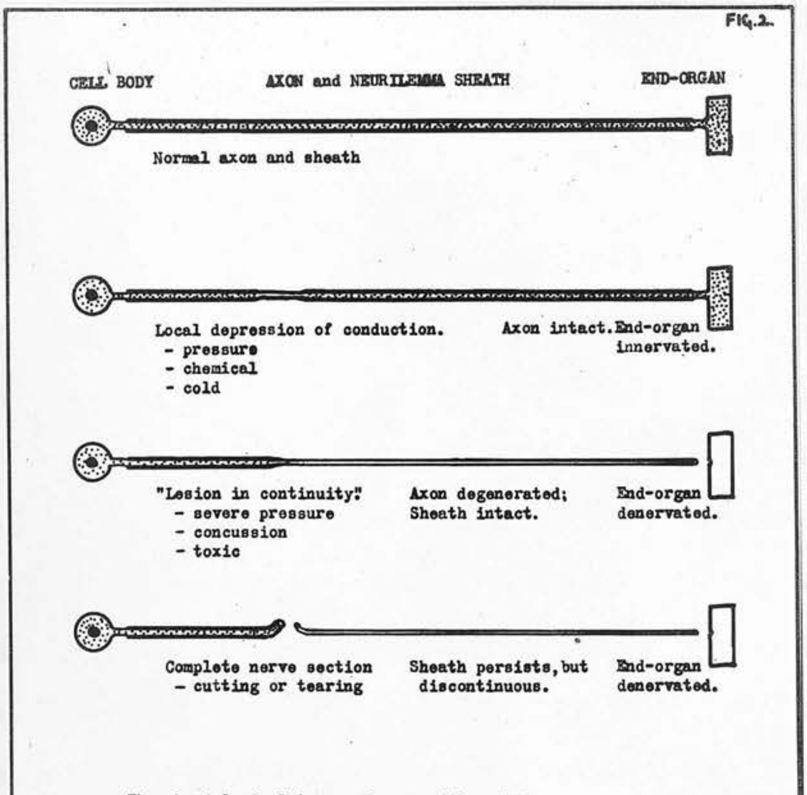
Thirdly, in "Neurotmesis", we encounter the common war injury where the mixed nerve has been cut or torn right across, whereby continuity is lost, and the distal portion remains as a bundle of empty neurilemmal tubes. This is the injury which so often requires surgical intervention to oppose and fix together the severed ends in order to allow regeneration every chance. In this lesion of complete section with anatomical separation the pattern or arrangement of the neurones in the nerve is essentially destroyed, for the regenerating axon tips approach and enter at random a neurilemma tube on the distal side of the gap which may or may not lead them to the right /

right variety of end-organ, and at the best cannot be expected to re-occupy their original positions. Features of this regeneration across gaps, and through interpolated grafts, have been systematically examined and investigated in animals and man by many workers, and have recently been reviewed by Young (1942) who has been responsible for much of the knowledge that we now possess on the subject.

Although these two latter types of nerve injury - axon section and complete nerve section - bear such widely different prognosis as regards ultimate result, it is important to appreciate that they cannot be distinguished one from the other by examination of the region of sensory loss or of the paralysed muscles; for, once Wallerian degeneration has taken place, the end-organs are completely denervated in both instances. Short of exploratory operation, only the extent and rapidity of recovery can differentiate axon section in continuity from nerve section with its accompanying axon shuffling. It is in respect of early detection of recovery that physiological investigation is most valuable.

A diagrammatic presentation of these types of nerve injury is given in Fig. 2, but clinically we can add a further type of disability which is not uncommonly /

Fig.2.



The physiological types of nerve fibre injury.

uncommonly encountered as a complication. One must remember that a neurone - cell body, axon, and end-organ - may be intact anatomically and physiologically as a unit, but may remain inactivated from the point of view of function. Functional or hysterical palsies are relatively common, often associated with structural injury, and have to be taken into account as a form of physiological damage.

A further complication arises in the fact that not all nerve injuries in practice correspond definitely to any one of these four types. In pressure palsies and axon section particularly the extent of damage may be differential as amongst components of the same nerve. It is well-known that, broadly speaking, the larger diameter fibres in a mixed nerve are the most sensitive to mechanical pressure or contusion, whereas the smaller fibres in the same nerve are more affected by chemical or toxic injury. Mild pressure palsies very often present a picture of motor paresis with little or no sensory loss; local anaesthesia characteristically abolishes pain readily without interfering until much later with motor impulse propagation in the same nerve trunk. Moreover, even in complete nerve section, the curious chances of missile injuries may result in partial /

partial section of a nerve, with or without contusion to the remaining portion, and anatomical anomalies of nerve distribution are more common than formal anatomical teaching makes evident.

It is in respect of the assessment of denervation and recovery of end-organ function that physiological methods have a value as clinical adjuncts, and this portion of the thesis proposes to describe the methods in common use, with an attempt at estimating their particular worth over a series of cases. Physiological techniques as applied to the clinic must be judged on a basis of practicability as well as on value, for a delicate and complex system for measuring some function may be useless as applied to the routine examination of scores of patients. We are not here concerned primarily with the measurement itself as with some simple routine application which can yield sufficient information to be of value. Limitations of investigation in respect both of simplicity and of value will be emphasized throughout the following account.

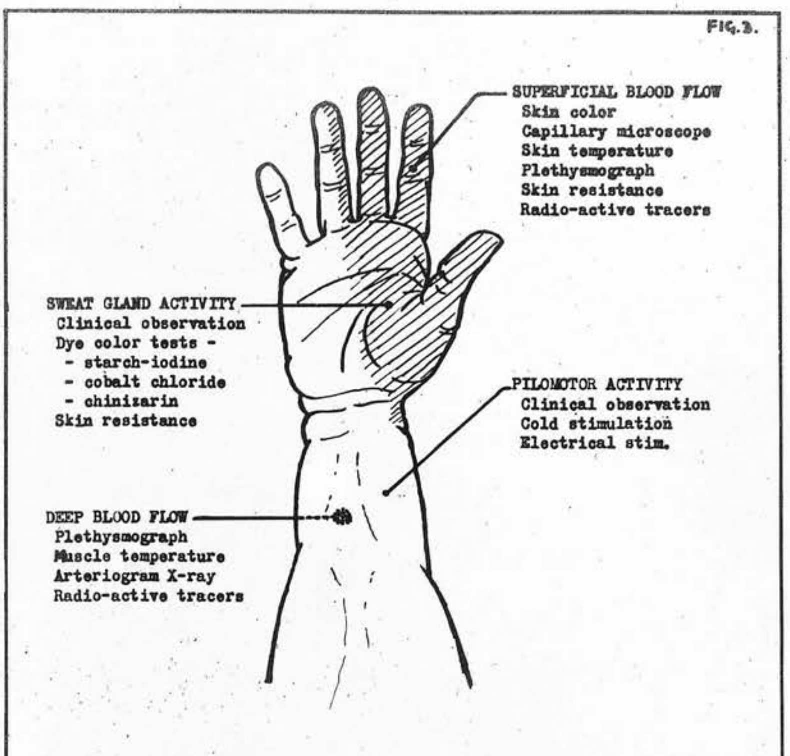
2. THE INVESTIGATION OF AUTONOMIC DENERVATION.

Section of the autonomic component of a peripheral nerve gives rise to the familiar clinical picture of loss of vasomotor control, absence of spontaneous sweating, and abolition of "goose-flesh" or pilomotor reaction in the area supplied by the severed fibres. This area, in any given mixed peripheral nerve, is a relatively small one, and there appears to be a very extensive overlapping of autonomic fibres in their peripheral distribution; this distribution, moreover, is extremely variable and inconstant from one individual subject to another. The area in which autonomic denervation can be demonstrated after mixed nerve section corresponds roughly to the area in which sensory defect occurs, but is usually rather smaller and more variable. The principal anatomical features of autonomic denervation, demonstrated by various methods, have recently been described by List and Peet (1938), Guttmann (1940), Richter and Woodruff (1941), Shumacher (1942) and Richards (1943).

In the initial examination of cases of peripheral nerve injury, the inconstancy and relative unimportance of the autonomic defect render its evaluation of secondary significance, and the investigation /

investigation of peripheral autonomic defect after nerve injury is undertaken usually to detect early signs of regeneration. There are a great many methods of study available, but most of them have been designed and employed for the examination of autonomic function itself, and not as adjuncts to nerve injury diagnosis. In the majority of nerve injuries to the extremities by missiles, the mixed nerve is damaged at a relatively high level in the limb, and the distal region in which autonomic defect occurs is of much less importance, both from the view-point of diagnosis and prognosis, than identification of, say, the most proximal muscle affected. This does not apply to low injuries to the same extent, and in nerve injuries at wrist level autonomic re-innervation is often the earliest sign of recovery.

In order to present a complete account of methods of investigation of nerve injury cases, we will outline the techniques in common use, and comment briefly upon them. Any one, or all, of the autonomic functions can be examined as an index of activity, and the general summary of the investigation is shown diagrammatically in Fig. 3.



The methods of assessment of peripheral autonomic activity.

2.1. The measurement of vasomotor activity.

The measurement of peripheral vasomotor activity in man has been studied in connection with vascular disease and injury rather than with traumatic nerve damage. In the nerve injury cases of war, in young and healthy persons, the vasomotor defect is of very minor importance. Immediately following on nerve section or block, the vessels where autonomic fibres have been put out of action are deprived of the normal constant vasoconstrictor tone, and dilate to a degree determined by their natural elasticity. In nerve injury at any rate any vasodilator elements in the human mixed nerve are of no practical significance. This dilatation is reflected in the skin colour, the skin temperature, and the superficial blood flow; and also, though less certainly, in the blood flow through the deeper tissues. All these effects can be estimated and used as indices of autonomic denervation. The flushing of the skin which is usually very obvious in young people shortly after the injury has been reduced to a standard comparison scale by Lewis (1929). Skin temperature is best measured by means of a thermocouple junction and galvanometer (Grant, 1935 and blood flow by plethysmographic methods (Freeman, 1935). Deep blood flow and its variations can only be /

be estimated by elaborate and careful technique; a recent paper by Barcroft, Bonnar, Edholm and Effron (1943) gives a good account of the difficulties involved, using a combined thermocouple and plethysmograph method.

The dilatation which results from abolition of vasoconstrictor impulses does not persist in human subjects for more than a few weeks, and the denervated vessels take on the power to expand and contract in response to local circumstances. Richards(1943) points out that, in this country, denervated digits are usually cold and blue after the initial flushing has passed off, because the prevailing climate provides a cold environment.

Such denervated vessels can still dilate in response to local heating or to local infection or drug administration, although they are no longer under remote nervous control. A review of methods and significance of skin temperature measurements has been given by Murlin (1939).

A new method of estimating blood flow in man is now being made possible by the production of radio-active isotopes of physiological elements; chemically identical with the element in the body, the radio-active form can be administered and detected by /

by its radiation. The production and detection of radio-active substances have been developed to a very great extent already by physicists and chemists, but await application to human physiology; a preliminary report has been published by Smith and Quimby (1944). We have tried one such experiment in a case of damaged digital circulation from frost-bite; because it was impossible to secure the correct radio-active tracer substance, we were forced to use a weak natural substitute, and the experiment was a failure in result, though not in principle. The recording gear is complex in design, but not in operation, and the method has great possibilities once normal standards have been established for blood-flow in various parts of the body by such technique. The design of the recording gear has very much improved during the War, and there is no doubt that it will be of clinical application within a few years at most.

2.2. The measurement of sweat gland activity.

The second feature of peripheral autonomic activity in man which can be measured as an index of damage and recovery is the secretion of the skin sweat glands, which goes on continually to a greater or less degree under the influence of sudomotor impulses in the autonomic nerve fibres. Clinical observation describes the denervated peripheral area as hot, from vasomotor denervation, and dry, from sudomotor interruption, and as regeneration proceeds, return of sweating is one of the earliest signs of recovery. Minor degrees of sweating, especially in the prevailing climate in Britain, are difficult to detect or assess, and two methods in particular have been developed as clinical adjuncts for estimation and recording of sweat gland activity.

The first, or chemical, method depends on the use of substances which change colour on contact with moisture; any such chemical, if suitable in other respects for application to the skin, will differentiate between a normally sweating area and the dry area of autonomic denervation. Slips of filter paper soaked in cobalt-chloride and dried in an oven are blue as long as they remain dry, but turn pink on application of small amounts of water (White and Smithwick, 1941). Minor's method (1928) involving a /

a paint of iodine and castor oil followed by dusting with starch powder has been very widely used, and is convenient for photographic record purposes, as the sweating area turns a blue-black colour, leaving the denervated region light. Guttmann (1940) describes a similar chemical sweat-detecting method using the dye chinizarin, which also gives a deep blue colour in presence of moisture, and is rather more convenient in use than starch and iodine.

The second method for measurement of sudomotor denervation makes use of the fact that the electrical resistance of the skin is greatly altered by presence or absence of sweat secretion. With reasonable appreciation of the difficulties the accurate measurement of skin resistance is a straightforward and rapid procedure. Skin resistance measured between two electrodes on the skin is varied not only by sweat gland activity but by vascular changes in the tissues below the epidermis. When the ordinary type of electrodes using contact paste or saline-soaked pads are used, vasomotor changes alter the inter-electrode resistance considerably, as can be seen in the fact that the resistance of the warm hand is markedly lower than that of the cold hand, sweat being ruled out by thorough cleaning immediately before /

before measurement. But when dry metal electrodes are used, the resistance component due to the epidermis far outweighs the component due to underlying tissues, hot or cold, and alterations in sweating are by far the most variable factor. It is not advisable to apply a direct current, such as from a battery, to living tissue for any length of time, as polarization occurs which lowers the resistance and causes a steady increase in current. This can readily be observed by maintaining the electrodes in a fixed position for several seconds and noting the steady decrease of resistance. A very good quantitative account of this phenomenon in man is given by Bourguignon (1923), and a review of the general problem by Levine (1933). More reliable results can be obtained in practice by the use of alternating (AC) current, which causes no polarization because of the periodic reversal of flow. Most of the measurements of skin resistance have been carried out with battery and galvanometer recording direct current, but we have found that measurements with alternating current are simpler and more definite. The technique and design of skin resistance measurement is considered in Part II of this thesis, and will not be elaborated here.

In our experience skin resistance measurement /

measurement has been a very rapid and simple method of assessing autonomic denervation. If a permanent anatomical record is desired, the margin of the high resistance area must be marked with a skin pencil; using a 1 cm. square electrode it is very easy to define a sharp line of demarcation between normal and non-sweating regions. In this connection, one finds that in the first few weeks after autonomic denervation the non-sweating area reduces in size, and this long before any true regeneration can have taken place. Furthermore, just as the full vasodilatation passes off gradually, so does the very high resistance of recent denervation, although the denervated area will show a resistance higher than normal until regeneration occurs. The changes in the initial period after autonomic section are described by Smithwick (1940).

From the point of view of early detection of recovery, measurement of sweat gland activity is certainly the simplest and probably the most valuable index of autonomic re-innervation, and its detection by skin resistance levels accordingly a valuable one, especially in the case of nerve injuries at a distal level. At the same time we must bear in mind that an indication of autonomic recovery alone is of academic /

academic significance in a hand with motor and sensory loss; autonomic regeneration is not necessarily followed by motor and sensory recovery, and motor and sensory loss isoften encountered without corresponding autonomic defect, by reason sometimes of anomalous distribution, and sometimes of differential fibre damage in the mixed nerve, as already described.

Recent accounts of sweat gland denervation in man after nerve block or injury, both from the anatomical and physiological sides, and by dye and resistance methods of demonstration have been given by List and Peet (1938; 1939), Guttmann (1940), Richter and Woodruff (1941), Richter (1942) and Shumacher (1942).

The actual values of resistance measured by experiment vary very widely with the technique used. As actual values are of great importance in the design and operation of stimulating instruments, we shall discuss the variations in detail in Part II. Figures are only of value if made consistently with the same preparation of the patient, the same electrodes and the same recording instrument. We have found it of great value to employ the same electrodes for stimulation as for resistance measurement, and the stimulator which we have designed and used for investigation /

investigation of motor defect incorporates a simple addition whereby the resistance between the electrodes can be measured at any time by operating a switch. The actual figures found in a series of measurements are presented in Fig. 4. These resistance measurements were carried out by means of the cell and galvanometer technique, as we did not initially appreciate the advantages of alternating current. Electrodes as used for muscle stimulation comprised one large indifferent electrode and one small 1 cm. diameter one, used either dry or with a saline pad according to the measurement required. The palmar skin was measured in every case, and normal control figures taken from the unaffected hand wherever possible.

The results expressed in tabular form are given below:-

A. Normal palmar resistance with saline electrode and saline-soaked skin:

Range in thousands of ohms.	No. of individuals
Below 10	15
10 - 20	81
20 - 30	50
30 - 40	32
40 - 50	28
50 - 60	35
60 - 70	25
70 - 80	9
Total No. of measurements	275

B. /

B. Normal palmar resistance with dry skin and dry electrode:

Range in thousands of ohms.	No. of individuals
Below 50	10
50 - 100	108
100 - 200	101
200 - 300	59
300 - 400	19
400 - 500	10
Total No. of measurements	307

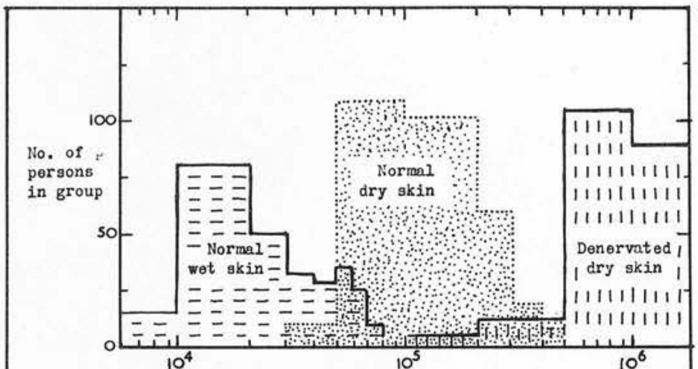
C. Denervated palmar skin resistance with dry electrode:

Range in thousands of ohms.	No. of individuals
Below 500	18
500 - 1000	104
1000 - 1500	91
1500 - 2000	22
Over 2000	3
Total No. of measurements	238

It will be seen from these figures and from their graph in Fig. 4 that there is a wide and fairly constant difference between the three groups. The normal dry skin resistance averages, in 307 persons, with this technique about 100,000 ohms, while that of denervated non-sweating skin in 238 persons has a mean value approximately 10 times as much. It is important to appreciate that these figures refer to measurement of the skin with a dry electrode and in its /

Fig.4.

FIG. 4



THE RANGE OF VARIATION OF SKIN RESISTANCE

Distribution of measurements of skin resistance in normal and denervated palmar areas. Dry measurements with bare metal electrodes; wet with saline pad and saline-soaked skin. Electrodes: one indifferent 10 X 5 cm. on forearm; one small disc 1 cm. diameter, as used for muscle stimulation. Current from dry cells; maximum one milliampere.

its natural condition. The distribution of measurements of normal skin well-soaked with saline and taken with a saline pad shows a mean value of about 10 - 20,000 ohms., and this order of resistance arises whether the skin is denervated or not. The soaking of the epidermal layer with saline entirely obscures any natural differences due to sweat gland activity, as might be expected. For this reason the electrodes used for muscle stimulation (for which purpose they are always wet) cannot immediately be used for assessment of sudomotor denervation, but must be dried, or a second pair used. The absolute figures given correspond fairly well with those given by other authorities using a similar technique (Whelan and Richter, 1943), but are in any case of secondary significance, the important feature being the relative order of magnitudes of normal and denervated dry skin resistance. It is very important that the skin be unbroken where the small electrode is placed, as even minute abrasions or punctures of the corneous layer will lower the resistance to a few hundred ohms., which represents the resistance of the deeper vascular tissues. Occasional very low values are encountered in hyperhidrotic cases, where the reason is obvious to the eye. Very high resistance skins may be /

be encountered in patients recently removed from plaster or other rigid splints. Both these conditions are sufficiently obvious not to cause confusion; apart from these there are no other sources of misinterpretation, and the measurement is a very simple one.

2.3. The measurement of pilomotor activity.

The plain muscle strands which when contracting pull on the hair follicle so as to cause erection are innervated by autonomic fibres, and autonomic denervation results in the abolition of this power of hair-erection, usually described from the skin appearance as "goose-flesh". From the clinical point of view pilomotor function has very little importance, as it is not easy to produce reliably, and is not capable of exact measurement. In cases where autonomic defect extends centrally from the extremities, the denervated area is often well shown up if the individual is in a hot bath, or is suddenly exposed to cold. Sudden exposure either to heat or cold will promote widespread pilomotor action in most people; application of a block of ice to the shoulder or axilla usually results in goose-flesh over the arm in a matter of a few seconds. This goose-flesh, very obvious in a suitable light, is absent over the denervated area, which is often very well demonstrated by the contrast. The method is however less precise and convenient than the alternatives already described, and has the drawback of being inapplicable to the most important region in routine examinations of nerve injuries, namely the hands and feet.

In /

In addition to the abolition of spontaneous pilomotor activity, autonomic denervation may or may not abolish the local pilomotor reaction to an electric stimulus, depending on the level at which the denervation has been carried out. This will be discussed in the next section when the reflex levels of autonomic activity in general are described.

2.4. The Peripheral Autonomic Reflex Levels.

In the preceding sections we have outlined the clinical features produced by peripheral autonomic denervation in man as they appear from lack of spontaneous activity; this inactive area can be compared statically with the surrounding normal region by various methods of measurement. But in the examination of peripheral nerve injuries autonomic denervation is more commonly estimated on an "active" as opposed to a "static" basis, and for that purpose certain reflexes are artificially provoked so as to throw into contrast normal and affected regions of the limbs.

There is a large number of such true physiological autonomic tests, which operate over different levels of the nervous system, and afford information as to the absence or integrity of the various axon paths involved. We will describe them briefly according to the pathways over which the reflexes operate.

(a) Reflex Tests over Central Nervous System Pathways.

The reflex vasodilatation test, described by Gibbon and Landis (1932) as a clinical test for vasomotor activity, has been widely used in the study of peripheral autonomic denervation, and the results recorded at the Gogarburn Nerve Injuries Unit published /

published by Richards (1943: 1945). In this test, exposure of any part of the body (conveniently the normal extremities) to heat produces after a short time a reflex opening-up of the blood vessels in the other extremities. The test is commonly carried out by observing the skin temperature of the area to be tested by means of thermacouples (Bedford and Warner, 1934) and immersing the other limb or limbs in water at 45°C. Temperature rise in the tested region implies vasomotor innervation of some degree; the extent of the rise, or its delay before appearance, as compared with normal control regions affords a quantitative measure of partial innervation. In this way the active response of an area, and not merely its basal level of activity can be measured; the denervated region where efferent pathways are damaged does not respond, and stands out by contrast.

A similar test uses sudomotor activity as its indicator of response; this may be measured by the dye methods already described, or by measurement of skin resistance. The skin resistance alteration consequent upon sensory stimulation, although presenting difficulties for routine use, can be developed into a very delicate and rapid test of autonomic activity. It is familiar to the psychologist as the "psychogalvanic" /

"psycho-galvanic" reflex, and even to the newspaper public as the once-popularized "lie detector". The psycho-galvanic reflex tends to lay emphasis on the afferent aspect of the reflex, and its absence is not, except under carefully controlled conditions, truly significant of sudomotor denervation; Carmichael, Honeyman, Kolb and Stewart (1941) point out that the response can be observed on any portion of the normal body surface if the subject is maintained sufficiently warm and comfortable. These workers employed the reflex to measure the velocity of sympathetic nerve fibre conduction in man. Darrow (1937) has reviewed the entire mechanism of the psycho-galvanic reflex.

Pressor reflexes in man, with the response detected as a rise of general blood pressure, have been widely used in investigation of autonomic activity. Perhaps the best known test is the "cold pressor" response described by Hines and Brown (1932) wherein one hand is immersed in water at 4°C for 1 minute; and the blood pressure rise consequent on this standard stimulus is measured 30 seconds and one minute later. A "muscle pressor" reflex of similar nature was described by Alam and Smirk (1937) wherein the stimulus consisted of exercising muscles whose circulation had been temporarily arrested by a proximal sphygmomanometer /

sphygmomanometer cuff. The degree of response in these pressor tests is very constant in normal subjects tested under standard conditions.

All these reflexes involve central nervous pathways of some complexity, and their efferent outflows operate over both pre-ganglionic and post-ganglionic neurones. In so far as the reflex is dependent on the integrity of the sensory side of the reflex arc as well as upon the motor, they may be used as indications of sensory activity, and in all cases the interpretation of their presence or absence must be done with due consideration. The cold pressor response, for example, can be used as a test of intact afferent cold sensation fibres from the hand immersed in the cold water; and the muscle pressor response might be employed clinically for the detection of sensory muscle afferents.

When these reflexes are employed in peripheral nerve injury examination, they are used primarily as indicators of integrity of the post-ganglionic autonomic fibres, although they are also abolished by section B of the pre-ganglionic fibres, or by damage to the sensory afferents invoked.

(b) <u>The Post-ganglionic axon reflexes.</u>

From the physiological point of view a very interesting /

interesting series of reflexes persists after section of the pre-ganglionic autonomic fibres, and such reflexes can be adapted for peripheral nerve injury examination. Pre-ganglionic section, by interruption of the efferent pathway, abolishes all spontaneous activity in the effector-organs involved, and also abolishes the complex reflexes just described; but such pre-ganglionic section does not result in denervation of the effector organs, which remain supplied by the intact but apparently useless post-ganglionic axon. Because of the branching of each terminal post-ganglionic axon, and its attachment to several effector organs of the same type, local reflex responses to stimulation can be elicited over a limited area. Thus stimulation of the skin of the arm with a strong faradic current results, after a few seconds' interval, in an area of goose-flesh, of local sweating, and of reddening which surrounds the electrodes for several centimetres. These appearances are due to activation of the autonomic effector organs over the sympathetic plexus in the skin, and constitute a true axon reflex involving antidromic propagation of nerve impulses over part of the network (Lewis and Marvin, 1927; Wilkins, Newman and Doupe, 1938). Such reflexes are not dependent on sensory afferents or pre-ganglionic /

pre-ganglionic pathways, and disappear only when the post-ganglionic neurons are damaged and have degenerated to their extremities; they are, therefore, strictly a test for post-ganglionic integrity.

These local axon reflexes are, naturally, demonstrable in normally innervated areas, where the local network exists, but because of the rather high intensity of stimulus required, are uncomfortable to elicit. In cases of peripheral nerve injury, however, because of the rough correspondence of sensory and autonomic territories of a given nerve, they may sometimes be elicited painlessly, or more commonly, can be attempted painlessly; reflex response without pain implies autonomic integrity with pain fibre interruption, which is relatively rarely found except in some recovering lesions; absence of reflex response, and of pain, implies total superficial denervation of that region. In general, these axon reflexes have not proved to be of significant practical use in nerve injury examination, probably because of their relative insensitiveness. We have tried out the axon reflex as an indicator of returning innervation after nerve injury, and have consistently found that autonomic function as revealed by skin temperature or visible sweating is a more sensitive index than the local axon reflex /

reflex, which reappears two or three weeks after re-innervation has been detected clinically.

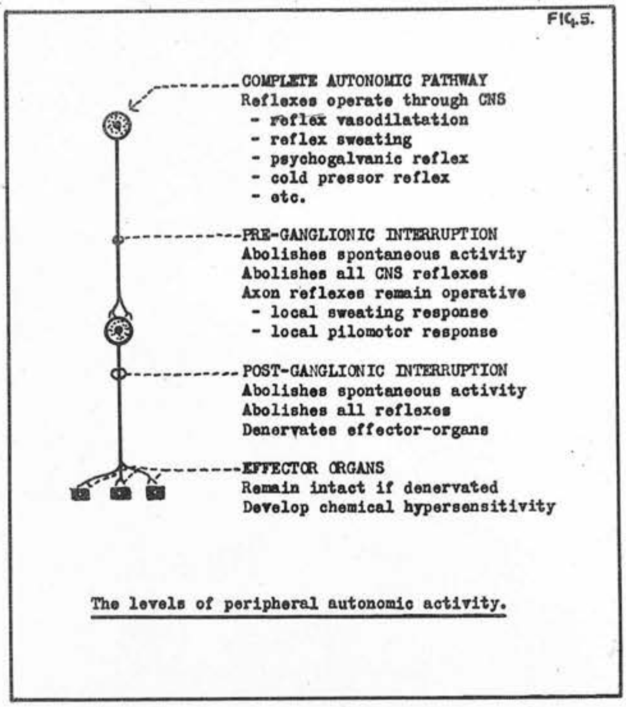
(c) Effector organ sensitivity.

At a yet lower level of complexity we have to consider the function of the terminal effector organs when they are completely denervated, as they are by the post-ganglionic section which severe peripheral nerve injury inflicts. The denervated effector organ - plain muscle of blood vessel or hair follicle, or sweat gland - does not itself degenerate, but remains in a potentially active condition for an indefinite time provided its nutrition is unimpaired. As such an organ is completely devoid of nerve supply, it cannot be operated by any form of reflex, but can yet be rendered active by chemical substances reaching it *via* the blood stream, or from adjacent tissue. Not only does this chemical sensitivity persist, but it is usually augmented very considerably, so that minute amounts of appropriate substances may produce, in the denervated organ, exaggerated effects. This chemical sensitization has been considered by Cannon (1939) as a general "Law of Denervation", and applied not only to autonomic effector organs but also to ganglion cells and to voluntary muscle fibres. From the practical aspect this sensitization presents the surgeon /

surgeon with a problem, for post-ganglionic sympathectomy will abolish spontaneous activity of the effector organs (which may be desirable on therapeutic grounds) but by denervation will sensitize them to substances which may be in the blood stream or to tissue metabolites. The excessive response of denervated arterioles to adrenalin, and of sweat glands to acetyl choline make the adequate therapeutic operation one which abolishes spontaneous activity but does not denervate, namely pre-ganglionic section. In cases of peripheral nerve injury the autonomic damage is post-ganglionic, and for a period after injury vasoconstrictor tone is removed from the affected blood-vessels, the sweat glands are inactive, and goose-flesh no longer appears; but after a few days, or weeks, the denervated effector organs acquire a marked power of response to local conditions, as we have already considered in connection with the common "cold phase" following vasomotor fibre interruption. This sensitization of the effector organs is not made use of for diagnostic purposes, and indeed tends to obscure the theoretically simple results of autonomic injury.

Fig. 5 represents these physiological levels of autonomic activity in a schematic way.

Fig.5.



The levels of peripheral autonomic activity.

2.5. Summary: Assessment of Autonomic Denervation.

Autonomic defect arising from peripheral nerve injury can be measured in a variety of ways utilizing sweating or vasomotor reactions under static or reflex circumstances. Of the various available methods, the psycho-galvanic reflex is the most delicate, but not suitable for routine use by reason of its complexity. Measurement of skin resistance is the most rapid and simple method of accurately delineating denervated non-sweating skin, provided such measurement is correctly done. Reflex vaso-dilation tests, with skin temperature as response indicator, are very satisfactory in practice. There is no evidence that either of these two methods is superior for the detection of the earliest sign of autonomic regeneration; in both cases their use in this respect is limited by the small and distal distribution of the autonomic component in mixed nerve, and by the fact that partial lesions which affect the autonomic component slightly or not at all, are in practice fairly common.

3. THE ASSESSMENT OF SENSORY DENERVATION.

Division of the sensory component of a mixed nerve produces clinical manifestations which are well-known, but whose physiological basis remains a subject for conjecture and experiment. In the simplest descriptive terms the resulting region of sensory loss consists of an area wherein light touch, as with cotton wool, is not appreciated, and a somewhat smaller inner area where the sensation aroused by a pin-prick is also absent. As in the case of autonomic distribution there is a considerable overlap between adjacent nerve territories, and individual variation is common and considerable.

Many attempts have been made to interpret these findings in terms of anatomical arrangement and physiological activity. The original description of the results of sensory nerve section given by Rivers and Head (1908) remains as the standard of clinical observation, although the well-known theory of "protopathic" and "epicritic" sensory mechanisms is inadmissable in the light of modern neurophysiology. Walshe (1942) in a critical review of the subject of cutaneous sensibility stresses the view that sensation depends on two peripheral factors; the anatomical overlap /

overlap and distribution of the terminal nerve endings to a "sensory unit" of appreciable size including several end-organs, and the known existence in the sensory nerve of several components having different threshold values for excitation and different rates of conduction. In so far as this attitude depends on data which can be directly verified microscopically and experimentally, it is a very attractive one, and has recently been given additional experimental support by Bishop (1943: 1944) employing a new technique for the stimulation of individual sense organs in man. Several authorities, however, feel that this explanation does not adequately account for certain clinical findings, and Lewis (1942) has postulated the existence of a dual skin mechanism. One part of this mechanism, the so-called "Nocifensor" network - is not directly afferent to the central nervous system, but is concerned with a local chemical release arrangement which serves to lower the threshold of the afferent nerve endings to painful excitation. Livingston (1943) has published a monograph on pain mechanisms in relation particularly to peripheral nerve injury.

It must be admitted that the neurophysiologist has had less to contribute in this field than in any /

any of the other aspects of nerve injury, and from the practical aspect, the pin and the cotton wool test are the instruments of choice. The difficulties of precise assessment of sensory impairment and improvement are partly fundamental. Within a few weeks of injury the boundaries of the "touch loss" area tend to become smaller, with no evidence of regeneration of the interrupted fibres; it is almost certain that this is due to the extension into the margins of the denervated area of sensory branches from the surrounding normal regions. There is as yet no valid quantitative expression of sensory impairment, and recovery can be judged objectively only by anatomical decrease in the denervated area; even this is very largely dependent on the subjective character of the patient.

Appreciation of recovery by the patient's own description of a "different" feeling has to be judged purely on its merits in a particular case, and even the delineation of areas may be quite inaccurate from one examination to another on the same subject. Examination results are further complicated by the fact that sensory loss is very inconstant both in degree and extent; partly because in partial injuries considerable numbers of sensory fibres may be spared while motor axons are interrupted, and partly because there /

there is a great deal of intercommunication of sensory elements between peripheral nerves in the limbs, and a high complete lesion not uncommonly results in very little sensory loss, the sensory component having joined the mixed nerve in question below the lesion level.

From the practical point of view it is very desirable to establish if at all possible some method of assessing sensory impairment on an objective basis, for in many lesions sensory recovery is the earliest sign of regeneration. This is especially so in low lesions at the level of wrist or ankle, where the length over which sensory fibres have to regenerate before restoring function is relatively short. At the same time we have not been able to devise any satisfactory technique up to the present. The pressor reflexes already mentioned have been tried as depending on cold sensation for the cold pressor test and muscle afferents for the muscle pressor test, but have been of very little use; they do not appear to commence operation until sensation has obviously returned to the area, as judged by ordinary means. Faradic excitation of the skin with minute electrodes is a very poor alternative to the clinical needle and wool, although we have not had the opportunity so far of /

of testing Bishop's spark technique.

There is at least one obvious possibility which must have occurred to many neuro-physiologists, and that is the recording of sensory action potentials in the mixed nerve trunk above the lesion. If action potentials could be demonstrated to appear and cease on appropriate stimulation of a skin region, an entirely objective assessment of the nature and degree of innervation could be made. But the technical difficulties are extremely great at the present time; detection of the potentials is possible, and their identification feasible, but the method as a practical clinical adjunct has not yet been developed. Rusinov (1943) has reported the successful recording of sensory activity in a mixed nerve trunk in man, and claims to have identified the impulses subserving pain sensation; but I have made many attempts, with apparatus considerably superior in delicacy and reliability to Rusinov's, without any measure of success. The potentials can, quite readily, be recorded and identified in an exposed nerve under general anaesthesia; but confirmation of Rusinov's report must be awaited before it can be accepted that recording from the surface overlying a mixed nerve can give reliable information.

This /

This problem represents one of the contributions which applied electronics may well make to physiology in the course of the next few years, with the advance of technical methods, and the development of such methods up to the present time will be discussed in Part II of this thesis. The biological and medical implications of an objective method of describing peripheral sensory mechanisms are very great, and the subject accordingly worth intensive study.

Summing up, we believe that methods of assessing early sensory recovery in man after nerve injury cannot at present be counted as effective as that available for autonomic activity estimation. Seddon, Medawar and Smith (1943) in a paper on the rate of regeneration of peripheral nerve have pointed out that sensory methods are very difficult to gain information from; they point out that Tinel's sign (1917) is sometimes, but rarely, useful, and often absent, and this has certainly been our experience also. Examinations delineating the margins of sensory loss are the best available method of assessing sensory recovery; for these the classical testing with needle and cotton wool is as good as any; even this is difficult and unreliable in many patients.

4. THE ASSESSMENT OF MOTOR DEFECT.

4.1. General considerations.

Muscular weakness or paralysis is perhaps the most obvious and dramatic result of peripheral nerve injury, and is the main feature to which attention is directed with intent to repair. Although certain sensory defects may be gravely disabling - for example median nerve anaesthesia in the hand - the majority of surgical procedures and therapeutic measures are undertaken to restore muscular function to the defective limb, and thereby to give the patient, if at all possible, a useful hand or leg as the case may be. From the point of view of assessment of damage and recovery, the neuro-muscular system affords many opportunities for study and measurement, and the next portion of this thesis deals with them in considerable detail. We have concentrated especially upon neuro-muscular investigation for several reasons. Autonomic activity was concurrently being studied by Dr Richards at the Gogarburn Unit, and has been described by him in several places (1943; 1944; 1945); and we have seen that attempts to measure sensory activity in man, though most important physiologically, are at present unlikely to give results: and as the

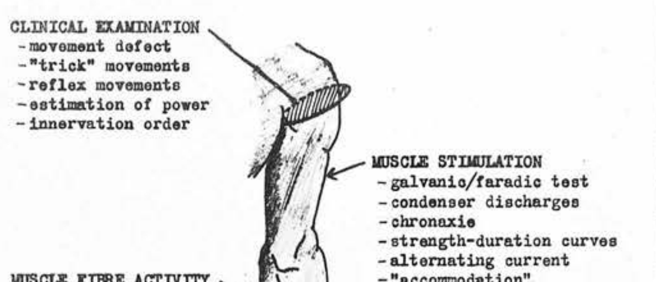
Nerve /

Nerve Unit was intended primarily for treatment and disposal of Services casualties and only secondarily as a field for research, we decided at the outset to investigate motor function in the first place.

There are three main lines of approach to the practical problem, and each covers a wide field in itself. In the first place there is the straightforward clinical examination of muscular weakness, with the refinements that systematic recording of cases and experience can give. Secondly, the artificial stimulation of muscles by electric currents has long been used in the diagnosis and treatment of neuromuscular damage, and, at the time of starting the Nerve Unit was due for consideration and development in the light of modern neuro-physiology. Thirdly, a physiological technique, developed during the past decade, allows us to record and measure the currents of action produced in the contractile muscle elements themselves, and thereby to appreciate differences in various pathological conditions. Finally, in exceptional cases, one may have the chance of direct inspection of the muscular tissue after biopsy, but such opportunities are rare. These methods are presented schematically in Fig. 6, and we shall proceed to discuss each method separately.

Fig.6.

FIG.6.



The assessment of motor defect.

4.2. Clinical Examination.

At first sight it might appear a very straightforward procedure to examine a limb, and to detect and note which particular muscles were active and which were not. While this is so in many cases, in a large number of patients identification of affected muscles may not be an easy matter. There are two main difficulties encountered. The first is the rapid development in certain patients of so-called "trick" movements, whereby the patient has learnt to operate a joint with muscles other than those which normally carry out that action. Such movements appear very commonly in patients who are intelligent and keen to recover, and who are not oversplinted; such patients often claim to have recovered certain lost movements, which is of course true from their point of view but very misleading to the examiner. The other main source of confusion is the fairly common occurrence of anomalous innervation in limb muscles, particularly the small ones of the hand; the interossei, for example, are quite often innervated by the median nerve, and remain active after complete ulnar lesions. In addition, painful recent wounds, scar tissue, adherent tendons, and joint stiffness and oedema may severally make voluntary /

voluntary action reluctant or difficult to detect. The systematic clinical testing of individual limb muscles has been described in M.R.C. War Memo. No. 7: (1943; revised 1944) prepared by the Surgery Department of Edinburgh University from experience and material at the Nerve Unit. The tests there shown are intended as far as possible to avoid confusion by trick movements.

The clinical recording of muscle defect is one of the most important single features of examination. We have regularly used charts which list the limb muscles in order of innervation, so that the level of the injury, and also retrogression and recovery, can be seen at once. A portion of one of these charts is reproduced in Fig. 7, which summarizes the principles of clinical recording; the chart provides for the recording of galvanic, faradic, and voluntary response on successive examinations. The section reproduced in Fig. 7 is that applicable to a patient H. S., who sustained a complete median nerve lesion above the motor supply to the pronator-flexor group of muscles; accordingly, on first examination, all the median-supplied muscles were inoperative voluntarily or faradically, though the response to galvanic current persisted. After median nerve suture, /

Fig.7.

Fig.7.

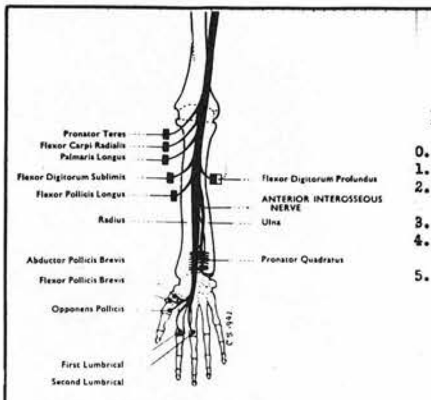


DIAGRAM OF MEDIAN NERVE MUSCLES.

RECORDING OF VOLUNTARY POWER.

0. No contraction.
1. Flicker or trace.
2. Active movement, with gravity eliminated.
3. Active movement against gravity.
4. Activity against gravity and resistance.
5. Normal power.

NAME. H.S. Median nerve suture.

MEDIAN MUSCLES. DATE	6/3/43			11/12/43			25/3/44			24/6/44			7/10/44		
RESPONSE	G.	F.	V.	G.	F.	V.	G.	F.	V.	G.	F.	V.	G.	F.	V.
Pronator	+	−	0		−	1		+	2?		+	4		+	5
Flex. carp. rad.	+	−	0		−	1		+	2		+	4		+	5
Flex. dig. sub.	+	−	0		−	0		−	1		+	4		+	5
Flex. poll. long.	+	−	0		−	0		−	1		+	3		+	3
Fl. dig. prof; 11 & 111.	+	−	0		−	0		−	0		±	3		+	3
Abd. poll. brev.	+	−	0		−	0		−	0		−	1		+	2
Opp. poll; fl. poll. brev	+	−	0		−	0		−	0		−	1		?	2
Lumb. 1 & 11.	+	−	0		−	0		−	0		−	?		?	2
Recorded by -	O.T.R.			O.T.R.			O.T.R.			O.T.R.			O.T.R.		

THE CLINICAL RECORDING OF MUSCULAR ACTIVITY AND POWER.

suture, voluntary response as a mere flicker reappeared in the most proximal muscles nine months after operation, extended gradually to the more distal muscles, and increased in power in the proximal. Nineteen months after nerve repair the most proximal muscles are charted as being normal in power, and the small hand muscles operating voluntarily, though weak. In this case, as in many, voluntary activity is detectable shortly before faradic excitability returns.

Seddon, Medawar and Smith (1943) have discussed in detail the use of such charting methods in estimating rate of regeneration in peripheral nerves in man; for accurate work they found difficulty, as we have, in securing sufficiently frequent observations on a given patient during the long period of recovery; but for practical purposes, once recovery has been definitely detected, examination at monthly or even three-monthly intervals is enough, and the muscle response chart shows at once whether regeneration is proceeding satisfactorily.

4.3. The Electrical Excitation of Nerve and Muscle.

4.3.1. Introduction.

The main clinical part of this thesis consists of the description and development of methods of artificial excitation of human muscle. The investigation was originally undertaken to test out existing methods and, if possible, to develop new ones which would yield the maximum amount of valuable information together with the minimum complexity in routine operation. Although the scope of the investigation has broadened greatly with the appreciation of new problems and possibilities, the important question of the diagnostic value of electrical stimulation has been the primary one followed up. A great number of techniques have been described for the percutaneous stimulation of nerve and muscle in man. Electric currents have the advantages over other possible excitor agents that they are clean, harmless, and transient, and that their action on the physiological nerve-muscle preparation has been worked out in almost tedious detail for many years past. The configuration of electric currents can be altered in three ways, separately or together, and the efficiency of such currents as tissue depolarizers depends /

depends on several factors. Currents may vary in intensity or amount; in length of application or duration; and in their temporal configuration, i.e. they may be applied suddenly or gradually, or may reverse in direction during their application. Any stimulus applied to a nerve or a muscle provokes that nerve or muscle, if it does so at all, by depolarizing the surface layer of the excitable tissue; whereby a propagated disturbance, the "nerve impulse" in axons, or the contraction of muscle fibre, arises at that region, passes over the rest of the cell concerned and dies away as the normal polarization of the layer is restored. It is not intended here to elaborate the physico-chemical mechanism as it is at present known; I have recently given a simplified review of the present knowledge in a Honyman Gillespie Lecture (Ritchie, 1945). The important basic fact from the point of view of stimulation is that this depolarization process requires certain characteristics from the applied stimulus; these can be measured, externally, by electrical means, and the properties of the excitable tissue assessed on a basis of the adequate stimulus. It is this sort of assessment of tissue excitability which is fundamental to all diagnostic electrical methods, and the variety of techniques to be /

be described are concerned mainly with different forms of applied stimuli and their utility from the point of view of detecting excitability changes.

The first man to adopt electrical methods for stimulation of human muscle was Duchenne of Boulogne (1806-1875), who in 1855 published a book on local application of electric currents to man in which the distinction between galvanic and faradic currents is drawn, and the use of electrical stimulation to prevent atrophy described. In 1868 Erb described the galvanic-faradic test in its present form, and produced charts of the "motor points" of human muscles which are in use today. Hoorweg (1892) gave formal physiological expression to this test by appreciating that the duration of a current is a factor of like importance to that current's intensity or volume; Du Bois-Reymond having pointed out long before (1845; 1862) that rate of change of current was an important factor.

All the diagnostic methods to be described under the heading of stimulation make use of these three fundamentals, together or separately - the volume of current, its temporal duration, and its rate of application are all factors which affect the efficiency of the electric current as a depolarizing, and /

and thus exciting, agent.

Our original intention was to make simultaneous measurements on the same patient by several techniques, and this was done in the early stages of the investigation; but it became apparent, on systematic comparison, that one method in particular had especial merits in simplicity and yield of information, and the greater part of the work has been carried out with that method alone. But we shall proceed to describe and compare them all, with reference to their shortcomings and difficulties.

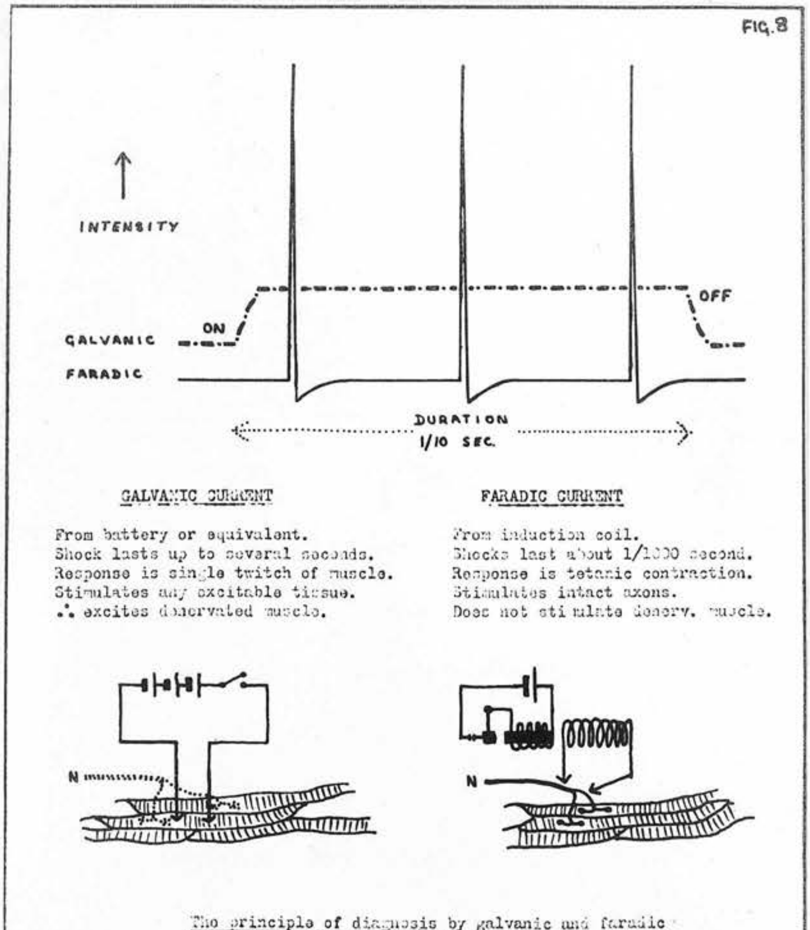
4.3.2. The Galvanic-Faradic Test of Denervation.

Electro diagnosis of neuro-muscular damage by means of the galvanic and faradic currents was introduced by Erb in 1868, and is still the standard adjunct to direct clinical detection of paralysis. The test involves application to a suspected muscle of (a) direct or galvanic current stopped and started at intervals of a second or more and (b) the short intense shocks from the secondary winding of an induction coil. The condition of the muscle is interpreted in terms of its response to these currents. Muscle, whether innervated or not, responds by contraction to an application of direct current, if sufficiently strong; normal innervated muscle, with intact nerve endings responds also to faradic current; denervated muscle cannot be made to contract by faradic shocks. "Response to faradism" has therefore come to imply in the clinic that the muscle so labelled has an intact motor nerve supply. In general, this statement is true, and the galvanic-faradic test has the important advantages of being well understood by most persons who have to deal with nerve injury cases, and of being carried out with instruments which are familiar, robust, and involve no calculations.

Healthy nervous tissue, specialized for easy and rapid depolarization, can be "triggered off" by /

by the induction coil shocks at a tolerable intensity, and hence normal innervated muscle can be caused to contract by faradic excitation of the nerve axon elements in it. Denervated muscle, after a few days of nerve degeneration, possesses no excitable axon elements, and is itself as muscle a less readily depolarizable tissue; but application of the long-lasting galvanic current can, if adequately applied, directly depolarize the muscle fibres and initiate contraction. As Erb appreciated seventy years ago, there may be a final stage of damage or disease where no contractile elements persist in a "muscle", as after long fixation or ischaemia, and in such conditions no current, galvanic or faradic (or any other agent) can excite response. The faradic current is ordinarily described (Cumberbatch, 1941; Kruzen, 1941) as consisting of sudden spikes of current lasting about one-thousandth of a second and being repeated as rapidly as the trembler mechanism of the coil permits, usually at such a rate (25-50 per second) that neuromuscular response is tetanic. Galvanic current as ordinarily used consists of direct current from a suitable source of variable voltage administered in shocks by a metronome or hand-key and lasting at least one-tenth of a second and often several seconds. Fig. 8 illustrates these /

Fig. 8.



The principle of diagnosis by galvanic and faradic stimulation of normal and denervated muscle.

these currents approximately to scale, with their effects. The shocks are applied by means of saline-padded electrodes to the muscle concerned; we shall consider the effect of size and position of electrodes in a later section.

Although the galvanic-faradic test enjoys a wide reputation, it is nevertheless an out-of-date and primitive method, and, as all clinicians know, is liable in practice to gross misinterpretation. It is satisfactory as a confirmation of denervation or innervation in cases where the diagnosis is clinically simple, but is far from reliable in the really dubious instances where it may be needed to take the place of direct clinical evidence. The main defects are as follows. Neither galvanic nor faradic current are readily expressed in quantitative figures; although it is possible to measure galvanic current, it is not possible to measure faradism in any reliable way. Moreover, the erratic action and lack of standardization of faradic coils, not only from one coil to another, but from one occasion to another of the same coil, make any quantitative assessment futile. In Part II of this thesis we shall present cathode-ray oscillograms to prove this point, but all workers with nerve injuries have encountered anomalies where denervated /

denervated muscle has been excitable to faradism (as it may be with a powerful coil and an anaesthetic skin area beneath the electrodes) and where obviously normal muscle has been recorded as "no faradic response" (as it in turn may be with an inefficient coil and a low skin resistance). Such anomalies are not as a rule more than misleading, but the galvanic/faradic test has a further serious drawback in its diagnostic use. Because it is impossible to calibrate, no precise record can be kept of a given muscle's excitability on successive examinations, and therefore the finer gradations either of retrogression or recovery cannot be detected. Finally, muscle testing by galvanic and faradic current is uncomfortable for the subject, and can often not be pushed to the point of decision; "faradic response" is very often missed because of the patient's intolerance of adequate amounts of current.

Muscle which is found to be inexcitable to a particular faradic coil we have frequently shown to respond to the shocks from another instrument which happened, through superior design or adjustment, to be delivering longer and stronger pulses of current, and it is common experience that physiotherapists prefer to use a particular instrument which they have found /

found by trial to be a "good" coil, i.e. an effective one. A report of inexcitability to faradism must therefore be accepted with due allowance for the individual operator and their methods.

Galvanic current, by reason of its relatively long duration, is always uncomfortable to the patient, for it excites all sensory end-organs in the skin very readily, including the pain fibre twigs. Lack of galvanic response, implying entire absence of contractile elements in the muscle concerned, should be accepted as absolute only if performed under anaesthesia, and with a known amount of current passing. This point will be discussed in a later section. At the same time, galvanic current as commonly used diagnostically is unnecessarily brutal. The usual length of pulse used in testing is of the order of one second; there is in fact no need to use more than one-tenth of a second's flow of current to estimate galvanic response, as we shall show later. Many commercial testing sets producing galvanic current from alternating current mains have an alternating ripple super-imposed on the direct galvanic current, which is uncomfortable, and quite unnecessary. Many keying arrangements are such as to allow sparking and erratic contact at the make and break, and any /

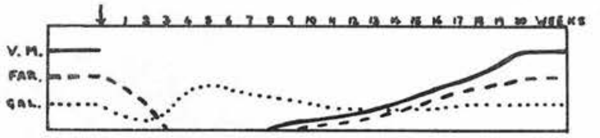
any such irregularities lead to discomfort. We shall later describe a new instrument which has overcome these defects, and which has proved very satisfactory in use.

Moreover, the faradic current is an unsuitable one with which to detect early signs of regeneration. Apart from the fact that it cannot be estimated in reproducible units, the faradic current does not appear to be an efficient stimulus for newly innervated muscle. Most of the modern authorities in describing the Reaction of Degeneration test agree that in a recovering lesion voluntary movement appears a short time before faradic response in the same muscle (Kruzen, 1941; Kovacs, 1942), and this point is brought out in Fig. 9, which is redrawn from a French translation of Erb's original work. Fig. 9 represents Erb's findings of seventy years ago; they correspond exactly with the modern teaching. Erb's diagrams are not intended to be to scale, but rather to represent the increase and decrease of excitability in a simple way.

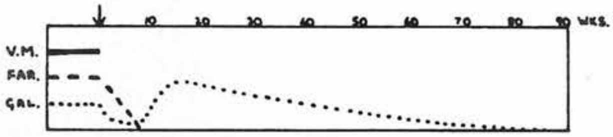
Summarizing, the galvanic-faradic test for the Reaction of Degeneration has the merits of antiquity, simplicity and wide appreciation, and on the whole gives satisfactory clinical results. It is not, /

Fig.9.

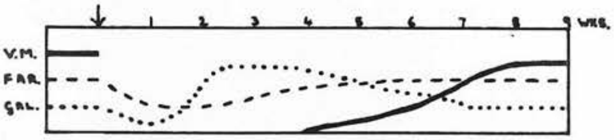
FIG.9.



Paralysis and recovery from nerve damage and degeneration. Faradic response absent for five weeks; reappears two weeks after first trace of voluntary movement. Galvanic response never absent; increased in denervated interval.



Incurable paralysis with permanent loss of motion - cause not stated. Faradic response lost early. Galvanic response increased for a time after denervation, and then gradually disappears as muscle elements replaced by fibrous tissue.



Partial degenerative reaction. Both faradic and galvanic responses present; faradic depressed. Denotes conduction lesion of nerve without Wallerian degeneration.

<u>The galvanic and faradic reactions in various nerve injuries.</u>

<u>Redrawn from Erb's "Traité d'électrotherapie", 1869.</u>

not, however, capable of expression in a quantitative way, is not of value in prognosis of recovery directly, and is an uncomfortable procedure for the subject.

4.3.2. The Condenser Discharge Test.

In 1914 Cluzet, as a result of some years of animal experiment, put forward the suggestion that electrodiagnosis of muscle condition might be carried out in man by means of condenser discharges. An electrical condenser charged from a source of E.M.F. and allowed to discharge through a resistance does so in a calculable manner and in a time depending upon the capacity of the condenser and the value of the resistance. Thus by using a number of condensers of different capacities and discharging them through the electrodes and intervening tissue, one may apply shocks of constant initial intensity but varying duration.

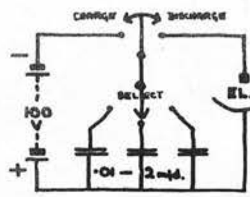
Cluzet's original method was not employed to any extent in practice, but modifications of his technique due to Lewis Jones (1915) and to Hirsh (1920) were used in peripheral nerve injury centres during and after the 1914-18 War. Accounts of the principle and apparatus are to be found in most of the electro-therapy texts at the present day, but very little quantitative data has been published on the results; Worster-Drought (1920) gives a reasonably detailed account. The Lewis Jones Condenser Test Set officially supplied to certain American Army units /

units in 1917 consisted of a bank of twelve condensers, ranging from 0·01 mfd. to 2 mfd. (a range of 200: 1); each of these condensers, selected by a switch, could be charged to a standard potential of 100 volts, and discharged by a hand key through electrodes and patient. The standard electrodes consisted of one large indifferent electrode plate, and a small half-inch diameter active testing electrode. It was said (Worster-Drought, 1920; Cumberbatch, 1933; Kovacs, 1942) that normal muscles responded to the discharge of condensers from 0·01 - 0·1 mfd; partially degenerated muscles to those between 0·1 and 1 mfd; and full denervated muscles only to capacities exceeding 1 mfd: in all cases the initial charge being to 100 volts. No clinical records are given in confirmation of these claims.

In view of the simplicity and widely-published accounts of the condenser set test we thought it desirable to carry out a clinical control. The mathematical principles of condenser testing are shown in Fig. 10. A charged condenser, removed from its source of E.M.F., and discharged through a resistance, will deliver up its charge according to an exponential law; if the capacity be C microfarads, and the resistance R megohms, after a lapse of time RC seconds 37% of /

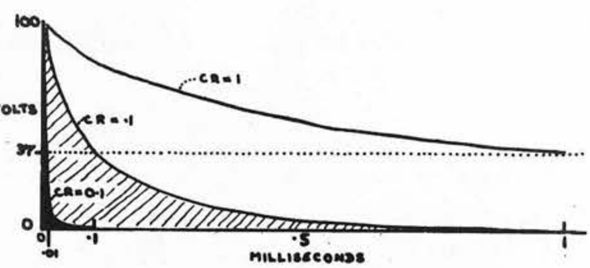
Fig.10.

FIG. 10.



Normal muscles respond	0.01 - 0.1
Partly degen.m's	0.1 - 1.0
Fully degen. m's	over 1 mfd.

The principles of condenser discharge testing.



The nature of the condenser discharge shocks; scale drawing.
A condenser of capacity C microfarads discharged through a resistance of R megohms takes RC seconds to fall to 37% of its initial voltage. The diagram represents the wave-forms of condensers of 0.01, 0.1 and 1 mfd. discharged through a resistance of 1000 ohms, which is that given by Lewis Jones for muscle testing with one small half-inch electrode and one large indifferent electrode.

of the charge will remain; after time 2 RC seconds 13%, and after 3 RC seconds 5% only of the original charge will be present. Theoretically the condenser will require infinite time to discharge completely. In Fig. 10 we show to scale the discharges theoretically expected by Lewis Jones; he assumed, and the figure has been repeated in later texts, that the resistance of the tissues was fairly constant at 1000 ohms using the electrodes already mentioned. On this assumption the RC values of his condenser bank (that is, the time for the electrode voltage to fall to 37, having started at 100) ranged from 0·01-2 milliseconds, as drawn.

Fig. 11 gives the results of two sets of clinical records obtained by the exact technique specified by Worster-Drought (1920) for condenser testing. In the upper graph we give the variation in capacity for threshold stimulation of the same muscle, in the same patient, from day to day over a period of three weeks. To make the record more valuable, we selected a patient with a known denervation at a high level, and the graph therefore records the variability of the method both for normal and for denervated muscle. It will be noticed that the results are very inconstant from one examination to another, /

another, and that even in a single individual, there is no decisive separation of denervation from normal. The range of variability is 13: 1 for normal muscle; 4: 1 for denervated muscle.

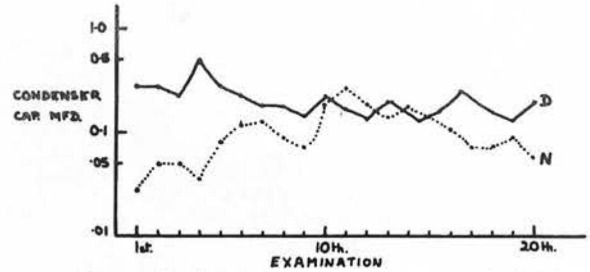
The lower graph of Fig. 11 represents a series of measurements of condenser thresholds taken on a large number of patients. The patients are selected in two groups, normal and denervated, and the condenser capacities plotted for each. No attempt was made to group corresponding muscles together, so that each group represents a composite of various hand and arm muscles; but for each denervated muscle that was recorded, the normal contralateral on the same patient was measured as control, so that the groups are not biassed one against the other. It will be seen at once that the overlap between the groups is very considerable, and that response to condenser capacities around 0·1 mfd. may be given either by normal or denervated muscle. As already explained, this is not so likely to be found in any one patient, but renders it impossible to compare records from one patient to another. Those figures are taken from a series of patients over 150 in number.

We conclude that the condenser test does

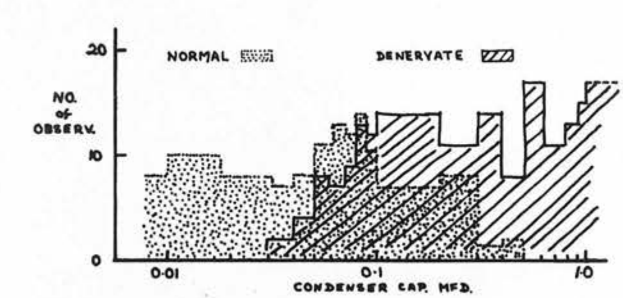
not /

Fig.11.

Fig.11.



The records of condenser testing the same muscle at intervals. Minimum capacity needed for excitation at 100 volts of First Dorsal Interosseous M.s on the same patient. Successive examinations at daily intervals. N = normal muscle; gives range 0.03 - 0.4 mfd. D = denervated m.; gives range 0.15 - 0.5 mfd.



The records of denervate and normal muscles from assorted patients, as given by condenser test. 120 normal muscles fell into the dotted groups; 163 denervated muscles into the lined area. Condensers of about 0.1 mfd. stimulate denervated muscle as often as they do normal.

not give reliable quantitative information as to muscle denervation; either as distinguishing normal muscles from denervated, or as following recovery in a single patient. We have not therefore continued condenser testing after the experimental series presented.

It is worth while enquiring briefly into the reasons for the variability of the test, as they formed a basis for the design of a more satisfactory test to be described in detail later. In the first place, the assumption of 1000 ohms as inter-electrode resistance is quite wrong. We have already presented evidence from a series of 275 cases that normal (and denervated) palmar skin resistance between electrodes of approximately the same size as those prescribed by Lewis Jones is most commonly between 9000 and 12,000 ohms, and tends towards the higher limit over areas other than the palm. It is true that Kovacs (1942) says "1000 ohms represents the resistance to the short condenser discharges" implying that resistance to a brief shock is lower than to a steady current measurement; but we shall later present evidence that even transient resistances of the order of 1000 ohms are very uncommon. In the second place, as we shall show later, the form of condenser discharge through living tissue does not follow /

follow the theoretical exponential law, because in fact the tissues cannot be regarded as a pure resistance. This can only be proved by cathode-ray oscillograph examination, and was not known to Lewis Jones or to Worster-Drought. Thirdly, a great deal of the erratic behaviour of the test is due to mechanical causes; the peak instantaneous current at the moment of closing the key to initiate the stimulus is of the order of 100 milliamps, and causes a very considerable spark at the key contacts. Oscillographic observation of the discharges shows that, in fact, no two are identical, being variously distorted and initiated according to the accidents of the key contact surfaces. It is clinically very obvious that with the pre-determined threshold capacity in circuit, and the electrodes held over the same spot on the muscle, several successive depressions of the key may or may not elicit contraction - in other words, the threshold, under the very best circumstances, is not precisely determinable.

These findings have been of great value in development of new apparatus.

4.3.4. Chronaxie Measurement.

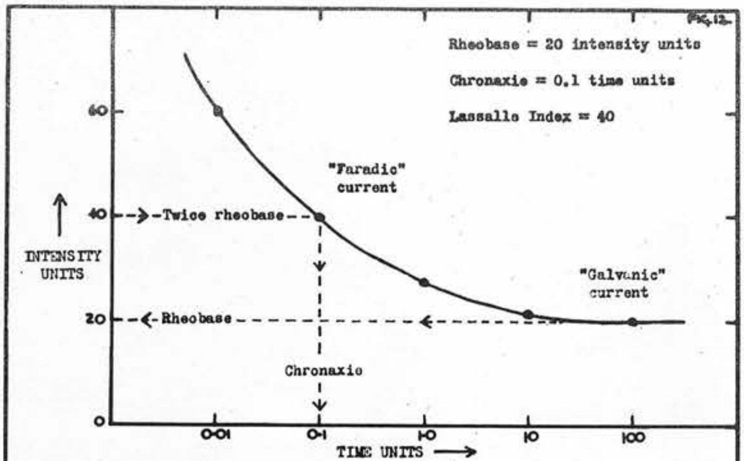
In the years following 1906 Lapicque introduced the conception of the excitability index "chronaxie" into neuro-physiology, and it has been very widely used and discussed in laboratory work since that date. The basic principle underlying the use of chronaxie as an index is to specify excitability in terms of a temporal measurement and thereby to avoid many of the factors which confuse a measurement of electrical intensity.

A stimulus which lasts for a long period will bring about depolarization of excitable tissue when applied at a relatively low intensity; the lowest effective intensity will in fact be that of an indefinitely persistent stimulus, and this lowest effective intensity is named the "rheobase". No lesser intensity will produce response, unless the circumstances of the experiment alter; and in practice we find that indefinite duration is not strictly necessary. The so-called "temps utile", or effective duration of the rheobase stimulus is of the order of one-tenth of a second for mammalian skeletal muscle, and prolongation of the stimulus beyond that does not result in a lowering of the threshold intensity. But if the duration of the stimulus be reduced /

reduced below the "temps utile", then the rheobase intensity is no longer adequate to produce depolarization, and the threshold stimulus becomes one of short duration, and high intensity.

As we have seen, this effect is the basis of the galvanic/faradic test, and can be completely described in terms of the relationship between intensity and duration of threshold stimuli for the same tissue under the same conditions (Fig. 12). We shall consider the value of such measurements in a later section. Chronaxie is defined as being that duration of stimulus of twice rheobasic intensity which is required for threshold excitation, and is therefore specified in units of time, and gives no account of the actual rheobase value. Chronaxie measurement has this great advantage over the excitability tests already described, that it obviates to a great extent variations in experimental conditions. It is obvious that, from time to time, the amount of tissue resistance in series with an excitable fraction such as a nerve will vary, and the amount of fluid resistance in shunt with the nerve will also vary unpredictably, so that rheobase measurements, which are in electrical units of voltage or current, will represent the current through all these elements in combination, and not the current through the excitable /

Fig.12.



THE INTENSITY-TIME GRAPH OF TISSUE EXCITATION.

The effectiveness of a stimulus depends on its intensity and on its duration; the shorter the stimulus, the more intense must it be to produce response. Three points on the complete curve are defined and named:-

RHEOBASE is the minimum effective intensity for a stimulus of indefinite duration; below this value no stimulus, however protracted, will excite.

CHRONAXIE is that duration required of an effective stimulus of value twice rheobase. Although defined with respect to the rheobase, the chronaxie figure is independent of the numerical value of the rheobase.

LASSALLE'S INDEX is defined as the square of the rheobase multiplied by the chronaxie, and takes into account the absolute values of both.

Galvanic and Faradic currents are not measured in actual figures; they correspond to long and short stimuli respectively.

excitable tissue itself. In other words, a tissue which has in fact constant excitability characteristics in itself may, when tested by externally applied stimuli, show considerable variations in rheobase due to alterations in surrounding media.

The chronaxie measurement, by doubling the rheobase regardless of actual value, and considering the duration of the stimulus at the double value as the excitability index, disposes in part of this difficulty. If the external circumstances vary, the rheobase will alter, and therefore its double value also; but the duration of the double-rheobase stimulus will not alter to the same extent, if at all, and is found to be a reproducible figure from one experiment to another.

The validity of chronaxie as a single measure of tissue excitability under laboratory conditions has given rise to a great deal of controversy which does not concern us in this discussion of its practical value in muscle-testing, and the recent views of the principal workers in this field have been expressed by Lapicque (1935) and Rushton (1935), while a critical review of the physiological aspects of chronaxie has been given by Davis and Forbes (1936).

From /

From the point of view of clinical value the classical monograph of Bourguignon (1923) entitled "Chronaxie sur l'Homme" contains a very full account of the technique and difficulties of the method as applied to man. It is evident that one of the technical problems is to produce stimuli of known short duration whereby chronaxie can be assessed in terms of time. A number of ingenious instruments have been devised for the mechanical production of short duration shocks, and are described by Bourguignon as being unsuitable for clinical use. Weiss (1901) described a pistol whose bullet severed two wires placed at a variable distance apart; Keith Lucas (1906) a heavily-weighted pendulum which touched two contacts at the bottom of its arc; Strohl (1920) a falling-weight device of rather similar design; and Sachs and Malone (1922) a rotating disc with peripheral projections. None of these devices are practicable, for apart from the difficulty of contact irregularity it must be remembered that in order to produce a shock lasting 0.1 millisecond with contacts separated by as little as one millimetre, a peripheral speed of ten metres per second is required of the breaker device. Bourguignon accordingly abandoned the mechanical principle, and produced his time-calibrated shocks by /

by means of condenser discharges. We have already seen that a known size of condenser discharges through a known resistance in a calculable definite time and manner, and Bourguignon devised a shunt and series circuit for the electrodes which presented to the condenser an almost constant discharge resistance regardless of variations in subjects' resistance. It is important to note that this ballast circuit was intended to stabilize the time of condenser discharge, and not the voltage or current through the patient; the rheobase was determined with the electrodes in position, doubled, and condensers charged to the double potential discharged through the electrode circuit without any movement of the electrodes. It is also important to realise that the configuration of the discharge corresponded to the exponential voltage decay already figured.

This condenser-discharge chronaxie technique enabled Bourguignon to obtain reproducible figures for excitability of human muscles, and he describes in detail the causes of error and inaccuracy in routine use. He found a very marked and constant difference between the chronaxie figures of normal and of denervated muscle; chronaxie for normal limb muscles ranged from 0.15 milliseconds to 0.8 milliseconds, the /

the extensor muscles tending to possess the longer figures. Denervated muscle, by contrast, gave chronaxie values ranging from 10 to 60 milliseconds, and could thus readily be distinguished by this index alone. As a result of the examination of a relatively small series of nerve injury cases followed from complete nerve section to recovery, Bourguignon came to the conclusion that intermediate chronaxie figures during the stages of degeneration or re-innervation are not found in practice, and that the chronaxie rather suddenly changes from the normal value to the degenerated figure. This rendered the method of no great value as regards prognosis of recovery in nerve lesions. A similar conclusion has been expressed by Turrell (1929), Cumberbatch (1939) and Bauwens (1941), although none of these workers has published precise figures for specific cases, and it is a striking feature of the subject in general that despite numerous opinions and claims for chronaxie as a diagnostic measure, very few case records have been published. Bauwens (1941), in a very interesting theoretical discussion, points out that chronaxie measurement fails to give a quantitative account of the condition of muscles in which healthy and denervated motor units co-exist. He believes that this is so because /

because in chronaximetry no account is taken of the absolute value of the rheobase, so that however few normal motor units there may be in a partially innervated muscle they will provide the normal chronaxie figure if they are sufficient in number to produce a detectable response; if the few present are not strong enough, then the chronaxie will revert, without intermediate values, to the high figure characteristic of the bulk of denervated fibres in the muscle. In order to obtain stimulation of a few normal units situated in a bulk of denervated muscle fibres, a high rheobase intensity may be required, but this is not recorded in chronaximetry.

The bulk of opinion, therefore, is that intermediate chronaxie values do not occur in partial muscle denervation, and that chronaximetry is of little value in the assessment of such lesions.

We shall, however, show in a later section, that this opinion is only valid as applied to one particular technique of chronaxie determination, and that where chronaxie is measured by precision instruments and a favourable configuration of stimulus, intermediate values do in fact occur, and are of value in prognosis. It does not appear to have been realised that the actual chronaxie figure depends to a great /

great extent on the technique of determination, and we believe, as a result of a series of many thousands of measurements, that many of the discrepancies and arguments which have arisen over chronaxie are in fact due to non-recognition of this fact. The chronaxie figures from condenser discharges, and those from rectangular waves of current, or of voltage, are different, and differ in practical value.

Bourguignon, in evaluating exponential waveforms in terms of rectangular co-ordinates, arrived at an empirical formula for expressing condenser discharges; from experiments with Weiss's pistol and his own condenser lay-out, he concluded that a condenser discharge of time constant RC (see section 4.3.3) was equivalent to a rectangular application of 0.37 x RC seconds. (It is important here not to confuse this conversion constant of 0.37 with the similar figure mathematically involved in consideration of exponential decay. RC seconds, the time-constant of a condenser and resistance combination, is the time for the charge on that condenser to fall to 0.37 of its initial value. This RC value, multiplied by 0.37, is, according to Bourguignon, the biologically equivalent stimulus duration of rectangular shape).

We shall show that this is, in practice,

not /

not borne out, and that had Bourguignon conducted his experiments with the pistol device instead of with condenser discharges, he might have detected intermediate chronaxie values in recovering nerve lesions. As, however, chronaxie determinations have been incidental to a more extensive measurement of muscle excitability, we shall present the results in a separate section later on.

The pistol technique was of course quite impracticable for routine use, and it is only within the last few years that we have been able to produce rectangular pulses of known short duration with sufficient accuracy and convenience for muscle testing. Even with such rectangular pulses, the properties of living tissue so distort and modify the stimuli, that widely different chronaxie figures can be obtained from the same tissue by different methods of stimulus application, and this has only very recently been appreciated (Ritchie, 1944; Walter and Ritchie, 1945). We shall discuss the problem in detail later on.

4.3.5. The Intensity-Duration Relationship.

We have already seen, in considering chronaxie, that there is a definite relationship between the duration of a stimulating shock and its intensity. At one end of the scale we have the rheobasic stimulus, of long duration and minimal intensity; at the other end a very brief stimulus, which to produce response must be of great intensity. These two features, therefore, can be represented relative to one another by an "Intensity-Duration" graph, as theoretically drawn in Fig. 12. The chronaxie index is now seen to be merely one defined point on this curve expressing excitability, and the value of recording the complete cruve as compared with isolated chronaxie measurements has been emphasized by many workers (Rushton, 1935; Tower, 1939; Bauwens, 1941).

The first requisite being some method of obtaining stimuli variable, and measurable, both in respect of intensity and of duration, there are several technical approaches, and all do not give the same results. The simplest method is to employ a set of different sized condensers, and charge them to a variable but known voltage. Technically this is a simple matter, and the resulting records are known as "Voltage-capacity" curves. It is most important /

important in considering this work to adhere to a rigid terminology to avoid confusion; "intensity-duration", or "strength-duration" is used to express the theoretical concept, but is not adequate for actual curves obtained in practice.

Voltage-capacity curves have been published for re-innervating human muscle by Marble, Hamlin and Watkins (1942), but for a few isolated cases only. Such records suffer from two very serious drawbacks, and have no merit beyond simplicity. In the first place, the temporal configuration of the stimulus is exponential; and, secondly, the time scale, given in terms of condenser capacity, is not absolute, and depends on the resistance of the tissues of the particular patient at the particular time of examination. This means that such records are not necessarily comparable from one time to another, or from one patient to another, and while voltage-capacity measurements are interesting in exposed-nerve laboratory preparations, they are not valid for clinical testing.

A number of workers have devised apparatus for delivering rectangular schocks of varying duration. These include the mechanical devices referred to in the section on chronaxie, and a number of more recent electronic instruments which produce the shocks /

shocks without mechanical breakers by means of thermionic valves. These will be discussed in detail in a later section of this thesis. There is however very little published work of actual clinical experiment, and almost all of these designers have been ignorant of the basic properties of living tissues. It is not difficult to produce rectangular shocks of known duration, and the duration can be specified in true time units. The duration range of stimuli needed for human intensity-duration curves is very great, covering some five decades, from very short stimuli of a few microseconds' duration to an upper limit of about one tenth of a second. The durations are therefore conveniently specified in millisecond units. Stimuli of longer duration than 100 milliseconds are unnecessary for human muscle testing, as the rheobase intensity is reached at that value, and longer stimuli do not result in a lower intensity threshold.

The problem of intensity measurement is very much more complex. Apart from technical difficulties of measuring very short electrical pulses (which can be overcome) the properties of tissues with respect to electric current passage are of very great significance. In the ordinary way, intensity can be specified either in terms of volts pressure, or /

or current density, and it has been often assumed that the two are equivalent. Volts and current are related by Ohm's Law in simple relationship for an object which is a pure resistance, and can replace one another (in correct proportion) according to the actual value of the resistance. Put in another way, a rectangular shock measured in volts pressure will result in a rectangular current flow, provided that the material traversed is a true and uncomplicated resistance. But, as we shall show, living tissues are not straightforward resistances, and a rectangular pulse of voltage does not give rise to a rectangular current pulse in the deeper layers, nor is the rectangular configuration of a stimulus measured as current maintained across the excitable elements in the muscle or nerve. This very important phenomenon will be described in a separate section. Its significance lies in the fact that intensity-duration curves measured at the instrument as current-duration curves do not correspond with intensity-duration curves measured as voltage-duration curves. The actual figures for each duration (and, therefore, the chronaxies read off such curves) differ by as much as ten times.

It is therefore essential, if rectangular waves are used, to specify the records as "voltage-duration", /

"voltage-duration", or"current-duration" curves, as the case may be, for the two are not interchangeable.

Very few complete clinical records of current-duration curves have been published, though Bauwens (1941; 1943) has devised a very precise method of taking them, and has given several theoretical interpretations of such curves without published experimental evidence.

I have myself recorded some ten thousand voltage-duration curves on various nerve injury subjects, and will present them in due course in this thesis. There is no evidence that voltage-duration curves are superior to current-duration curves in respect of information gained from their study, but there seems little doubt that in practice voltage-duration curves are technically easier to produce, and considerably more comfortable for the patient. The reason why they are more comfortable lies in the tissue distortion of voltage pulses to be described. This conclusion was verified and strengthened by a comparative test of voltage and current instruments by Grey Walter (1944), who further comfirmed the discrepancy in actual numerical values of the two techniques. He suggests, and I agree, that failure to realise the difference in result has been at the root of a great deal /

deal of the controversy regarding anomalous chronaxie values in experimental work.

So recently as 1943 we find Denny stating ". . the patient can be regarded as a purely resistive load . . ." If this incorrect view is adopted, then comparison of intensity-duration curves and chronaxies obtained by various workers using their own methods becomes very misleading and confusing, as similar tissues may yield figures differing by some ten times under apparently identical conditions. It is essential, therefore, to specify the exact technique in every case in which such intensity-duration measurements are made.

The evaluation of intensity-duration curves from one patient to another, and from the same patient at different times, must be done graphically, as no single index figure can account for rheobase level and curvature satisfactorily. We have seen that chronaxie is a defined point on the curve, but does not specify rheobase value; Lassalle (1928) proposed an alternative index, shown on Fig. 12, which was calculated from the formula rheobase squared multiplied by chronaxie, and this Lassalle Index varies both with rheobase and with chronaxie. Although no use appears to have been made hitherto of the Lassalle index /

index, we have found it a more valuable one than chronaxie, and the voltage-duration curves to be presented will include both chronaxie and Lassalle index values with each curve. The expression rheobase squared times chronaxie has the unit dimensions of energy, and not of time, and is a more logical single representation of the curve. It has two drawbacks; firstly that any error in rheobase determination (a measurement which is liable to error) is magnified by squaring, and, secondly that as chronaxie is defined as the duration of shock of twice rheobasic intensity, the steeply curved portion of the curve at very short durations is not taken into account. We have not thought it worth while to pursue calculations towards a further new index, as graphical presentation is by far the best way of examining a family of such intensity-duration curves.

4.3.6. The measurement of "Accommodation".

The previous sections concerned with excitation of nerve and muscle have been concerned with stimuli which are suddenly applied, last for a certain time, and (in the case of rectangular stimuli) are suddenly withdrawn; and we have seen that the excitability of a tissue to this type of stimulus can be completely expressed in terms of an intensity-duration graph. But in addition to intensity and duration of a stimulus there is a further feature which governs its effectiveness, and that is the suddenness or rapidity with which it is applied.

As far back as 1845 Du Bois Reymond remarked that absolute volume of current as such is not a stimulus, but that in order to effect excitation that volume must fluctuate from moment to moment; he maintained that the effectiveness of stimulation was proportional to the magnitude of change of current, or to the rate of its fluctuation. This, and subsequent work by the same author (Du Bois Reymond, 1862) aroused a great deal of interest in rate of change of current as a factor in excitation, and by the close of the nineteenth century a considerable amount of quantitative data on the behaviour of the cold-blooded muscle-nerve preparation had been compiled, /

compiled, notably by the German workers Bernstein (1862), von Kries (1884), Schott (1891) and Gildemeister (1904). The fact was established that the most efficient form of stimulus was that which rose instantaneously to its threshold value (as does the "make" of a current applied through short wires and a good key), and if the rise of current were to be delayed so that it sloped gradually up to its limit, then the threshold peak value at which response occurred was notably higher than in the case of the instantaneous current.

This is merely one experimental presentation of the basic fact of adaptability or accommodation to stimuli which is shown by all tissues in varying degree. Response occurs readily to a rapid change of environment, and less readily if the environmental change be more gradual. This general principle holds not only for nerve and muscle, but for all the sensory end-organs, which exhibit adaptive qualities according to their various functions (Adrian, 1928). The fundamental mechanism is unproven, though on the basis of the semi-permeable membrane conception of axon activity it appears that the tendency of the polarized membrane is to maintain itself in that condition. Gradual attempts at depolarization /

depolarization are therefore nullified to some extent by the natural processes of restoration, so that a greater ultimate external force is necessary to bring about the degree of depolarization needed for response.

Keith Lucas (1907) described this accommodation process in the frog's sciatic nerve in terms of the minimal current gradient required to bring about excitation. He found that if an instantaneous current of strength one unit (that is, a current which rises from zero value to one unit in a few microseconds) was just effective in producing response, an ultimate peak strength of about 50 units might be required after one second, if the current were allowed gradually to reach that value. In other words, during the seconds' gradual application of stimulus, the nerve's threshold increased some 50 times. This current gradient of 0 to 50 units in one second represented the slowest rate of stimulus progression that was effective, and if the gradient were lower than this the adaptive process kept as it were ahead of the stimulus so that excitation never occurred within physiological limits of current strength. This publication attracted a great deal of attention amongst neuro-physiologists, and several workers devised techniques of measurement, notably Laquerriere (1907), Becher /

Becher (1912) and Lapicque and Laugier (1910). Interest in this problem appears to have lapsed during the war years of 1914-18 and thereafter, but, following on the publication of two papers by Blair (1931) and Schriever (1931), a concerted attack on the problem was made from the point of view of theoretical analysis of the effectiveness of graded currents. The more important papers, among many, are by Delherm and Laquerriere (1931), Liberson (1934), Hill (1936) and Solandt (1936; 1937). The subject has been well reviewed in recent monographs by Katz (1939) and Schaefer (1940), but there is no information of practical value in respect of application of these methods to nerve injury diagnosis in man; although Solandt, in 1936, observed that the measurement of accommodation in man could be made by a relatively simple technique, and published some figures for the time-constant of accommodation in the ulnar nerve of thirteen normal subjects.

As far as I can discover the first measurement carried out on denervated human muscle was that made by Bordet in 1907, who at that time noted that denervated muscle had a much lower minimal current gradient than normal muscle, and therefore possessed very poor powers of accommodation. In view of the fact /

fact that this observation has recently been repeated and suggested as a basis for electro-diagnosis of denervation, it is only fair to credit Bordet with the original appreciation of the fact. The use of the so-called "progressive" currents in therapeutic muscle stimulation has been advocated by physio-therapists for many years past. Turrell (1926; 1929), Cumberbatch (1941) and Kruzen (1942), in modern editions of text-books of electrical treatment all make the statement that slowly alternating current (of frequency about one per second) or gradually applied galvanic current has the power of stimulating denervated muscle to the exclusion of normal surrounding muscles. They point out the potential value of this fact in artificial exercising of paralysed muscles without excitation of the more powerful surrounding normals. None of these authorities accounts for or explains the phenomenon, and, in practice, it is made little use of in physiotherapy. It is however quite true, and a valuable adjunct to therapeutic technique, as we shall describe. The very considerable accommodative power of normal human muscle enables it to "evade" excitation by a gradually progressive current, while denervated muscle, poorly accommodative, is stimulated to contraction.

There /

There is another observation of physiological importance which arises from the property of accommodation. When a stimulus of constant and protracted amplitude is applied to a tissue which has power of adaptation, the response of the tissue to the stimulus will gradually decrease, although the stimulus persists at a steady value. This is readily appreciated subjectively in the sensation of touch, for if an object be touched the initial contact is detected at once, but if the pressure and position are maintained steadily the sensation of contact rather rapidly diminishes and disappears. It is well known that muscle or nerve response to a long galvanic shock occurs only at the "make" and at the "break" of the current, with no response occurring during the steady passage of the stimulus. Hoffmann(1910), using Wedensky's (1883) method of detecting human muscle action potentials by means of needles connected to a telephone ear-piece, noticed that normal muscle responds with only a few action potentials to an applied galvanic shock, whereas denervated muscle very commonly shows continuous activity for several seconds. Recently Doupe (1943) has published very beautiful records of this phenomenon using modern appliances, and has shown that denervated muscle has a repetitive response /

response to galvanic stimuli, as judged by its action potentials. Doupe comments on this repetitive response as being due to lack of accommodation, and suggests it as the basis for the well-known sluggish contraction of denervated muscle when stimulated electrically. Similar records for mammalian preparations have been published by Skoglund (1942) and his work represents the latest exposition of the older work on accommodation repeated with modern technique and recording.

There appears no doubt, then, that there is a great difference in the powers of accommodation in normal and in denervated muscle, and some recent attempts have been made to use the differences as a quantitative method of electro-diagnosis. In August 1942 a restricted-circulation progress report from the U.S.A. Medical Research organization noted that Pollock was developing a method of employing progressive currents for diagnosis in cases of peripheral nerve injury. Details were not given beyond the fact that he had found that denervated muscle behaved as an irritable substance without the power of accommodation. Using progressive currents of very long duration (up to sixteen seconds) Pollock found that the minimal current gradient for denervated muscle was of the /

the order of 2 - 10^{o}. As re-innervation occurs, he states that the power of accommodation rather suddenly returns, and the minimal current gradient becomes of the order of 20 - 40^{o}. Up to the present time no complete publication has been made of his findings on human muscle, but Pollock, Golseth, Arieff, Sherman, Schiller and Tigay (1944) have dealt with the results of progressive current stimulation on normal and denervated cat muscle. In this paper they claim that neurotization of denervated muscle is accompanied by a sudden rise in accommodation, and also by a decreased threshold to instantaneous galvanic shocks. While not disputing the general findings, we feel that this work is liable to serious technical criticism. A mechanically operated potentiometer was used to grade the current (described in later technical section) and the skin over the muscle was perforated several times with a needle before the electrodes were applied. Our objections to this are threefold: firstly that currents applied for the several seconds specified by Pollock bring about a great deal of polarization, which may be differential in the various tissue layers (so that although the current may be increasing regularly at the electrodes its distribution may be varying unpredictably in the deeper tissues) and that no account /

account was taken of this; secondly, that response was never checked by action potential recording; and thirdly, that the decreased threshold to galvanic currents is a misleading observation, and does not occur in man. In a large series of cases we have never found the galvanic threshold or rheobase increase on innervation - indeed, the reverse has always been the case. Our opinion is that the discrepancy arises from the technique of skin puncture prior to stimulation. Re-innervation of a muscle implies in nearly every case the appearance of a "motor point" at which current has ready access to the innervated motor units <u>via</u> the nerve fibres. (It is not intended to imply, of course, that the current traverses the nerve fibres, but rather that it has "access" in the sense of being able to excite from a distance). In denervated muscle there can be no such "motor point", as the muscle fibres are directly excited by the current, which is accordingly spread over a relatively large bulk of tissue; but, once innervated motor units have appeared, these can be excited simultaneously by a relatively smaller amount of current so applied as to excite the group of nerve fibres. Puncture of the overlying skin, without adequate search for a "motor point" of maximum sensitivity, will therefore tend to mask /

mask the decrease in threshold which we find invariably accompanies neurotization. We shall show that <u>avoidance</u> of skin puncture is an important practical consideration in muscle testing by quantitative methods.

A recent publication by Kugelberg (1944) gives an excellent review of the measurement of accommodation in man, with very advanced technique (details in technical section later), but has not dealt with the problem of denervated muscle. Kugelberg gives details of a large series of measurements under various conditions of circulatory disturbance, with statistical evidence of the error of his method and the normal range of variation, and the paper is by far the most practical and precise that has yet appeared on this subject. We very much regret that clinical circumstances did not permit of his examining nerve injury cases.

We have case records from nerve injury cases where the accommodation figures were measured by a modification of Skoglund's (1942) technique, but we found the method inferior, from the practical routine point of view, to strength-duration measurements. The most unsatisfactory feature of the method is the uncertainty of response detection, which may occur at any /

any time during the gradual rise of the current. In order to figure the results, it is necessary to know the time of rise, and the peak current value reached, and these can only be registered simultaneously with response by very elaborate means. Moreover, in the cases where motor response does not appear, as often in normal muscle with a slowly rising current, the current may ultimately rise to a very high value and cause considerable sensory distress or burning of the skin. The measurement of the accommodation constant for a given muscle may take half-an-hour, or more, and the amount of material examined correspondingly limited. There is no doubt that many of these difficulties could be overcome by simultaneous recording of action potentials as index of response, but such elaboration would remove the method from the realms of a routine clinical adjunct, which latter was one of our chief aims.

We did not find intermediate values of accommodation during degeneration or re-innervation, and although our case numbers were too small to warrant conclusions about this matter, we abandoned accommodation measurements on hearing that they were being systematically examined in America. No clinical report has so far been published in any detail /

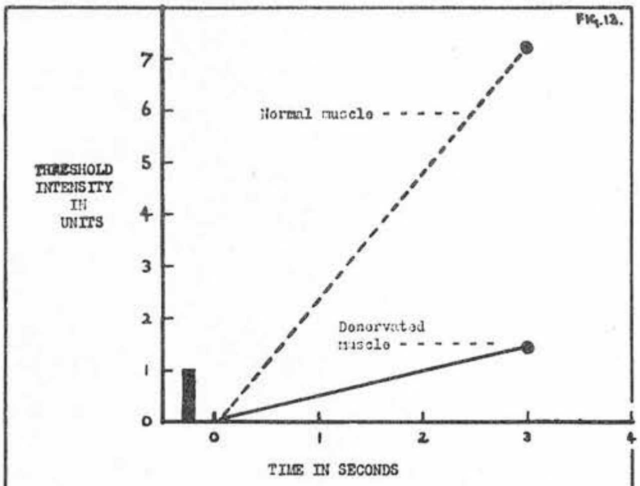
detail, so far as we are aware.

Our clinical report consists of measurements on 14 cases of known total denervation, the cases being selected a few days after surgical division of the motor nerve (prior to suture) and therefore tested at a period too early for any motor regeneration to have taken place. The rheobase to rectangular voltage shocks of 100 milliseconds duration was first measured for each muscle and this figure (which varied somewhat with the particular muscle) was taken as one unit - the threshold unit for instantaneously applied shocks. A 100 millisecond shock is found in practice to be as long as need be used for rheobase determination, even in denervated muscle. To avoid the complexities of measuring both time and peak voltage reached, a fixed time increase of three seconds was chosen. The apparatus, which is described later, was an electronic device whose output was not affected by resistance variations in the load consisting of electrodes and patient, hence non-polarizable electrodes are unnecessary. [This compensating feature, while valuable, does not of course compensate for variation in current distribution in the patient's tissues due to differential polarization in tissue layers.]

The /

The results are presented in Fig. 13. On these 14 cases, 39 individual muscles were examined, and, as controls, the corresponding normal contralateral muscles. The variation from one muscle to another muscle on the same patient is of the order of 5-10%, and from one muscle to the same muscle on another patient about the same. These variation figures substantially agree with the fuller observations of Kugelberg (1944) published subsequently to our determinations. We have plotted the mean of all the observations only, and find that the difference in accommodation between normal and denervated muscle is of the order of six or seven times, far beyond the extreme limits of individual or instrumental variation. Denervated muscle is seen to possess very little power of accommodation, and increases its threshold only 1·4 times after three seconds gradual current application. Normal muscle, by this technique, appears to raise its threshold some 7 - 8 times during the same period. Detectable twitch of the muscle concerned was the criterion of response, and each measurement was repeated several times. The measurement is a laborious one, and, in our opinion, not suitable for routine use.

Fig.13.



Stimulus "Accommodation" in normal and denervated muscle.

Mean values from 39 muscles in 14 cases. Threshold to instantaneous stimulus of 100 msec. = 1 unit. Stimulus applied rising gradually for three seconds: normal muscle raises threshold 7.2 times; denervated muscle only 1.4 times. Power of accommodation decreased approximately six times by denervation.

4.3.7. Stimulation by Alternating Current.

The type of stimulus obtained from an induction coil secondary winding may be said to be alternating current in that it possesses components of either polarity (though these may be unequal - Fig. 8), but in modern radio and engineering practice an alternating current is one which obeys a sine law of voltage and current, is symmetrical about the zero axis, and is maintained at a constant amplitude. This type of current is very widely used in the distribution of domestic electric power, the frequency in this country being normally 50 complete sine waves per second. But sinusoidal alternating current may vary in frequency over very wide limits, from a very slow alternation of one wave in several seconds to the very rapid alternations of many millions per second used in radio communication and in medical diathermy.

Hitherto we have been considering the effect of relatively isolated stimuli on muscle and nerve, and have appreciated that the three important variables for effective excitation are intensity, duration, and rate of change, with respect to each single stimulus. In stimulation of living tissue by alternating current, these three variables are all related to the frequency of /

of the current waves, and are interdependent. Before considering the relation of these variables to tissue excitation, there are two important practical points to note about AC stimulation. Firstly, the response of the muscle concerned is tetanic - i.e. a contraction sustained as long as the stimulus is applied - and not the sudden transient twitch produced by a single shock. Secondly, because of the symmetry of the AC waves above and below the zero line, no resultant polarization occurs in the tissues even if the current is applied for some considerable period.

Considering the application of sinusoidal alternating current to excitable tissues with constant amplitude but variable frequency, we see that the important variable factors are (i) the duration of each half-cycle wave, which decreases as the frequency increases, and, (ii), the rate of rise of current for each half-wave, which increases as does the frequency. These two factors, then, operate in opposite senses from the point of view of effective stimulation; a high frequency AC current will have waves of short duration (and thereby will be relatively inefficient) but will necessarily have a rapid rise of current, which makes for effective stimulation. Theoretically, therefore, for any excitable tissue of given excitability /

excitability characteristics, there will be an optimum frequency of alternating current for stimulation, that is, one which will be effective at a lower amplitude than frequencies either higher or lower. Laboratory work has confirmed this, for Hill, Katz and Solandt (1936) found that AC of frequency 200 cycles per second was optimal for excitation of the exposed sciatic nerve of the frog. At frequencies above and below this the threshold intensity rises. Katz (1939), in a monograph dealing with excitation of nerve from the laboratory and theoretical aspects, points out that this optimal frequency effect is to be expected from the facts that nerve is not excited by current if the current either does not last long enough, or does not alter rapidly enough; as these two factors operate in opposing senses, there will be a certain frequency at which a balance is struck, so to speak, between the two opposing components. Katz further emphasizes that there is no need to postulate a "resonant" mechanism (Coppee, 1936) to account for this optimum frequency phenomenon, for it can be observed with any form of current which varies its duration and rate of rise simultaneously but in opposite senses; it has been demonstrated for frog preparations by Fabre (1927) using isolated triangular waves of current.

Up /

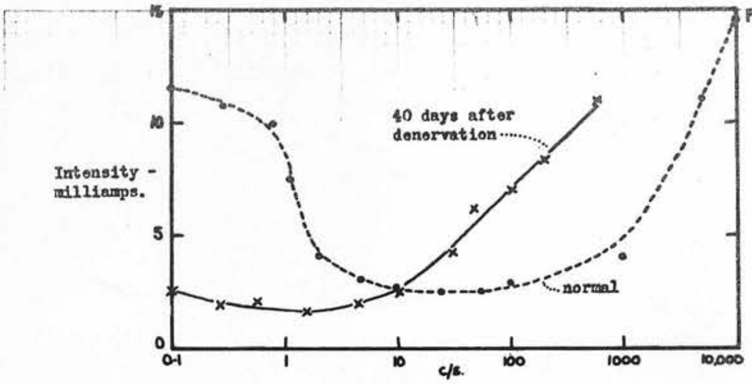
Up to the present time no systematic study of the use of variable frequency AC in human muscle-testing has been published, although several workers have come very close to the practical problem. Grodins, Ivy and Osborne (1942) suggested the determination of the optimum frequency in normal and denervated muscle as a means of diagnosis, and have followed this up with two important papers on AC stimulation of mammalian muscle (Osborne, Grodins, Mittelmann, Milne and Ivy, 1944; Grodins, Osborne, Johnston and Ivy, 1944). Employing the gastrocnemius muscle of dogs, both normal and denervated, they applied variable frequency AC from a generator of very advanced design (Mittelmann, Grodins and Ivy, 1943) and identified the optimum frequency for the two conditions of muscle. Two important discoveries resulted from their researches, which we shall consider in summary. In the first place, as was predicted from the known excitability differences in normal and denervated muscle, the optimum frequency differed very considerably for the two. Normal dog muscle, under experimental conditions, has a minimum intensity threshold for AC in the 60-100 c/s. region. (Curtis, in 1941, predicted from calculation that the ordinary power supply frequency of 60 c/s. as is general in America represented as dangerous a form of /

of current for accidental injury as could be chosen). For denervated muscle the optimum frequency was in the region of 1 - 1·5 c/sec. for threshold stimulation. Fig. 14 is redrawn from one of their papers to illustrate this finding.

The second important discovery of Grodins and his co-workers was that the optimum frequency for denervated dog muscle was not constant, but varied with the amount of force demanded of the muscle concerned. They found that for a powerful contraction of denervated muscle, a frequency of 25 c/s. was the most effective, although for a just perceptible response 1·5 c/s. had been the best frequency for the same muscle (Fig. 15). These results were obtained under laboratory conditions where the load and tension developed could be assessed with precision. The authors comment on the practical application of these results to clinical material, and come to the general conclusion that the AC frequency method is unsuited to diagnostic work because of this variation with response strength. They do not, however, give figures from human subjects under ordinary test conditions. They also point out that from the practical aspect of artificial exercising of paralysed muscles, 25 c/s. current might be a more satisfactory agent than the very /

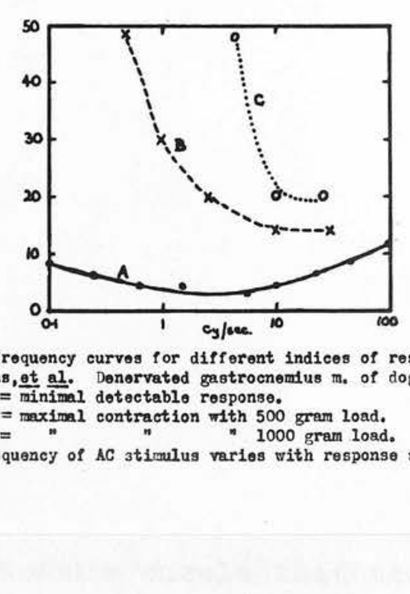
Figs.14 & 15.

FIG.14.



Intensity-frequency curves for normal and denervated dog gastrocnemius muscle; from Grodins, Osborne, Johnson & Ivy. 1944. Am. J. Physiol: 142, 216. Most effective frequency of AC for normal muscle about 60 c/s.; about 1.5 c/s. for denervated muscle. Thresholds are for minimal detectable steady tetanic response.

FIG.15.



Intensity-frequency curves for different indices of response.
From Grodins, <u>et al.</u> Denervated gastrocnemius m. of dog.
Curve A = <u>minimal</u> detectable response.
Curve B = maximal contraction with 500 gram load.
Curve C = " " " 1000 gram load.
Optimum frequency of AC stimulus varies with response strength.

very low-frequency current commonly recommended by physio-therapists.

The unqualified transfer of these results to human material seems to me to be open to a great deal of practical criticism, both on the diagnostic and therapeutic grounds. We are compiling a series of human case records on these lines, thanks to the kindness of Dr McDonald of the Birmingham Sound Reproducers Company, who has lent me a precision oscillator for the production of variable frequency AC current, and although a sufficient amount of material will not be accumulated in time for presentation here, a few comments must be made at this stage.

With regard to the diagnostic side of the use of AC current, we are of the impression that Grodins' rejection of the principle is unjustified. The minimum detectable twitch in human muscle, intelligently positioned so as to reduce load as far as possible, is such a very small fraction of the potential tension of the whole muscle that the optimal frequency for denervated muscle is in fact very constant at 1 - 3 c/s. in the several cases we have so far examined. The optimum frequency for normal human muscle appears in practice to be rather higher than that suggested by Curtis, and is in the region of 100 - 120 c/s., but /

but is more inconstant than Grodins et al. suggest.

From the other point of view, that of therapeutic exercising of denervated muscle, Grodins, Osborne, Johnson, Arana and Ivy (1944) have published an account of the prevention of atrophy in denervated rat muscle by 25 c/s. AC stimulation, and there appears little doubt that it does appear the most effective agent under these circumstances. But atrophy-preventing measures in animals are traditionally and practically not transferable to human muscle, and there are many other factors to consider. The main claim for physiotherapeutic employment of the very low-frequency current (0·5 - 1·5 c/s.) in denervated muscle exercise was its ability to stimulate such muscle without at the same time producing contraction in normally innervated antagonist muscles, and as we have seen in Section 4.3.6, this claim is true, if the procedure be carefully carried out. This does not apply to 25 c/s. AC, which is not far removed from the optimum for normal muscle, and which certainly has no selective action on paralysed. Our limited experience so far has been that 25 c/s. AC is not well tolerated by the subject; Grodins et al. in decrying the use of 1·5 c/s. AC do not point out its advantage in avoiding a good deal of sensory stimulation also. Moreover, it is very difficult /

difficult to avoid stimulation of adjacent normal muscle, which with its lower threshold tends to violent and uncomfortable activity. We feel that the transfer of the results of animal experiment to man are in this instance misleading, and hope to publish human case-records in due course.

From some aspects the use of alternating current is most attractive; it avoids the difficulties of polarization, and as we shall show later, is not distorted in the tissue layers to the same extent as rectangular or exponential pulses. The drawbacks are numerous; AC is not well tolerated in general, and a tetanic response is always less readily detected and assessed than a twitch. The generators, although costly, are readily obtainable in commercial form requiring very little modification for clinical experimental use. The problem of stopping and starting the train of waves is a vital one for precision work, and one which Grodins does not refer to. Katz (1939) pointed out that if AC is started suddenly, it will sometimes start at the peak intensity, and sometimes at zero, and, far more often, at some random value in between. In other words, the impact of the first wave will alter in a random way, and may give rise to quite false tissue responses. This was recognised

by /

by Coppee (1934), who applied AC to his laboratory preparations in gradually increasing intensity, and by Hill (1936) who accepted steady tetanic response as the only satisfactory criterion of excitation. Neither method is quite suitable for human application, as gradually developing or steady tetanus is very inconvenient to detect, and often very uncomfortable for the subject. We have found it convenient to apply the current in short bursts, with blank intervals, and it is technically possible to ensure that each burst begins at the same point in the cycle. It is in fact essential to do this, as the errors in detecting incipient clinical tetanic contraction are very considerable as compared with threshold measurements for interrupted trains of current. This is one of the important practical differences between clinical and laboratory technique; in the latter mechanical registration of response is simple and reliable, but in routine clinical muscle-testing the operator's judgment of response must be assisted by every means, as upon it depends the accuracy of the threshold determinations.

The matter must await publication of adequate clinical data.

4.4. The Recording of Muscle Action Potentials

Having reviewed the methods and value of examination of motor defect by means of clinical examination and artifical electrical stimulation, we turn to a third method which has more recently been developed. Just as the propagation of the nerve impulse along a fibre is accompanied by a transient electric potential, so is the contraction of a muscle fibre accompanied by a similar action current. It is not practicable to record nerve action potentials in man except from nerves exposed at operation (although methods for this are being developed) but it is relatively easy to detect the muscle action potentials in an unanaesthetized patient. Although the human electromyogram has only recently become a practicable routine procedure, Wedensky (1883) noticed over sixty years ago that discontinuous electrical activity could be detected in human muscle. Employing one of the early telephone earpieces connected to two fine steel needles inserted into muscle substance he described the "rushing" sound which occurs during contraction, and the absence of sound during relaxation. This experiment deserves to be more often repeated. Hoffmann (1910), in an isolated examination of one case of nerve injury, noticed that the action potentials /

potentials resulting from galvanic stimulation were repetitive in the denervated muscle, though single or very few in normal muscle. From that time until after the 1914-18 War there are no records of electromyography in man, although the appearance of muscle action potentials super-imposed on electrocardiograph records was well-known.

The development of electronic technique during and after the 1914-18 War brought new instruments into the hands of the neurophysiologist, and the advent of the thermionic valve amplifier rendered the detection of small and transient potentials a common laboratory procedure. Adrian and Bronk (1929) described a new technique for muscle potential recording in man, using a hypodermic needle with an insulated wire core leading to an amplifier and thence to a cathode ray tube and a loud-speaker; and this method, which is presented schematically in Fig. 16, has been very largely used since. The hypodermic needle forming the outer part of this so-called "concentric" electrode may be of the finest size, and inserted into muscle without anaesthesia. The tip is large in comparison with individual muscle fibres, but is comparable with the blocks of fibres which are innervated together and which form the "motor unit" components of skeletal /

skeletal muscle. The manufacture and properties of various types of concentric needle have been fully described by Lindsley (1935), Hoefer and Putnam, (1939) and by Gilson and Mills (1941), who describe the resultant records in normal subjects. Denny-Brown and Pennybacker (1938) as a result of a study of several cases of nerve injury in man, defined and described the difference in the records obtainable from normal and from denervated muscle. They showed that the human "motor unit" consisted of some 100-150 muscle fibres normally working in unison, and that the normal electromyogram potentials resulted from activity of such units. Denervated muscle, on the other hand, which had lost the block organization of the individual fibres, exhibited minute "fibrillation" potentials, which Denny-Brown and Pennybacker thought to be due to single muscle fibre activity resulting from denervation sensitivity to circulating acetyl choline.

The application of electromyography to clinical testing of large numbers of nerve injury subjects was recently described by Weddell, Feinstein and Pattle (1943; 1944); the latter paper gives a very full review and account of the technical and clinical results, and the traces in Fig. 16 are reproduced /

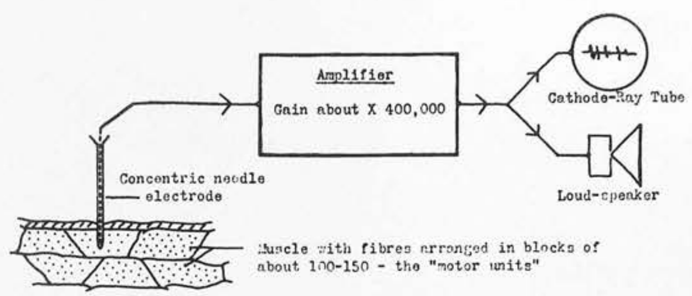
reproduced from that work. In view of the fact that we knew that this work was being done on a large scale, we have not made systematic electromyogram records on our cases, but have used the technique from time to time for confirming results of muscle stimulation. Weddell confirms the opinion of Adrian and Bronk (1928) that oscillographic examination is not strictly necessary for the appreciation of the difference between normal and fibrillation potentials, and that this can readily be done from the loud-speaker sounds; true action potentials are heard as deep loud thudding noises quite distinct from the sharp clicks of the very brief fibrillation potentials. For a full and very well presented account of electromyography reference should be made to the paper by Weddell, Feinstein and Pattle (1944) and we shall only summarize their findings in brief. The advantage of the method lies in the fact that the detection of normal action potentials in a muscle implies innervation without any doubt; as these motor unit potentials can arise only under the stimulus of the proper motor nerve impulses. Fibrillation potentials appear shortly after denervation, and persist until regeneration occurs, or until ischaemic processes abolish the contractile powers of the muscle fibres. Fibrillation potentials have been recorded /

recorded from muscles denervated for as long as eighteen years when no muscle ischaemia has occurred. In the case of muscles where nerve has undergone reversible ischaemic block (as in Bell's palsy) normal action potentials can be provoked by insertion of the needle, and this indicates the organization of the muscle into motor units by an intact though non-propagating axon. In re-innervating muscle, true action potentials appear before voluntary movement returns, though their identification is to some extent a matter of chance.

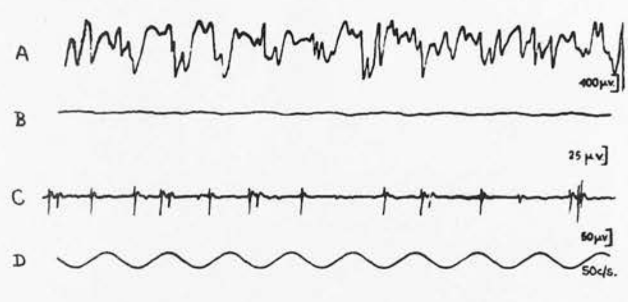
The method has the great merit of detecting directly the activity of muscle, and being independent of artificial approaches such as stimulation. The main drawback lies in the need for repeated needling in the early detection of regeneration; as the useful recording range of the needle is approximately one cm. from its tip, action potentials occurring in a scattered way in a bulky re-innervating muscle may be missed even after several needlings. There is no doubt that the work of Weddell et al. represents a very valuable and important contribution to practical handling of nerve injury cases. The electromyogram involves a certain amount of skilled handling, and with the inevitable discomfort of needle insertion, is not so simple or convenient for routine use as compared with stimulation methods.

Fig.16.

FIG.16.



Scheme of electromyogram for recording human muscle action potentials.



Representative oscillograms of muscle potentials under various conditions.

A. Record from maximal voluntary contraction of normal muscle.
B. Record from same muscle (Brachio-radialis) fully relaxed.
C. Fibrillation potentials from denervated Brachio-radialis M.
D. Time calibration trace; 50 cycles per second.

5. VOLTAGE-TIME STIMULATION IN P.N.I. DIAGNOSIS.

5.1. Introduction.

Having reviewed the various methods available for examination of peripheral nerve injury, we now present in detail a large series of quantitative records from actual cases. Measurements of autonomic activity (Section 2) were being conducted by one of our colleagues, and we knew that electromyographic examination was being systematically explored in another Peripheral Nerve Injury Centre; so that we have in particular studied the value of information obtained from muscle stimulation methods. After eighteen months initial experiment we came to the conclusion that recording of the Intensity-Duration curves for threshold stimulation combines the maximum information with the most simple and rapid routine technique, and the results are mostly of that type. Galvanic and faradic responses have also been measured on each case. As reported in section 4.3.6. we found accommodation measurements laborious and difficult in practice, and until recently we were unable to obtain adequate apparatus for investigating alternating-current stimulation, which has in any case certain practical drawbacks (section 4.3.7.).

If /

If any routine method is to be of regular value it must be capable of being applied simply and rapidly, of being reliable in operation over long periods, and of being readily interpreted. In all these respects, recording of intensity-duration curves has great merit. No apparatus suitable for carrying out this sort of measurement with simplicity or precision was available when the work was begun, and a portion of our time was spent on designing an instrument for this purpose and establishing a technique for its routine use, which we proceed to describe.

5.2. Technique of recording voltage-time curves.

As described in section 4.3.5. and shown in Fig. 12, the excitability of any tissue to electric current can be expressed in the form of an intensity-duration relationship; in such a record the intensities of shocks of various durations are measured at a value that produces a given degree of response, and one finds that the plotted curve is asymptotic at one end to the rheobase intensity (for long-lasting shocks) and at the other extreme to a shock of such brevity that no intensity, however high, will bring about response. Such a curve can be recorded with any number of points selected, and either the intensity or the duration may be continuously variable. The only available devices in the early stages were either mechanical contact-breakers, liable to error and clumsy in use, or condenser-discharge sets with their exponential decay wave-form and calculated discharge time. The first alternative is quite impracticable in routine use, and the condenser set proved unsatisfactory (section 4.3.3.) and we have designed a simple instrument using thermionic valves to produce shocks of known duration and intensity. The technical design /

design of this stimulator has been published (Ritchie, 1944) and will be discussed in a later section here. It delivers to the testing electrodes rectangular pulses of voltage selected by a switch to cover the five decades of duration necessary for the complete voltage-time record of human muscles. Five durations of shock were found adequate to plot the curves with accuracy, and they range from 0·01 milliseconds to 100 milliseconds, a range of 10,000:1 in duration. The length of each shock is adjusted in the instrument to the correct value, and is quite independent of the size, type, or resistance of the electrodes and intervening tissues; this is an important feature for quantitative work. The intensity control takes the form of a calibrated dial marked in volts from zero to 100, the upper limit being chosen as the usual limit of tolerance for most subjects with the electrodes used. It is not possible to make the intensity calibration completely independent of inter-electrode resistance without considerable complication, but from a large series of resistance measurements on assorted patients (section 2.2.) the instrument was so designed as to have a maximum error in this respect of 5%, and in practice this is obviated by the system of /

of central measurement on corresponding muscles of the normal limb.

The operation of the instrument, then, amounts to application of the electrodes in the correct anatomical position, the selection in turn of each of the five set "durations", and, at each duration, the increasing of the "intensity" dial until the muscle response appears; the intensity figure is recorded for each duration, and a graph plotted from the five resulting measurements. With practice this can be a very simple and rapid procedure, and a curve can be recorded from a muscle in a matter of thirty seconds; as this gives a complete account of the galvanic, faradic, and chronaxie excitability, the method is far simpler for qualitative routine use than any existing device for stimulation. For accurate quantitative work certain standard conditions must be observed to ensure valid comparison from one subject to another, and these will be discussed in due course.

A third control on the instrument allows the selection of shock frequency to be slow or rapid, so that single isolated twitches or tetanic responses can be obtained at will; we have found in practical testing /

testing that the single twitches separated by about one second's interval are easier to detect and better tolerated by most subjects, but many physiotherapists are accustomed to observe tetanic responses (as produced by their faradic coils), and the ability to obtain variable frequency stimulation is useful. Grey Walter (1944) has pointed out that the variable frequency facility is of great value in stimulation of brain cortex and other central nervous system sites, and it is of course most desirable for experimental work on the differential stimulation of fibres in a mixed nerve. All our records have, however, been obtained by the twitch response method.

As we have already mentioned (section 4.3.5.) rectangular voltage pulses and rectangular current pulses are not equivalent when applied to structures like nerve and muscle which are not pure electrical resistances, and this point will be taken up later on. Rectangular voltage shocks are easier to produce electrically by simple means, but, more important, are much better tolerated by patients, and it is this feature which governed the design of the machine. As complete recording of the curve implies use of fairly intense short shocks at one end of the scale, the patient's toleration is a matter of importance, and we /

we have found most emphatically in practice that a complete curve can be obtained by using relatively isolated voltage shocks on a patient who will not tolerate the ordinary faradic current.

Finally, the instrument is small and compact, and has proved quite reliable in regular use. Fig. 17 is a photograph of the original hand-made model with which over 10,000 voltage-time curves have been recorded in the past three years. With its publication, a number of copies have been made, and it is now possible to obtain a commercially-built model of superior finish and design, which has been widely recommended for tissue excitation and therapy in general.

As one of the important facilities of quantitative stimulation is to be able to compare results from one time to another on the same subject, and from one subject to another, we commenced the work with some experiments on the factors which varied under different circumstances, and thereafter established a technique of examination which, although reasonably simple, must be rigorously adhered to if the results are to be valuable. The main variables encountered in routine examination of numerous patients are resistance of skin and tissues, position of /

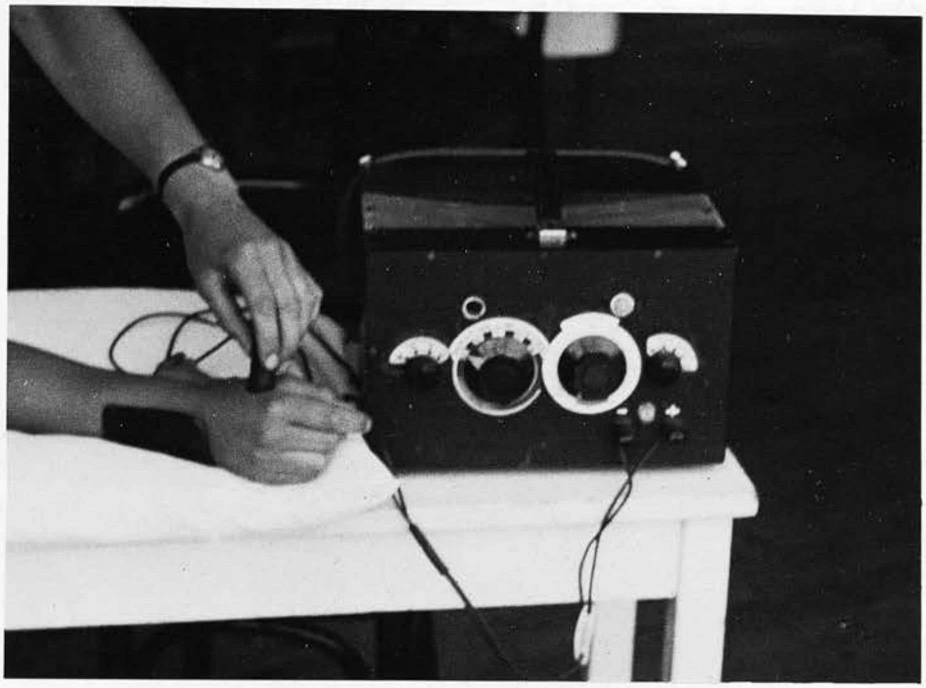


Fig.17. The square-wave stimulator and electrodes used in taking the Voltage-Time curves given in the text.

of electrode with respect to muscle, temperature of patient's limb, and strength of response used as indicator. The resistance of the average patient's skin, while variable, can be maintained reasonably constant by thorough soaking with saline; Fig. 4 (section 2.2.) shows that normal dry skin may vary from 50,000 to 300,000 ohms very commonly, but that normal skin well-soaked with saline has a much more restricted range, most commonly of the order of 10 - 30,000 ohms. If any individual patient has a particularly high skin resistance, the threshold intensities will all be higher than the usual values, and this may not be correctable by reference to the normal limb. In the majority of cases reference to the figures for the normal limb will settle the point, but in instances where the patient's limb has recently been removed from plaster, the skin conditions of the two will not be comparable. We were rather obsessed with this difficulty at the beginning of the work, and made measurements of every patient on whom voltage-time curves were recorded; a simple attachment to the stimulator allowed one to read inter-electrode resistance immediately before stimulation. In practice it is not important. We have never found a /

intensity of shock required for excitation is, however, the most important single source of inaccuracy. For all this work a standard size and type of electrode was used, consisting of a zinc disc one centimetre in diameter inserted across the lumen of a short piece of heavy rubber tubing the end of which was plugged with cotton-wool soaked in saline. This electrode is shown in Fig. 19, and has proved most satisfactory in practice. It is simple and clean, for the cotton wool plug can be readily changed; it is of constant contact area with the skin, even over the small muscles of the hand where the surface is not flat; mild pressure leaves a definite ring-like mark on the skin for several seconds, so that a displaced electrode may be replaced over the identical spot; and, most important of all, it may be held between two fingers which are themselves in contact with the underlying muscle. This latter point allows of faint muscular twitches being readily appreciated by palpation while the other hand manipulates the stimulator controls; the ordinary muscle-testing electrode with a disc on a wooden handle is quite useless in this respect. Many physiotherapists who have tried this type of electrode have used it regularly thereafter, and there is no doubt that minor details of this sort are important /

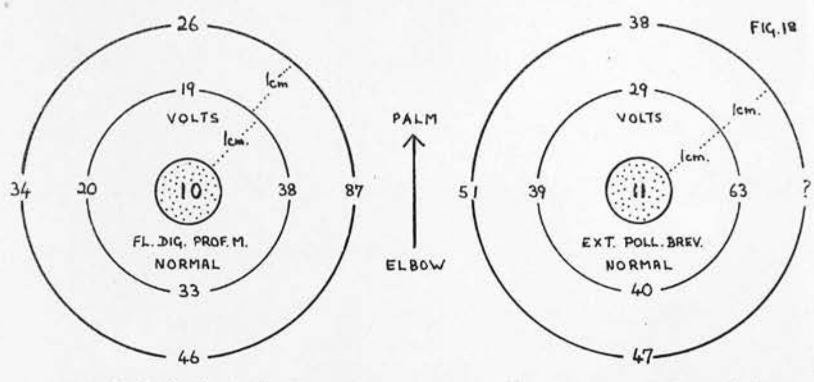
important, when taken together, in contributing to the success of the method. Such an electrode, connected as the cathode or negative pole, is used in conjunction with an anodal indifferent electrode, which is made up of a metal plate of zinc or lead covered with gauze or felt soaked in saline. These are obtainable as standard galvanic electrodes commercially, and the exact size is unimportant; three inches by four inches rectangular, of some stiff malleable metal such as lead is convenient, and allows of the indifferent electrode being "moulded" on to the limb and thus retaining its position without straps. The position of the indifferent electrode is not important; for examining muscles of the forearm or hand it is convenient to mould the large electrode round the wrist, as no unintentional excitation of muscles is likely to occur there from the use of high voltages. It is desirable to connect the large electrode to "earth", and this is best done within the instrument proper. We have described the electrodes in detail at this stage because it will be assumed throughout the rest of this work that such are used unless otherwise stated; that is, one active, negative, 1 cm. diameter saline-soaked wool contact, and one large, positive, earthed saline electrode. It may be mentioned /

mentioned in connection with electrodes that the use of bipolar stimulation with two small electrodes disposed longitudinally upon the muscle belly is quite futile, although often referred to in electro-therapy tests; such an arrangement works well enough for therapeutic stimulation of a muscle group, but is useless for identification and operation of individual muscles.

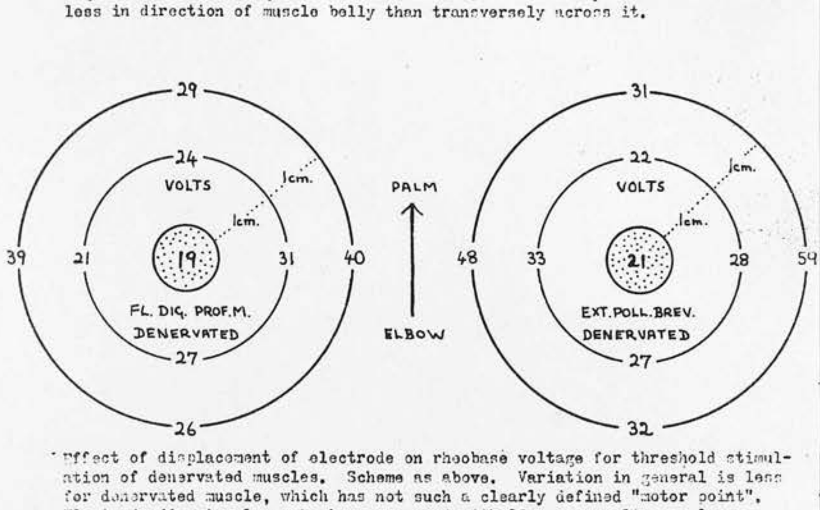
The disposition of the active electrode is a matter of great importance for quantitative work. All normal muscles, with the exception of one or two deep-set examples which cannot be used for artificial excitation, such as pronator quadratus at the wrist, exhibit a so-called "motor point", or surface spot at which the muscle is more readily excitable than anywhere else. This point corresponds to the skin area from which electric current has most ready access to the motor nerve branch to the muscle; the motor point commonly, but not necessarily, overlies the entry of the motor fibres into the "hilum" of the muscle, and in long muscles may be duplicated. Charts of the main muscles of the body and their motor points are included in all text-books of physio-therapy, but the actual point is variable with individual subjects according to build, posture, amount of fat or tissue fluid /

fluid and other factors, and the charts can only be regarded as guides. The effective motor point for each muscle of each patient must be identified by trial. Moreover it must be identified on each examination, for we have shown that marking the point by skin pencil or silver nitrate does not guarantee its exact location on subsequent examination, presumably because alterations of posture alter the relations of muscle and overlying skin. Precise location of the motor point by trial is not difficult with a quantitative stimulator, as it is a fairly restricted region at which the required intensity for a given degree of response is obviously lower than elsewhere. For this reason, an active electrode smaller than 1 cm. diameter is not recommended, as a very small electrode greatly increases the time spent in finding the most effective spot; a larger one is awkward for picking out individual muscles, and these reasons led us to fix on the 1 cm. size as standard. Fig. 18 presents the results of an experiment to determine the effect of electrode displacement on rheobase. The most effective spot for each of two muscles was identified with care by trial and error, and marked with the subject's arm in an ergograph clamp. The centre circle represents this position and the voltage required of a 100 msec. shock to produce a detectable twitch /

Fig.18.



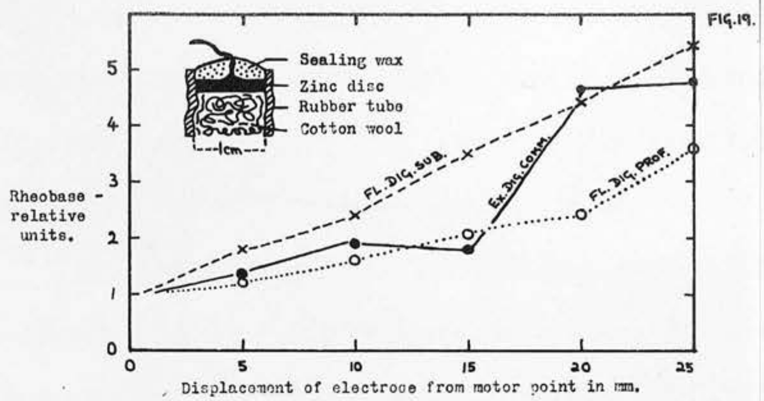
Effect of electrode displacement on rheobase voltage for threshold excitation of normal muscles. Centre circle = motor point; other figures represent volts required at the four quadrants 1cm. and 2cm. from motor point. Variation less in direction of muscle belly than transversely across it.



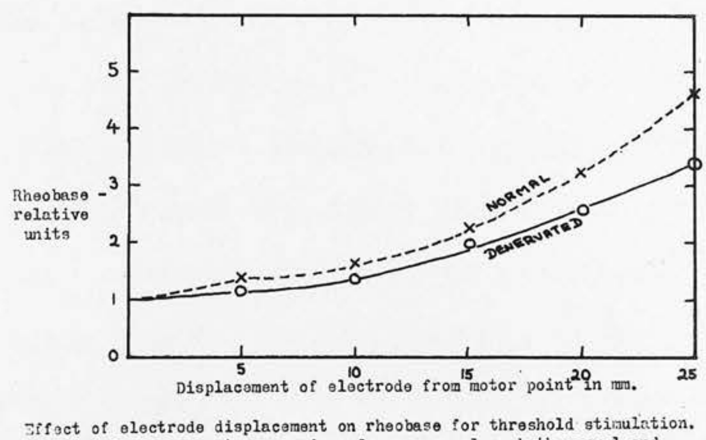
Effect of displacement of electrode on rheobase voltage for threshold stimulation of denervated muscles. Scheme as above. Variation in general is less for denervated muscle, which has not such a clearly defined "motor point". Electrode diameter 1cm: rheobase measured with 100 msec. voltage pulse.

twitch. The voltage required to produce a similar twitch was then measured at each of eight positions around the motor point, at the four quadrants of circles one and two cm. radius from the electrode margin at the centre point. We see that the voltage required is very much greater at all displacements, especially those transverse to the general direction of the muscle belly; a voltage of 10 at the true motor point may be equivalent to one of 40 or more only 2 cm. away. For the small muscles this applies more forcibly, if less deceitfully, for a 2 cm. displacement will result in stimulation of the wrong muscle, which is obvious. The same measurements for corresponding denervated muscles is given on the same diagram and here we see that the effect of displacement is less, though still considerable. As a completely denervated muscle can have no motor point in the strict sense, having no entering motor nerve fibres, the current excites the muscle fibres directly, and the electrode position tends to be less specific on that account. At the same time the effect is very considerable. Fig. 19 presents the effect of electrode displacement on rheobase voltage for several muscles, both normal and denervated, measured in the above way but expressed as means of several experiments.

It /



Effect of electrode displacement on rheobase; electrode 1cm. diameter. Mean values for 10 examples of each muscle. Threshold stimulation. Inset: Type of active electrode used.



Effect of electrode displacement on rheobase for threshold stimulation. Mean of 42 measurements on various forearm muscles, both normal and denervated. Electrode position is not quite so critical for muscle which is denervated.

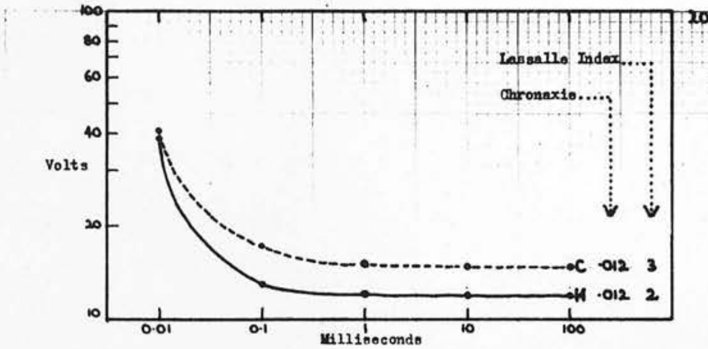
It will be seen that, roughly, a one-inch error in electrode position means a five-fold rheobase increase in normal muscles and a three-fold for denervated. The actual figures are of little value, as individual variation is very great, but the graphs emphasize the importance of careful electrode placing.

In practice, this is quite easy. The active electrode is placed in the region of the motor point, and the intensity control turned up until response is detected. The electrode is then moved over the skin; if the response becomes more violent the intensity is decreased; and so on until the most sensitive spot is located. With practice, also, the operator knows the order of intensity to be expected, and the search serves the useful purpose of accustoming the subject to the procedure, and of enabling the operator to determine whether palpation or inspection is the better method of observing the twitches. In most cases a few seconds' experiment will locate the electrode position properly. In moving the electrode about, positions will be encountered where the subject is most conscious of the shock; these are the most sensitive spots to him, and he may say so, but they have no relation to the motor point, which is determined quite objectively from /

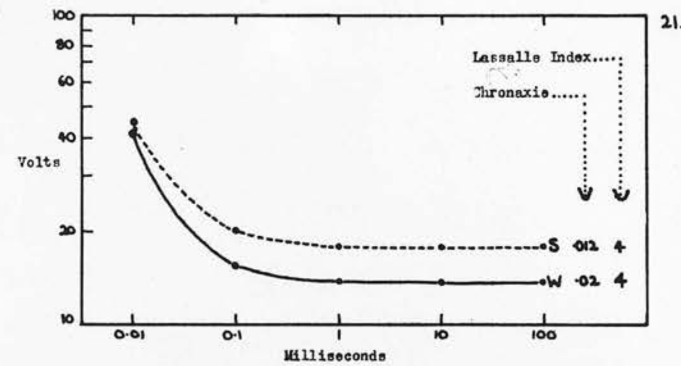
from the intensity dial of the stimulator.

The next variable factor is that of limb temperature, and the effect of this on the complete voltage-time curve is shown in Fig. 20. As this graph is the first complete one shown, the question of presentation of results may be briefly brought up here. Each V-T curve is drawn off 5 points, fixed or preselected as to time (horizontal scale) and freely variable in voltage (vertical scale). In view of the very wide range covered by the time axis, a logarithmic scale is essential, and it is convenient for appreciation of the curves to make the vertical voltage scale a logarithmic one extending over the single decade 10 - 100. The chronaxie is more readily calculated if the voltage scale be made linear, but the logical reason for logarithmic scales - the presentation of percentage differences - is then lost, and we have found that the vertical log. scale is more suitable for showing up significant differences between curves. At the right-hand, orrheobase end of each individual curve there are three applicable data; firstly a reference letter or number, secondly the chronaxie of that curve, specified in milliseconds, and thirdly the Lassalle Index mentioned in section 4.3.5. as being the square of the rheobase multiplied by /

Figs.20 & 21.



Variation in Voltage-time curves due to temperature. Curves from Flex. Dig. Prof. M. of normal subject. C = after 10 mins. immersion in cold water; H = after diathermy heating to greatest tolerated heat. Chronaxie is not altered; Lassalle index slightly decreased by heating.



Variation in V-T curves due to difference in strength of twitch end-point. Normal Fl. Dig. Prof. M. W = just detectable twitch used as indicator; S = violent twitch taken as end-point for each reading. Chronaxie slightly reduced with violent twitch; Lassalle index unaltered.

by the chronaxie. All the V-T curves to be shown are on the same scale and with the same conventions.

Fig. 20, then, shows the V-T curves forming own left Flexor digitorum profundus muscle at two extremes of temperature - after cooling in ice-water, and after heating in the inductotherm cable field to toleration. The curve from the cold muscle has a higher rheobase, and therefore a higher Lassalle Index, but its chronaxie is unaltered. The range of limb temperature normally encountered is far less than this, and has no significant effect on the curves. At the same time, a patient with warm comfortable extremities is easier to examine, more tolerant of handling, and more easily tested for voluntary power. It has therefore been our routine practice to expose patients for about ten minutes prior to examination to a source of radiant heat, so that they are seen with warm skin and comfortable movement as far as possible. This routine is the normal one for muscle-testing by any means, and is well known to physio-therapists. In the case of V-T curves, the corresponding muscles of the normal limb are used for control figures at each sitting, and if the pre-heating is not personally supervised the physio-therapy staff concerned must be instructed to direct the heat on to both the affected and /

and the normal part.

In Fig. 21 the effect of taking different twitch strengths as response is shown. This is potentially an important matter, for the curve is applicable strictly to the same degree of response for each of the five duration readings, and if the degree of response differs the curve may not be accurately recorded. Various adjuncts to response observation have been tested out, such as pointers stuck on the skin with Plasticine, small mirrors which reflected a point of light on to the wall, and several coarser ergograph methods. In our experience none of these are so satisfactory as straightforward clinical observation by palpation and inspection of the muscle. They all involve additional complication and introduce further apparatus to consider, and tend to distract attention from the actual muscle. All the curves to be presented have been recorded with the minimum detectable clinical twitch as response. This may be more readily detected by palpation of the muscle belly with the electrode holding fingers, as already described, or by inspection of muscle or tendon in a good light; it depends on the muscle and on the subject. The actual muscular force involved in such a twitch is very small, and quite insufficient to move the joint concerned; this is important, for joint pain or stiffness /

stiffness rules out any gross movement as indicator. In Fig. 21 the V-T curves are shown for one of my own muscles using as response first the minimal detectable twitch and secondly a twitch of considerable violence. In practice the two could not be mixed in the taking of a single curve, and we may conclude that, with reasonable intelligence, the minimal twitch detectable by clinical means is a reliable and fairly constant indicator. It can again be checked by reference to the normal contralateral muscles.

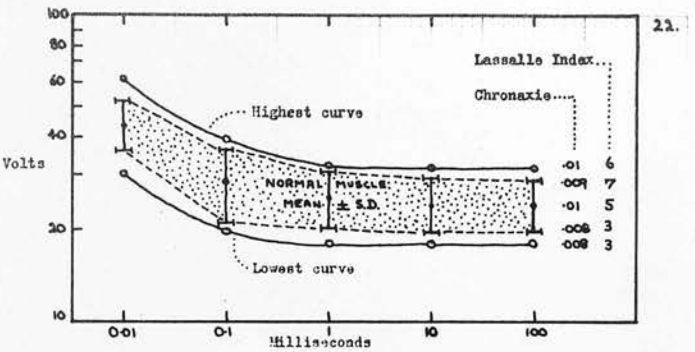
In ordinary recording of V-T curves with the stimulator, the necessary precautions and possible difficulties to be accounted for may be summed up briefly as follows. (a) The muscles to be examined, and the corresponding normal muscles, should be exposed to radiant heat for 10 minutes before testing. (b) The limb concerned should be disposed comfortably on a pillow, in a good light. (c) The indifferent electrode must be suitably placed round the wrist, and the true motor point identified by moving the electrode until response is shown with the minimum intensity. (d) The threshold intensities for each of the five durations are then noted in turn, with the active electrode held in place the whole time. One hand must be used for this, and for the muscle palpation, while the other manipulates the stimulator controls /

controls. (e) The figures should be repeated in the reverse direction, i.e. if the long duration impulse is used first, and the shorter ones thereafter, the threshold intensities should be recorded also in the reverse direction, starting with the shortest stimulus. The actual curve recording takes a minute only with practice. (f) A corresponding V-T curve should be taken from the contralateral muscle. (g) This procedure is carried out for each separate muscle, and careful notes kept of each examination. (i) The curves are later plotted on squared paper.

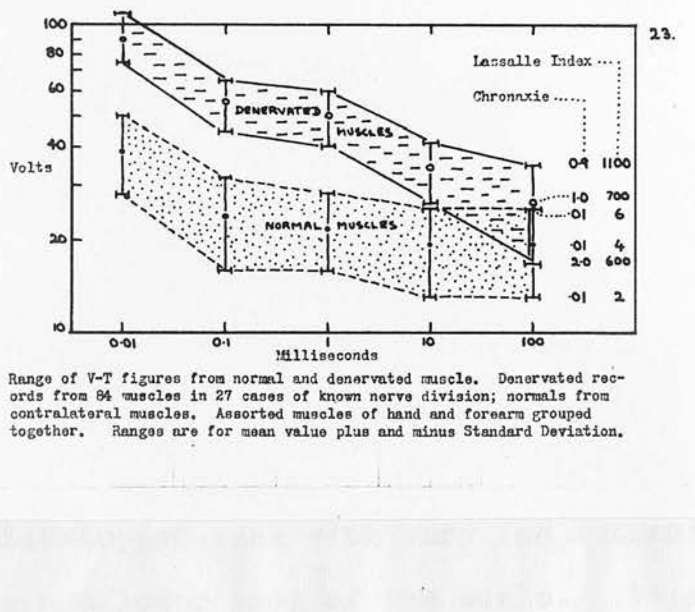
The actual graphing of the curves is an essential part of their appreciation, for only from the plotted curve can the chronaxie and the Lassalle Index be deduced, and the curves compared with those on previous or subsequent examination. When the instrument is used for qualitative muscle stimulation, we shall see that there is a very simple means of assessing denervation without recourse to written recording; but for the detection of regeneration careful graphing is necessary.

5.3. Voltage-Time Curves of Normal and Denervated Muscle.

The normal range of variation in a particular muscle of one subject was estimated by consecutive readings over a period of three months at daily intervals. By normal range of variation in this context is meant the spread of the results obtained on serial examination, including the errors due to the instrument and due to variation of circumstances such as temperature and response strength as well as any physiological variation which may occur from time to time. If the results are to be of quantitative value we must know the practical range of figures to be regarded as ordinary variability. I accordingly measured the V-T curves for the left first dorsal interosseous muscle of my own hand on one hundred consecutive days, observing the usual precautions just described. Each curve was measured in both directions - i.e. from the rheobase end and from the high-intensity end, and reference was not made at any examination to the figures for the preceding ones. The results are expressed graphically in Fig. 22, and a table of the important statistical points given below.



Range of V-T figures from one muscle of one subject at various times. Dors. Int. M.1. of hand measured 100 times over period of three months. Mean values plus and minus Standard Deviation; also highest and lowest single curves. Chronaxie and Lassalle index for each curve on right.



Range of V-T figures from normal and denervated muscle. Denervated records from 84 muscles in 27 cases of known nerve division; normals from contralateral muscles. Assorted muscles of hand and forearm grouped together. Ranges are for mean value plus and minus Standard Deviation.

<u>Muscle</u>: Left first dorsal interosseous of hand (A.E.R.). Normal innervation.

Duration in milliseconds:	0·01	0·1	1	10	100	Chron-axie	Las-salle Index
Mean of 100 exams, in volts:	44	28	25	24	24	·01	6
Standard Deviation, volts:	8·1	7·1	5·2	4·4	4·2		
Highest curve:	60	39	31	31	31	·01	9
Lowest curve :	30	20	19	18	18	·008	3
Mean plus S.D.	52	35	30	29	28	·009	7
Mean minus S.D.	36	21	20	19	20	·008	3

Several significant points can be noted from the figures. The highest and lowest figures recorded lie only slightly out with the Standard Deviation, and in fact 93 out of the 100 records fell within these limits, although the distribution between them was well spread. The spread is not therefore the so-called normal or Gaussian distribution, but has a flat-topped peak with very few extreme examples at upper and lower ends of the scale. It appears therefore that the variation to be expected in practical testing is a restricted one with definite limits at or about the Standard Deviation. This is of course a very favourable distribution for comparing one curve with another provided that the Standard Deviation /

Deviation is appreciated. Secondly, the chronaxie figures for the curves are in the region of one-hundredth of a millisecond, which is much lower than chronaxie numbers obtained by rectangular current or condenser discharge methods; they are however consistent. Thirdly, the Lassalle Index figures are all below 10, for this normal muscle, but show considerable variation with the rheobase of the particular curve, as is to be expected from the fact that the rheobase figure is squared in calculating the Lassalle index.

The method adopted of working out the Standard Deviation of voltage at each duration is decidedly unfavourable to the figures, as it implies that each voltage figure is independent of the other four in a given curve, which is of course not the case, as all five are measured successively at the same time and should, and usually do, lie on a fairly smooth curve. From the table given it would be possible to have a record in which the first voltage reading was the mean plus S.D. and the second voltage figure of the curve, at the next duration, was the mean minus the S.D.: this does not occur in practice. The statistical methods for working out deviations where each point on a curve is dependent on the others but the curve as a whole is variable are extremely complex /

complex, and the simple S.D's given represent the maximum error to be expected. For assessment of routine curves we have found that the plotting of the plus and minus S.D. range on transparent celluloid which can be superimposed on any particular graph gives a better idea of alteration from normal than any calculation. It should be noticed that the 'curves' given in the table and in Fig. 22 for Mean plus S.D. and Mean minus S.D. are not true curves from the muscle itself, but are calculated from the S.D's at each of the five variations separately, although chronaxie and Lassalle figures are given for them. Finally, it will be noted that the appreciation of V-T curves in tabular form is laborious and confusing, and apart from one other example, we shall present the curves in graphic form after this, both for clarity, and to avoid the very large tables which the many thousand collected records would occupy.

The next important point is to establish the difference in excitability between normal and denervated muscle as expressed by Voltage-Time curves. The following table, and Fig. 23 demonstrate the significant difference between these. In order to ensure that truly denervated muscles were measured, we have selected a series of cases encountered early in /

in the work where surgical division of a motor nerve was carried out prior to suture at operation. The intention in such procedures being to ensure regeneration if possible, the muscles were examined as soon after operation as the patient's condition and circumstances, such as dressings and plaster, permitted; and no muscle was accepted as denervated unless clinically completely inactive, to avoid the chance of anomalous or accesssory innervation. The muscles are assorted in the sense that the records are not all from the same anatomical muscle, and this results in a rather wider scatter, but more fairly represents the state of affairs encountered in practical muscle-testing. 84 muscles in all were recorded, by the usual method, on 27 different patients; that is, on any one patient several denervated muscles might be stimulated. For each muscle, of each patient, for which the V-T curve was recorded, the curve for the corresponding contralateral muscle of the same patient was recorded (except in two cases where amputation rendered this impossible). Therefore the "Normal" range in Fig. 23 is considerably more scattered than that of Fig. 22, because it includes several different muscles. It represents more fairly the range to be expected in routine testing. 72% or roughly three-quarters /

quarters of all the normal curves fell within the range of Mean plus and minus Standard Deviation. Chronaxie values are very constant at 0·01 millisecond, and the Lassalle Index in single figures.

Range of 79 normal muscles of hand and forearm.

Duration - milliseconds:	0·01	0·1	1	10	100	Chronaxie	Lassalle Index
Mean - volts	39	24	22	19	19	·01	4
Standard Deviation	11	8·1	6·3	6·0	6·1		
Mean plus S.D.	50	32	28	25	25	·01	6
Mean minus S.D.	28	16	16	13	13	·01	2

Range of 84 denervated muscles of hand and forearm.

Duration - milliseconds:	0·01	0·1	1	10	100	Chronaxie	Lassalle Index
Mean - volts	90	55	51	34	26	1·0	670
Standard Deviation	15	10	9·3	7·1	9·0		
Mean plus S.D.	105	65	60	41	35	0·9	1100
Mean minus S.D.	7	45	42	27	17	2·0	580

The range of Voltage-Time curves for denervated muscle is very different from that for normal /

normal muscle. The rheobase voltages at long-duration stimuli overlap considerably, but as the duration of shock is lessened the necessary threshold voltage increases rapidly. The Standard Deviation for each mean figure for the denervated instances is greater than that for normal muscle, although this is not immediately apparent from Fig. 23 because of the logarithmic intensity scale. 65%, or roughly two-thirds of all the denervated threshold figures fell within the range mean plus and minus the Standard Deviation. Chronaxie figures range from 0·9 to 2·0 milliseconds, approximately one hundred times those of normal muscle. The Lassalle Index figure is rather variable, because of the large spread of rheobase values, but is always over three figures, with a mean value of 700 as opposed to 4 for normal. Here again it must be realised that the "mean" curves are not true V-T curves as recorded, but are statistical conceptions. In the examination of any one patient, the difference between normal and denervated muscle is more obvious. The composite curves show, however, that the difference in quantitative excitability is very great. Using a stimulator capable of delivering a shock of one known fixed rectangular duration only, we see from the composite records that a pulse length /

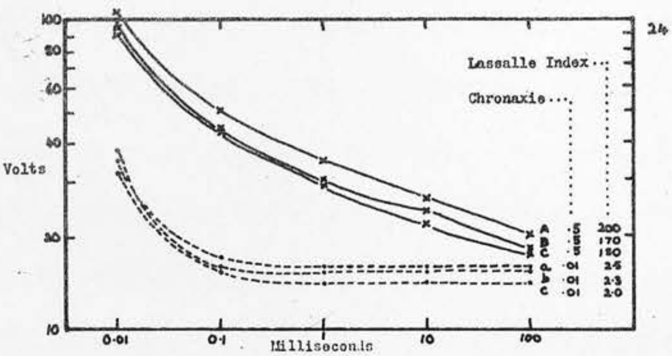
length of 100 milliseconds will not give very definite discrimination between normal and denervated muscle, since the rheobase voltages overlap considerably. A shock of 1 millisecond duration will however have a fair discrimination factor; between 30 and 15 volts it will very rarely excite denervated muscle, while below 25 volts it has never done so in our series of experiments. At voltages over 30 it will possibly excite denervated muscle, but will almost always stimulate normal muscle. The discriminating factor is greater if even shorter shocks are used, but in practice they are not advisable, for a fair proportion of patients will not tolerate the high voltage required to stimulate denervated muscle with a stimulus of 0·01 millisecond duration. A stimulator relying upon one duration of shock only should therefore have that duration of the order of 1 millisecond to give the best results in practice.

True V-T curves as measured from a nerve injury patient are shown graphically in Fig. 24. C.F. was admitted to the Nerve Injuries Unit four months after a bomb fragment would of the elbow resulting in a clinical radial palsy. Stimulation of the paralysed muscles on admission showed a typically "denervated" /

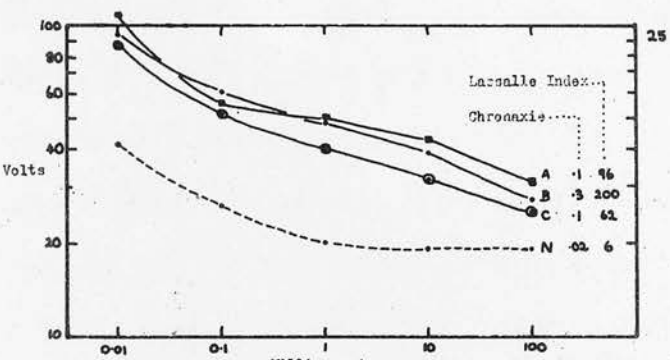
"denervated" type of V-T curve with chronaxie of 0.5 msec. and Lassalle index of 200. The curve for the extensor digitorum communis muscle only is given in Fig. 24, but these from extensor carpi ulnaris and the radial thumb muscles were similar. As on the first examination the patient's hand was swollen and oedematous, and testing difficult, he was given physiotherapy treatment for a fortnight and then re-examined with the result that the V-T curves had a slightly lowered rheobase, but were otherwise quite typical of denervation. At operation the radial nerve was found divided, and was sutured; knowing then that denervation was complete we recorded a set of curves five weeks after suture (before regeneration had proceeded to any length) and found them tally within the limits of variation. This case affords a very typical example of the difference between denervated muscle and normal, and of the sort of order of error encountered in routine testing by this method.

Two points may be emphasized. Firstly, the decision to operate is not governed primarily by the electrical diagnosis of total denervation, for such a circumstance can be brought about by a lesion in continuity which will not require suture for regeneration (Section 1; Fig. 2). The decision is made on consideration /

Figs.24 & 25.



Case C.F. The variation in V-T curves from one subject under usual conditions of clinical examination. Denervated Ext.dig.comm.m. - A,on admission, - B,after two weeks observation,and,C,five weeks after suture. Corresponding normal muscle curves dotted lines.



Case J.G. Denervated Ext.dig.com.M. A = on admission with arm oedematous; B = after massage for one week; C = after dispersal of fluid at end of 3 weeks physiotherapy. N = mean figures for normal contralateral muscle.

consideration of the site and nature of the wound having regard to the observation that the muscles are totally denervated. Secondly, the quantitative records of such a case become quite extensive when kept systematically. Although Fig. 24 shows the records from one muscle only, in fact we have altogether 33 V-T curves relating to the various muscles of this patient, including the central measurements. As the presentation of protocols of such curves for the various cases observed would not only be awkward to appreciate but would occupy some hundreds of pages, we shall present in graphic form only the curves relative to the muscle most proximal to the site of injury unless other features of interest can be made from further readings. In general in this type of work we are concerned practically with the most proximal affected muscles, in that they are normally the first to show signs of re-innervation. This is not always true, for in odd cases a distal muscle may recover early because of impediment to, or chance distribution of the growing motor fibres to the nearer muscles. Where this, or any similar observation has been made, records will be given in full. But in the great majority of our experiments the curves from the lower muscles have merely confirmed these on the upper ones.

Although /

Although the keeping and analysing of the full records is quite an elaborate procedure, Fig. 24 shows that there is a simple method of using the instrument to determine denervation without recourse to figures at all. It is quite characteristic of normal muscle that its rheobase to a 100 msec. voltage shock is the same as that for shorter durations down to 1 or even 0·1 millisecond. The point of inflection of the normal V-T curve is in the region of 1 msec. or less. The rheobase for denervated muscle, on the other hand, is at 100 msec. or slightly over, and with any reduction in duration intensity has to be increased considerably. This fact can be made use of in a very simple rapid test for denervation, which is far quicker and more certain than the standard galvanic-faradic test. The stimulator is set to deliver the 100 msec. shock, the electrode properly placed, and the voltage control adjusted until the twitch response appears. Then, leaving the voltage control at that position - the rheobase - the duration dial is rotated successively to 10, 1, and 0·1 msec. position. If the twitch appears at each of these, without any alteration of voltage, the muscle is certainly normally innervated. If, on turning the duration down to 10, the response disappears /

disappears and can only be recovered by voltage increase, and still further increase is required at 1 msec. duration, the muscle nerve supply is certainly damaged, and more accurate readings may be needed to get further information. As one or two twitches only are needed to ascertain response, this simple test for innervation can be carried out in a matter of ten seconds with very transient discomfort to the most sensitive subject and no more manipulation to the operator than turning a switch to four different positions in turn.

Case J.G., whose records are shown in Fig. 25, sustained a compound fracture of the humerus with damage to the radial nerve in December 1943. We have selected this example for graphing because it instances the greatest variation in V-T curves that we have encountered in a single muscle. On admission to the Nerve Injuries Unit in March 1944, four months after injury, the patient's arm was very stiff and oedematous from prolonged restriction in plaster on account of the bone fracture. On first examination, which was difficult, the radial muscles possessed chronaxies of the order of 0·1 to 0·3 msec., with Lassalle indices in the region of 100; the corresponding normal figures being 0·02 and 6.

Repeat /

Repeat examination after one, and three weeks intensive physiotherapy gave very similar figures, although the condition of the arm was very much improved, and might have been expected to cause gross alterations in the V-T figures. This patient has the least difference between denervated and normal curves of any we have examined, having a low rheobase for the denervated muscles and a high one for the normals. In spite of this, the differentiation between denervated and normal muscle is quite clear cut, and the reliability of the curves as an index very satisfactory despite the alteration in physical condition of the limb with physiotherapy.

We may fairly conclude that the method is able to distinguish with certainty between totally denervated and normal muscle; denervated muscle having chronaxie of the order of 1·0 milliseconds, and Lassalle index of several hundred, whereas normal innervated muscle has chronaxie of 0·01 millisecond and Lassalle index below 10.

5.4. Muscle Excitability in Cases of Pressure Palsy.

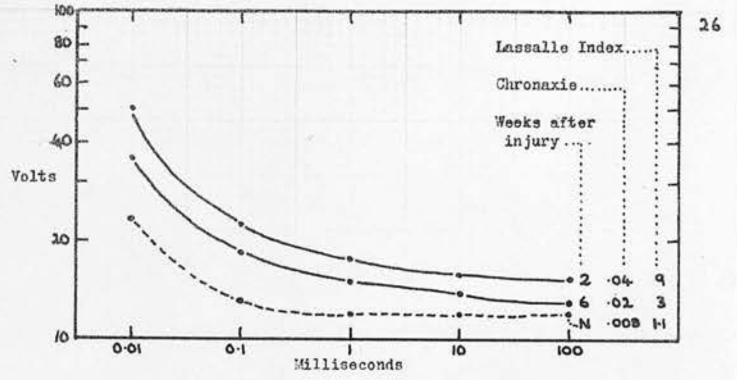
As described in Section 1, muscular paralysis can be caused by interruption of nerve impulse propagation in the course of the motor axons without necessarily involving Wallerian Degeneration of such axons. A mild degree of injury may abolish conduction but leave the nerve structure intact, and its function above and below the injury normal. Cases suffering from such injuries are in general grouped as "pressure palsies", as pressure on a nerve trunk is the commonest cause of the disability. As a rule paralysis is not complete, weak voluntary movement and faradic response being retained; the condition rather rapidly recovers without any treatment beyond removal of the cause. Denny-Brown & Brenner (1944) have shown that pressure alone does not abolish nerve conduction, but that the ischaemia resulting from pressure is responsible. As Erb (1876) pointed out, the electrical reactions are a valuable guide to the condition, especially in the very early stages where voluntary power may be very weak or even absent; the faradic response of the muscle is retained, and stimulation of the nerve trunk distal to the site of block produces contraction. This latter feature is not of great practical value, as the majority of pressure injuries /

injuries occur at a level below which the nerve is not accessible; the exception being ulnar nerve block at or above the elbow.

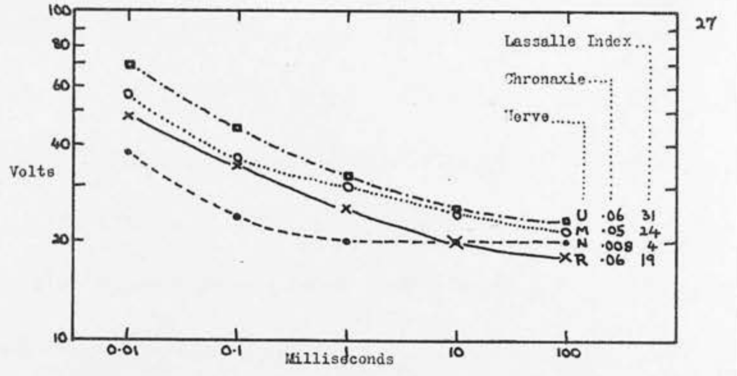
Case G.S. (Fig. 26) was admitted to the Nerve Unit with very marked weakness of the ulnar muscles of one hand and forearm; a mere flicker could be noted by ordinary examination, and there was some apparent wasting of the first dorsal interosseous muscle. He gave a history of employment as an R.A.F. telegraphist, in which occupation he operated a hand-key with his forearm resting on a ledge in such a position that the inner side of his elbow crossed the edge of the shelf. He had noticed progressive weakness of the hand, and became quite unable to operate the Morse Key, which is normally gripped between first and second fingers and moved both up and down by them. On examination the V-T curves from the affected muscles were slightly higher and steeper than the normal, but did not give figures suggestive of denervation, the average chronaxie being below 0·05 msec. and the Lassalle Index below 10. This was a singularly intelligent patient, a trained electrician, and took great interest in the procedure and recording of testing. Records were taken from seven of the ulnar-supplied muscles and from the corresponding /

corresponding normals; those from Flexor corpi ulnaris are given in Fig. 26. Without any specific treatment beyond removal from the telegraph key, G.S. recovered spontaneously; four weeks after the first examination the V-T curves were judged to have improved beyond the range of error and at this stage he exhibited a reasonable amount of voluntary power. In ten weeks his power and muscular contral was considered by himself to be completely normal. On admission, when Curve 2 in Fig. 26 was recorded he had a "doubtful" faradic response, in the usual clinical sense that the muscles only began to respond at the limit of tolerable faradic intensity; it was in fact this patient who pointed out to me the greater comfort of isolated stimuli of this type as opposed to the normal testing. The faradic response appeared definitely at the fourth week. Stimulation of the ulnar nerve just below the median epicondyle resulted in muscular contraction of the Flexor profundus and interossei muscles, and the diagnosis could have been made on this fact quite apart from the history.

Case R.A.C. (Fig. 27) was admitted with marked weakness of all forearm and hand muscles apparently dating from an operation in the elbow region (for removal of a bomb fragment which had no relation to the nerves, but was impeding joint movement /



<u>Case G.S.</u> Pressure palsy of ulnar nerve and spontaneous recovery after removal of occupational cause. Voluntary power weak but never absent. Fl.c.uln.M. N = normal contralateral.



<u>Case R.A.C.</u> Tourniquet palsy with muscular weakness in all muscles at elbow and below. Curves for three different muscles shown: U = Dors.int. 1.M.(ulnar); M = Fl.poll.l.M.(median); R = Br.-rad.M.(radial). N = mean for normal contralateral muscles. Spontaneous recovery took place in 10 W.

movement) during which a tourniquet had been applied to the upper arm for some 25 minutes to control bleeding. On examination, V-T curves were recorded from 11 of the forearm and hand muscles, and all showed chronaxies of the order of 0·06 m.sec. as compared with 0·01 for the corresponding normal muscles. Faradic response was present in all these muscles, and the ulnar nerve produced response when stimululated at the elbow, although the median and radial nerves did not do so at the limit of toleration. The V-T curves for the representative muscles are shown in Fig. 27; in this case the disposal of the patient, who required no special treatment, prevented a follow-up of the powers of recovery. Spontaneous recovery occurred, and on re-examination ten weeks after the first, no difference either in excitability or power could be detected.

We may conclude that the method of recording V-T curves has relatively little value in such cases, as the diagnosis can be made on history, clinical examination, and on the retention of the faradic response; it is noteworthy however that when the excitability is expressed in quantitative terms it is somewhat depressed, having an increased chronaxie and Lassalle index, though never to the extent of denervated /

denervated muscle.

The reason for this depression has been obscure. Below the level of the reversible ischaemic nerve block the axons and their motor end-plates in the muscle are intact. It is unlikely that the general depression of excitability is due to an admixture of normal and inactive fibres, for if this were so, the V-T curves would reveal a quite normal excitability; if sufficient normal motor units were present, they would respond at the lesser intensities, and give a normal curve. The possibility remains that the end-plate excitability may be diminshed, although its structure be intact. Denny-Brown and Brenner (1944) have demonstrated that restoration of the structure of the damaged section of the nerve may be very long delayed, if indeed it ever becomes completely normal. Conduction, however, appears to be completely restored. They do not report on the muscle histology, and in any case, minor impairments of excitability might come about through chemical deficiencies due to disuse or incomplete activity.

We have recently examined, through the kindness of Mr. Norman Dott, a number of cases of the most common and typical ischaemic nerve block - "Bell's Palsy" of the facial nerve - and the results are similar. Slight depression of excitability is invariably detected if there is muscle weakness, and this disappears as conduction is re-established.

5.5. Muscle Excitability in Functional Paralysis.

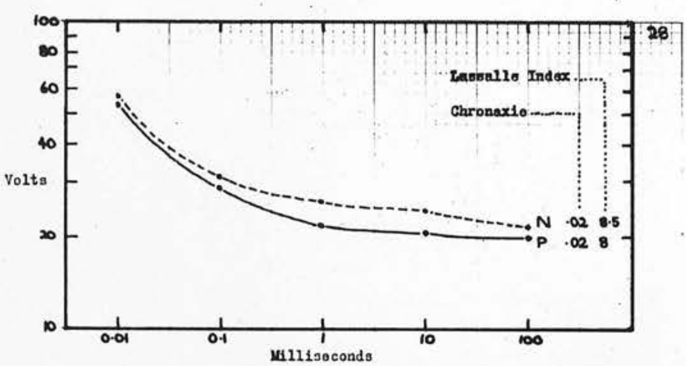
The diagnosis of functional or hysterical paralysis is usually readily made on clinical grounds. Certain muscular movements may be completely lost, and the prime mover muscles apparently paralysed, and yet the same muscles caused to contract as synergist or fixing muscles with other movements. In functional paralysis the neuro-muscular apparatus is unimpaired, the fault lying in the failure of the anterior horn cells to initiate discharges voluntarily, though they may still do so by reason of spinal reflex activity as in the instance of extensor reflexes already mentioned. One would expect therefore to find the excitability of the terminal neuro-muscular apparatus quite normal, and this is borne out by an examination of five such cases, of which we present two typical examples.

Case W.J.M. had, five years previously sustained a radial nerve injury resulting in complete drop wrist; I cannot now trace the nature of the original injury, but believe that it was a closed injury in continuity complicating a fracture of the humerus. At any rate, the subject had within a year made a sufficiently complete recovery to be graded A1 for military service. He was referred to the

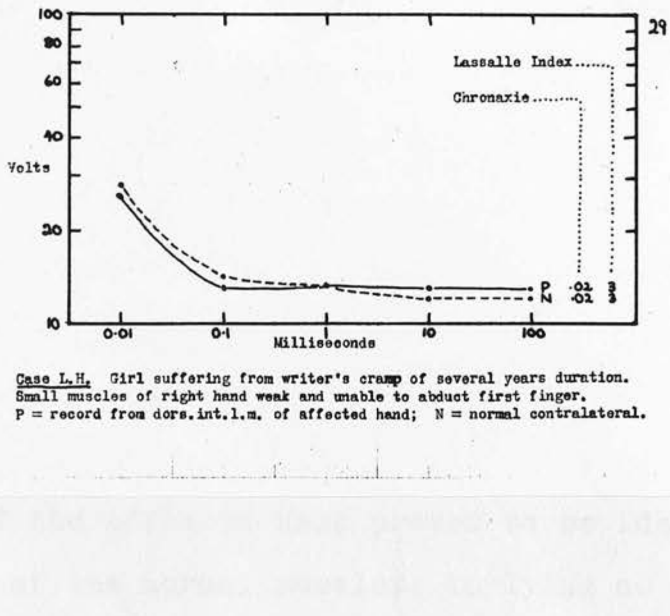
Nerve /

Nerve Unit after four years of arduous and unpleasant military duties with the B.E.F. 1940-43, having been in the retreat from Dunkirk and two minor coastal raids. W.J.M. was a heavily built man of 31 in apparently excellent physical condition, and made no complaint of distaste for Army life. On clinical examination the forearm extensors appeared totally paralysed for any dorsiflexion of wrist or fingers, but could be felt to harden when a full flexion grip was tested. V-T curves were recorded from ext. corpi ulnaris, the finger extensors, and from abductor pollicis longus muscle, and in all cases were almost identical with those from the corresponding contra-lateral muscle. Fig. 28 shows the curve for Ext. digitorum communis. The case is interesting as the super-imposition of a functional paralysis on a previous, recovered, organic nerve injury; a diagnosis of purely hysterical paralysis was made and the patient referred to the appropriate specialist for treatment.

The second instance selected is that of L.H. a young woman of 24 who was in employment as a laboratory assistant in the Medical School. She had been forced to abandon her previous work as a clerkess because of increasing inability to hold and use a pen or /



Case W. J. M. Functional paralysis in patient who had a previous nerve lesion followed by full recovery. Four years later paralysis re-appeared in the same muscles. P = Ext.dig.com.M. N = normal contralateral m.



Case L.H. Girl suffering from writer's cramp of several years duration. Small muscles of right hand weak and unable to abduct first finger. P = record from dors.int.l.m. of affected hand; N = normal contralateral.

of pencil. She came to see me of her own accord, having gathered that I was interested in the testing of muscles, and prefaced her history with an announcement that I was the twenty-seventh doctor she had visited! Clinically there was no evidence of paralysis in any of the small muscles of the hand when tested in the usual way; she was capable of manipulating burette taps and other small pieces of laboratory apparatus, but could not hold a pen in the normal way between thumb and forefinger of the right hand, and in this position the first dorsal interosseous muscle remained flabby. She could write, but not well, with her left hand, and had never persevered for fear of bringing on the same disability there. I gathered she had been in the hands of several psychiatrists.

On examination the excitability of the small muscles of the affected hand proved to be identical with that of the normal muscles, implying no damage to the peripheral neuro-muscular mechanism. Fig. 28 shows the records from the first dorsal interosseus muscle, which was that most inoperative in her attempts at writing.

V-T curve recording therefore demonstrates that there is no objective difference between normal muscles /

muscles and these useless from hysterical paralysis; this is the quantitative expression of the fact that faradic response is retained in such muscles.

Figs. 28 and 29, from normal muscles in two very different patients as regard build, give a very good idea of the upper and lower limits of normal V-T curves. All the four curves shown have chronaxies of 0·02 msec., and the difference in rheobase between the upper curves and the lower cause a difference of Lassalle Index of nearly three times, although the index remains below 10. Note that although these two sets of curves have the same chronaxie, their apparent curvature at first glance is different because of the logarithmic vertical scale.

5.6. Muscle Excitability after Ischaemia.

Impairment of muscular power as a result of ischaemia is seen fairly commonly in war wounds as a result of arterial injury, or vascular thrombosis after vessel bruising, and may or may not be complicated by nerve injury as well. In brachial plexus missile injuries both arterial and nerve damage are often present at the same time. We have already seen the effect of reversible ischaemic block of a nerve, and will consider here a few examples of muscle ischaemia. In general ischaemia of a limb is shown clinically by progressive impairment of muscle power as the limb is examined from the trunk towards the extremity, and the muscular weakness is not distributed in accordance with nerve supply in uncomplicated cases. In addition there may be sensory loss, also with peripheral and not neurological distribution, and impairment of skin circulation proceeding towards gangrene of the digital tips. In connection with the muscular apparatus, it must be realized that ischaemic muscular damage comes about in a very short time, and in general is irreversible. A limb which has suffered acute ischaemia from arterial occlusion will begin to show muscular changes within an hour, and within a few hours at most the muscles will suffer such structural damage /

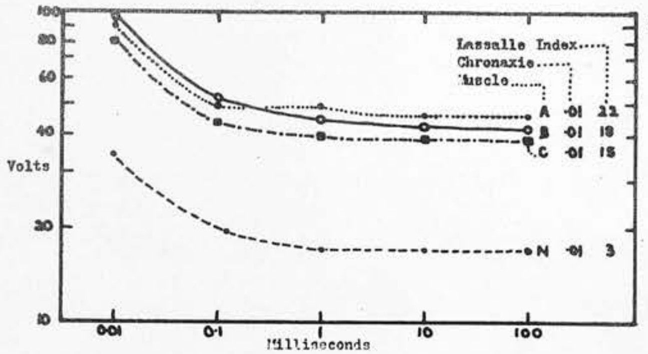
damage that relief of the ischaemia will not restore them to proper function. Therefore we may expect to find residual muscular impairment persisting indefinitely after an ischaemic episode which may itself have been transient and long before; and this impairment will be present even if the circulation has been restored to normal.

Moreover, all degrees of muscle damage may be encountered, from just detectable weakness and stiffness to complete replacement of contractile muscle elements by fibrous tissue. Observations on cases seen at the Gogarburn Unit have been described elsewhere by Blackwood (1944), Learmonth, Blackwood and Richards (1944), and in the British Medical Bulletin No. 7, 1944.

Methods of muscle-testing are not as a rule of great value in examination of such cases, as diagnosis is made on other grounds, but present certain features of physiological interest. Muscle which has been very severely ischaemic and been transformed into fibrous tissue is of course not excitable by any means whatsoever, as it contains no surviving contractile elements, and this has led to an opinion commonly expressed that ischaemic muscle is inexcitable to galvanic current. This is only true if applied /

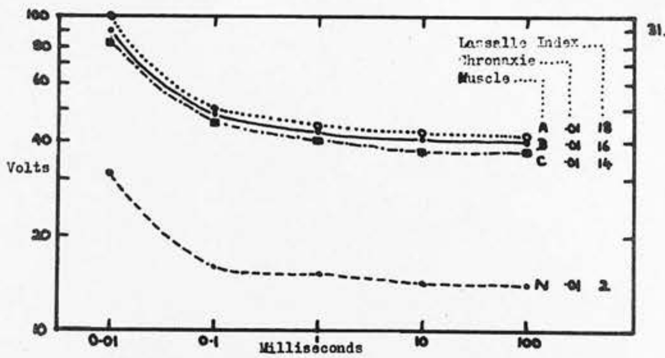
applied strictly to the severe cases. In mild cases the excitability of ischaemic muscle remains normal, but at a very high rheobase level, and testing may be impossible because of the very high voltages required. Inexcitability to galvanic current, adequately applied in known quantities, should only be regarded as definite if recorded under anaesthesia. The milder cases of muscle ischaemia, with impaired power and a rather rigid or "woody" feel on palpation, will often yield quite characteristic V-T curves.

Case W.A., shown in Fig. 30, is that of a man who sustained a fall on the elbow resulting in the onset of sensory loss in the hand, firmness and weakness of the forearm and hand muscles, and a very marked degree of oedema and bruising of the elbow region. When we examined this patient four months after the original injury he still had a very weak hand, although the circulation in the limb as judged by pulses and appearance seemed quite normal. V-T curves for several of the small muscles of the hand showed a very high rheobase, far beyond the normal range, but a chronaxie figure which was quite normal. This was so for muscles innervated either by median or ulnar nerves. As such curves could hardly result from any form of nerve injury, the suggestion of ischaemia /



30

Case W.A. Excitability of small muscles of hand five months after an ischaemic episode due to fall on elbow. Muscles all working voluntarily but weakly. Very high rheobase with normal chronaxie values. A = Abd. dig.min.m: B = Abd.poll.brev.m: C = Dors.int.1.m; N = mean of normals.



31.

Case L.W.W. Ischaemic paresis of hand muscles after bomb wound of elbow. Muscles working weakly. High rheobase and normal chronaxie significant of ischaemic muscle damage. A = Abd.poll.brev: B = Dors.int.1: C = Abd.dig. min: N = mean of normal contralateral muscles.

ischaemia was confirmed by a venogram X-ray taken immediately after injection of a radio-opaque substance, and this indicated probable thrombosis of the main deep veins in the elbow region. This thrombosis presumably resulted rapidly from the injury, caused the transient ischaemia, and was compensated by collateral channels later on, leaving the clinical picture of adequate circulation but residual muscle fibrosis.

A further example, Case L.W.W., Fig. 31, shows very similar records. In this instance the injury was brachial artery ligature for haemorrhage caused by a bomb fragment wound above the elbow. The muscles when examined felt firm, general hand circulation was poor, and the power very small. The characteristic features of normal chronaxie with very high rheobase are well shown. In this case the V-T curves afforded a piece of information of practical value, for it had been suggested that in addition to the arterial damage, median nerve injury had also occurred. That this was very unlikely was shown by the fact that Flexor digitorum sublimis and abductor pollicis brevis had normal chronaxies although very weak, indicating normal innervation with ischaemia as the cause of the impaired function.

In /

In the majority of ischaemic muscles, however, the records are not so clear cut as in the cases presented. Our conclusions are as follows. In mild ischaemia, the muscle chronaxies will be normal and the rheobase level very high. Whether galvanic or faradic response can be elicited depends entirely on the skill of the administrator and the patient's tolerance, for both responses are theoretically present. In more severe cases (and the severity refers of course to the initial episode, and not necessarily the limb's condition when examined) the above findings are probably present, but can rarely be identified because of the very great intensities required. It is probable that they could be detected under anaesthesia. In ordinary practice, both galvanic and faradic responses are lost, although ruthlessly applied galvanic shocks may be effective. Faradic response is, strictly speaking, present, but not detectable because of the subject's limit of tolerance. In very severe cases no muscular elements may be present, and therefore no agent, electrical or otherwise, can elicit response. In combined injuries of vessel and nerves, of which we have examined a number, electrical excitability is usually not found, for the good reason that as both denervation /

denervation and ischaemia tend to raise the rheobase, their combined effect raises the threshold to impossible values. We may conjecture that if the ischaemia is not too severe, a typical "denervated" V-T curve might be obtained, but the level would be so high that several hundreds of volts would be required. The muscle-testing of such subjects does not therefore serve any very useful clinical purpose, as a report of inexcitability may be misleading; absolute inexcitability must be reported only after testing under anaesthesia.

The reason for the elevation of rheobase with retention of normal chronaxie must be presumed to lie in the physical structure of partially ischaemic muscle, which consists of groups of histologically normal fibres surrounded by exaggerated quantities of fibrous tissue distributed, broadly speaking, fairly evenly throughout the muscle. Any electric current must first traverse inert portions of "muscle" before gaining access to the true innervated contractile elements, and to possess adequate intensity on arrival at these elements must be applied with greater intensity than normal. The muscle fibres themselves appear to be normal in excitability, and the raised rheobase due to the admixture /

admixture of muscle with inert fibrous tissue. We have pointed out that these findings only apply definitely to a certain stage of partial ischaemia, and that practical limitations prevent investigation in the majority of ischaemic cases.

5.7. V-T Curves during Muscle Re-innervation.

From the point of view of value as an adjunct to clinical examination of nerve injury cases, the most important information is that to be obtained from a study of the recovery of excitability in re-innervating muscle. We have seen in Section 4.3.2. that the galvanic-faradic test is of very little use in this respect, for voluntary power recovers clinically before the return of faradic response. In the account of the electromyogram technique in Section 4.4. it is noted that normal action potentials can be detected in recovering muscle before voluntary power returns, but that they may not always be so detected without very extensive needle exploration of the muscle; so that while a positive electromyogram means re-innervation beyond any doubt, a negative one does not necessarily mean absence of regeneration.

Neither action potential recording nor methods of stimulation can distinguish between the lesion in continuity and the complete nerve pattern disruption except by detecting recovery at a certain date after injury and deducing therefrom the probable nature of the injury. We have therefore examined as many cases as possible with a view to discovering whether precision methods of stimulation can give advance /

advance information of re-innervation of muscle before the clinical evidence of voluntary power makes regeneration obvious. The procedure has been the same for all the cases; V-T curves have been recorded from all muscles distal to the lesion (except such as may be quite inaccessible, or damaged by gross loss of substance or injury separate from the nerve lesion) at weekly intervals after admission, and after operation, if that was carried out. At each examination control curves were recorded from the normal muscles. We shall first show a number of individual case records before assessing the results as a group.

Case W.H.P., Fig. 32, sustained a blow on the upper arm from the airscrew of an aeroplane which he was starting by hand. The blade hit him a glancing blow on the arm, and an apparently more important blow on the thigh. The leg wound was a fairly deep cut; the arm wound caused no bruising or damage to the skin or soft tissues but resulted in complete radial paralysis. The first examination was carried out 4 weeks after the injury, when the radial muscles were quite inactive voluntarily. No sensory loss was detectable. The voltage-time curves from the muscles were quite typical of complete denervation, showing that the injury was not a severe pressure palsy, as might have been considered likely in view of /

of the history and the absence of sensory defect; high radial nerve section, however, not uncommonly leaves no impairment of sensation. It was considered advisable to explore the nerve because of the total denervation, and at operation the radial nerve was found completely divided as regards axon structure, and held merely by a thread of fibrous investment. The ends were trimmed and sutured together one month after the injury. This was a somewhat surprising state of affairs because of the relatively slight trauma which had caused nerve rupture.

In view of the early operation, and the closed nature of the injury without any complication of sepsis or haematoma, the case was followed with great interest; the patient himself was an intelligent and pleasant young man interested in the procedure of muscle-testing. As Fig. 32 shows, the first significant decrease in V-T curve, chronaxie, and Lassalle index occurred in extensor digitorum communis ten weeks after the suture operation; after 6 further weeks a flicker of voluntary power became detectable in the same muscle; only after a further nine weeks was faradic response - tested in the usual way, qualitatively - recorded.

These salient episodes are shown on the graph /

graph; curves were recorded in addition every week from the other muscles, in all 142 records being made on this subject. Brachio-radialis muscle, in spite of its more proximal anatomical position to the lesion, showed identical signs of recovery one week later than the muscle graphed. We have frequently found that the nearest muscle is not necessarily the first to re-innervate, especially after suture; in any case, ext. communis is an easier muscle to detect and examine. Unfortunately for the sake of investigation, we have not got regular weekly curves on many patients after the first sign of recovery is definite; this is only natural in the disposal of Service patients, who once known to be on the road to recovery, are kept on as out-patients, or sent to some convalescent hospital, where we review them only at intervals. This does not matter, of course, from the practical point of view, for once regeneration is known to have begun, no further procedure will be carried out surgically except in a few cases of arrest of nerve growth, and the patient will recover gradually on his own. But it means that we cannot present evidence from any large series about the course of recovery in more distal muscles. The difficulty is common to all clinical research workers, and Seddon, Medawar and Smith /

Smith (1943) make the same comment in connection with estimating rate of regeneration of human nerve. We shall sum up such results as we have at a later stage in this thesis.

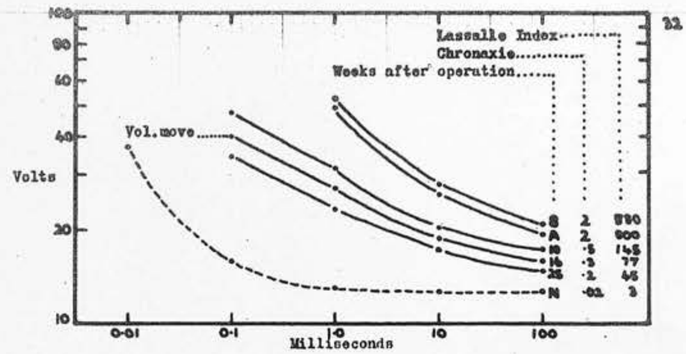
The interest in patient W.H.P. lies in the curiously minor cause of a complete nerve section, the very rapid (and ultimately complete) recovery of a radial nerve sutured under the most favourable conditions of early operation in a closed injury, and in the detection of recovery by means of excitability recording several weeks before clinical certainty. This was one of our earlier cases, and was very encouraging. In Fig. 32 we see that intermediate values for chronaxie and Lassalle Index do exist and are revealed by this method of examination. To be reasonably certain that alterations in V-T curves are significant involves a fairly elaborate procedure; the graphing of the variation range of the normal muscles, and the muscles as examined up to the 9th week, when they were still apparently denervated. The record at the 10th week from the muscle figured fell without the range, and the corresponding normal V-T curve did not fall without its range, so that the probability of instrumental or human error was largely obviated. Nor, in this case at any rate, could vasomotor /

vasomotor or sensory recovery have affected the passage of current or its toleration, for no such disability ever existed. A similar method of assessing the curves has been adopted throughout, and is probably unnecessary, as the significant alteration can, in our experience, be appreciated quite well by eye from the graph, and by chronaxie and Lassalle index calculation; however, the statistical principle adopted was a sound way of testing the method's value in the early stages.

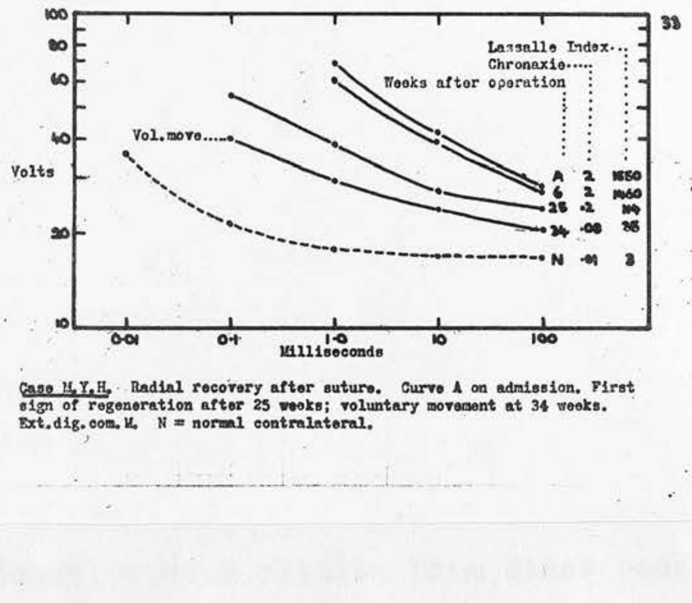
Another case of radial nerve injury and recovery after suture is shown in Fig. 33, that of M.Y.H., a WAAF truck driver whose vehicle was struck by a taxi-ing aircraft and overturned. She sustained a fracture of the humerus with immediate complete radial paralysis, and was admitted to the nerve unit four weeks after the accident. We kept her under observation for a further four weeks without detecting any recovery, and at that time open operation was performed, the nerve found divided, and sutured high in the upper arm. The graphed curves show that the records on admission, and 6 weeks after operation (being ten weeks after first examination) correspond almost exactly, and are typical of total denervation. No excitability improvement was noticed until the

25th /

Figs.32 & 33.



Case W.H.P. Radial nerve recovery after suture. Curve A on admission. First sign of re-innervation at 10 weeks; voluntary movement detected at 16 weeks. Ext.dig.com.M. N = normal contralateral M.



Case M.Y.H. Radial recovery after suture. Curve A on admission. First sign of regeneration after 25 weeks; voluntary movement at 34 weeks. Ext.dig.com.M. N = normal contralateral.

25th week after operation, when the chronaxie and Lassalle index suddenly altered; voluntary recovery was noted nine weeks later for the first time, and, in this case, faradic response returned simultaneously. The end result of this suture was very good indeed, in spite of the long delay before regeneration appeared definite; no doubt the high level of the suture and the disturbed condition of surrounding tissues account for this to some extent. The interval between "electrical" recovery and power was the longest in this case that we have encountered - nine weeks in extensor digitorum muscle, ten weeks in extensor carpi ulnaris, and ten weeks in abductor pollicis longus muscle. An interval of only five weeks was recorded for brachio-radialis muscle, and in fact we noticed the excitability improvement in extensor digitorum before that in brachio-radialis, although the latter showed voluntary movement a few weeks before. These findings will be discussed later on in conjunction with results from other cases.

This advance information of muscle re-innervation is of some practical value, saving some time in the long wait for recovery and informing the surgeon that the suture has been successful to the extent of fibre regeneration. It has been a regular observation /

observation in all the cases which we have been able to examine at weekly intervals, although the actual period between improvement of excitability and clinical recovery is variable. Out of a series of 17 cases of radial nerve degeneration followed up from the time of operation in this way, all have shown such an interval; averaging 4½ weeks for the higher muscles such as extensor communis and carpi ulnaris, and rather longer, 5½ weeks, for the more distal abductor and extensors of the thumb. The figures for the distal muscles are not so trustworthy, as the patients often were not available for weekly examination after the initial signs of recovery.

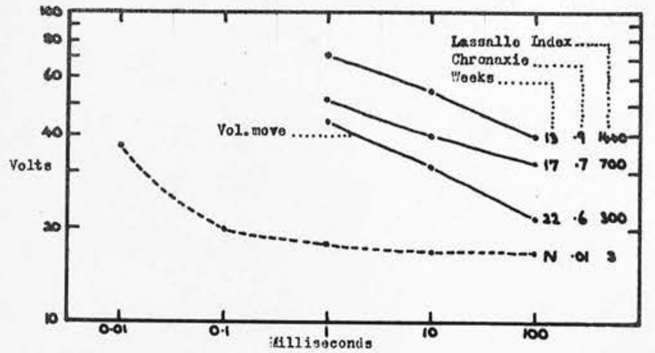
Cases W.H.P. and M.Y.H. already described are the two most obvious instances in our series; two more doubtful examples are shown in the next plate, Figs. 34 and 35. D.R., Fig. 34, was injured by mortar bomb fragments traversing the arm just above the elbow, and was admitted 10 weeks after the incident, which occurred in Italy. Brachio-radialis and extensor carpi radialis were both fairly strongly active, and had apparently been so from the early stages after the wound healed, but there was complete radial paralysis below that level. V-T curves recorded from the extensor digitorum communis muscle showed /

showed improvement five weeks before recovery of voluntary power, but the improvement was not marked, and was on the verge of the lower limit of this patient's variation. At the time no definite opinion was ventured, but the muscle did recover voluntary power in five weeks with a consistently lowered excitability curve. Faradic response was not present when this patient was sent to a convalescent hospital, although voluntary contraction of the finger extensors was quite obvious.

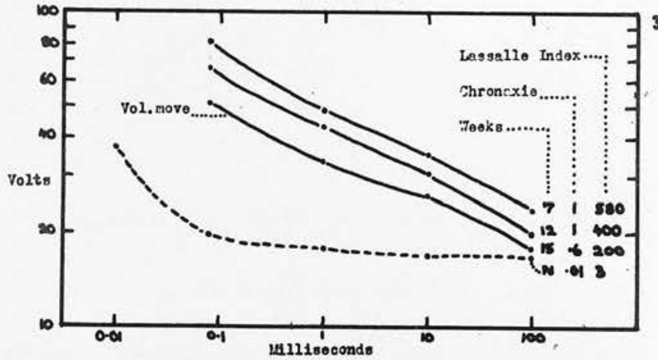
A rather similar case, C.N., Fig. 35, was wounded by machine-gun bullets in the elbow region, and the course of recovery in the proximal denervated muscle was followed. Improvement of excitability, of doubtful certainty for prognosis, was detected three weeks before voluntary recovery. This patient was then transferred to a hospital nearer his home, and was not followed up.

Neither of these last two examples were operated upon, and the recovery was spontaneous. We cannot tell definitely whether the nerve lesion was one in continuity, or a section with good apposition of the ends and consequent regeneration. Comparison with the time taken for recovery of sutured cases suggests that section was the lesion in both cases, as /

Figs.34 & 35.



Case D.R. Radial nerve recovery - spontaneous. Ext.dig.com.m. Doubtful signs of re-innervation 5 weeks before voluntary recovery.



Case C.H. Radial nerve recovery - spontaneous. Ext.dig.com.m. Doubtful signs of re-innervation 3 weeks before voluntary flicker detectable.

as the distance involved in regeneration was relatively short.

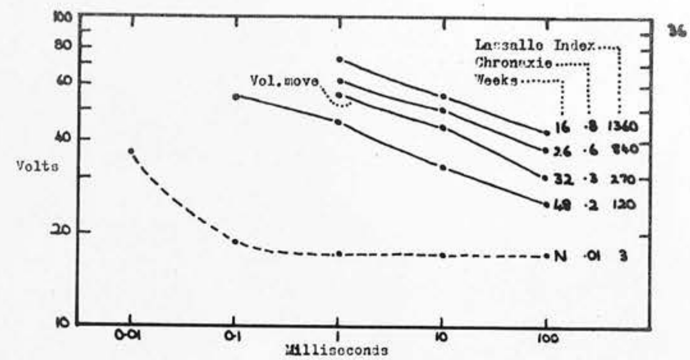
The occurrence of an interval between excitability improvement and voluntary power recovery is not confined to cases where the nerve has been sutured, or has regenerated across a gap, and therefore does not depend on the shuffling of fibres which inevitably disturbs the nerve pattern in such cases. It is not easy to be sure that one is dealing with a "lesion in continuity" without anatomical whole nerve section, as there is no certain test for this apart from surgical exploration; the experience of the Nerve Unit here has been that where exploration is carried out the nerve is usually found divided. In other words, it appears as if the classical lesion in continuity is rather rare, and that many of the cases where rapid recovery from denervation has been believed due to such an injury may actually have had complete nerve section with good apposition of the severed ends. We have not been able to collect more than five examples where the nerve lesion was reasonably certainly not a complete section and separation. Two of these are given in detail below.

Case W.G., Fig. 36, developed a complete radial paralysis shortly after an anti-tetanus injection /

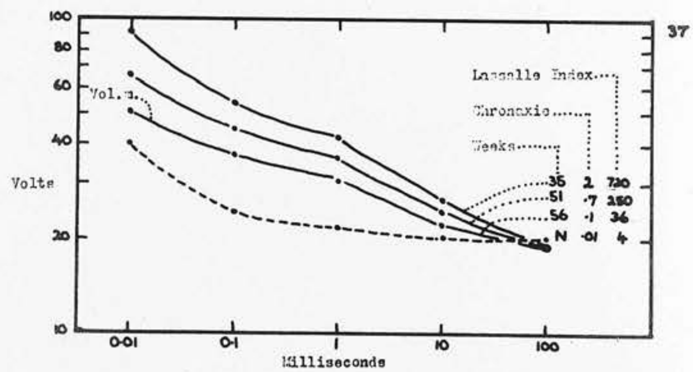
injection into the triceps muscle. This recovered spontaneously but very slowly, and the excitability records of the course of recovery parallel these four cases of known section and suture. After 26 weeks recovery was detected, preceding recovery of movement by 6 weeks, and faradic excitability by 9 weeks. In this case the V-T curves are from the brachio-radialis muscle, and the recovery therefore very slow. Ext. carpi radialis and extensor digitorum showed the same interval; the former recovering 2 weeks after brachio-radialis, and the latter 8 weeks after, which is about the average, so that we may conclude that the delay in regeneration was at or near the site of damage and not due to all-over slowing of axon growth.

Case P.C., Fig. 37, developed a radial paralysis from dislocation of the head of the humerus 8 months before our first examination, at which time triceps was active and fairly strong, brachio-radialis active but very weak, and the wrist and finger extensors completely denervated. Regeneration was evidently proceeding, but the patient was kept under observation because of the long delay in appearance of any further recovery. Good recovery did ultimately come about, but was very slow; 18 weeks after the first examination (just over a year from the accident) improvement /

Figs.36 & 37.



Case W.G. Closed radial nerve injury from ATS inoculation into triceps. Very gradual recovery - doubtful signs of regeneration 6 weeks before voluntary trace. Muscle still weak and poorly innervated after 48 weeks.



Case P.C. Closed radial nerve injury from shoulder dislocation injury. Signs of re-innervation 5 weeks before voluntary flicker. Ext.dig.com.m.

improvement in excitability appeared in ext. carpi ulnaris and ext. digitorum simultaneously, and was followed five weeks later by active movement in these muscles. This patient's records had the unusual feature of a very constant and rather low rheobase for the muscles, and this enables the curves to be compared readily on the graph; chronaxie and Lassalle index figures are typical.

The foregoing examples have been of radial nerve injuries, because in damage to that nerve muscular examination is the most important practical feature. As we have pointed out, complete radial section may result in very little, if any, sensory loss, and no autonomic functions can be used as signs of regeneration. It has therefore been in radial nerve injuries that the method of muscle examination has been of most practical value, and most often employed. But similar features hold good in the course of recovery in ulnar and median nerve injuries also.

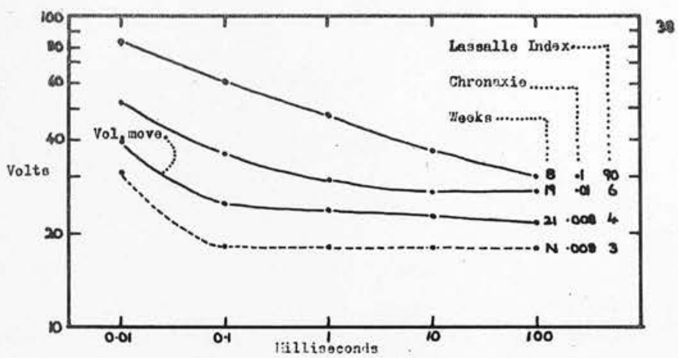
Case W.P., Fig. 38, had his ulnar nerve sutured just below the elbow after transection by a machine gun bullet. After 19 weeks the V-T curve of the first dorsal interosseus muscle suddenly came down to almost normal level, with chronaxie of 0·01 and /

and Lassalle Index in single figures; a trace of active movement appeared a fortnight later, and very little further improvement in power took place. 44 curves in all were recorded from this subject, and confirm what might be expected, that improvement in excitability gives evidence of regeneration, but no account whatever of the amount of ultimate recovery.

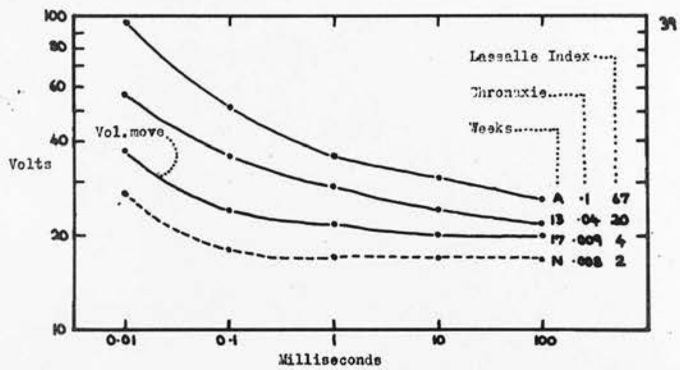
Case H.S., Fig. 39, required a median nerve suture about the mid-level of the humerus after a bomb fragment injury. 13 weeks after this operation, re-innervation became evident in the Flexor sublimis muscle and active movement 4 weeks later. Although fair power was ultimately regained in the forearm flexors, no signs of re-innervation appeared in the thenar muscles after 18 months. A slight amount of sensory recovery did take place over the palmar surfact of thumb and first two fingers, but regeneration evidently did not take place to the extremity of the median nerve's distribution. This is a common finding in repairs of the ulnar and median nerves, which have a very mixed composition of motor, sensory and autonomic fibres.

An interesting example of the possibility of muscle re-innervation unaccompanied by active power is shown by case W.T.A., Fig. 40, in whom one facial nerve /

Figs.38 & 39.



Case W.P. Ulnar nerve regeneration after suture. Dors.int.1.m. Injury below elbow. Recovered weak voluntary power after 21 weeks; no progress thereafter. Interval between first innervation and vol.power 2 weeks.

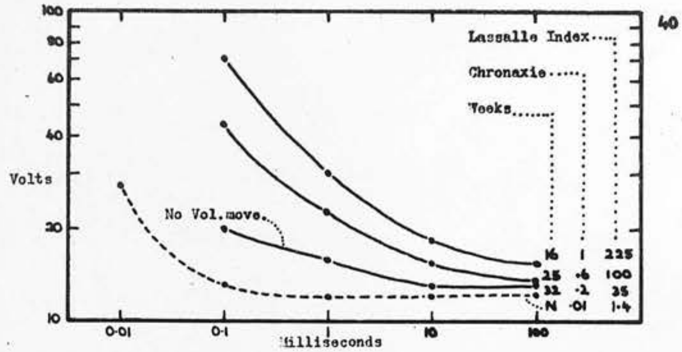


Case H.S. Median nerve recovery after suture. Fl.dig.subl.m. Signs of re-innervation 4 weeks before voluntary movement appeared. Fair strength regained in forearm muscles; no detectable re-innervation of small muscles.

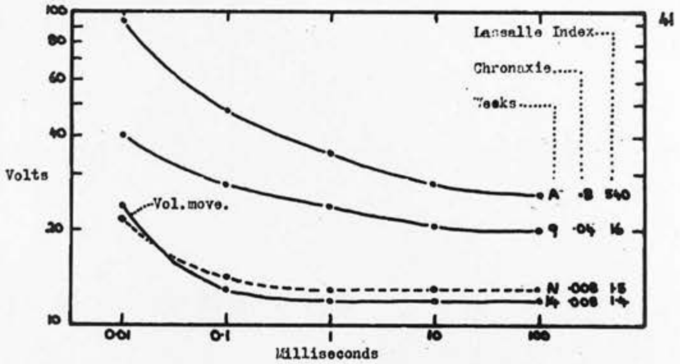
nerve was accidentally cut during an elaborate mastoid operation. Recovery in the histological sense undoubtedly took place, as the V-T curves gradually returned toward the normal over a period of seven months. A considerable amount of "tone" came back, and the patient was obviously improved clinically, but had no power to move the muscles at will. This is quite characteristic of facial nerve recovery after section; muscle tone is very often recovered, and the disability of drooping eyelid and mouth overcome thereby, but individual movement of muscles and the ability to alter facial expression is frequently never regained. We have observed 8 such cases in which the records and clinical course are almost duplicates of the above.

Case W.T., Fig. 41, is a further example of ulnar nerve recovery after suture, which was performed above the elbow for transection of the nerve by mortar bomb fragments. Excitability recovery indicating re-innervation appeared at 9 weeks in Fl. digitorum profundus muscle, 5 weeks before active movement. This is the longest interval recorded from ulnar innervated muscles. When voluntary movement re-appeared, the V-T curve was practically back to normal, and faradic response was regained.

The course of recovery as regards excitability /



Case W.T.A. Facial nerve recovery after section. Re-innervation at 25 weeks, clinical recovery of tone at 32 weeks, but no voluntary movement. Occip.-front.M. N = normal contralateral.



Case W.T. Ulnar nerve recovery after suture. A = on admission. Signs of re-innervation at 9 weeks; voluntary recovery delayed until 14th.week, when V-T curve normal. Fl.dig.prof.M. N = normal contralateral M.

excitability and voluntary movement can best be summarized in tabular form. The majority of the observations have been made on radial nerve sutures, and have been on the upper muscles of the forearm, for reasons of availability of patients for weekly examination. Re-innervation as reckoned by excitability improvement is assessed as previously described, by lowering of the V-T curve outwith the "denervated" range, and therefore only cases regularly examined can be included. Return of voluntary movement and faradic response is judged not by myself alone, but by the reports of the physio-therapy staff and other medical personnel.

<u>Nerve</u> /

Nerve & type of lesion.	Time between V-T improvement and voluntary recovery.		Time between vol. recovery and Faradic response.		No. of cases.
	Mean	Limits	Mean	Limits	
	Weeks		Weeks		
Radial nerve:					
High Section	5½	3 - 11	3	3 - 6	17
Low Section	5	3 - 9	2½	0 - 6	12
Continuity	4½	4 - 8	3	2 - 6	5
Median nerve:					
Section above elbow	3	2 - 7	4	2 - ?	6
" below elbow	3	2 - 9	1	1	7
Continuity	2	2	2	2	1
Ulnar nerve:					
Section above elbow	3½	2 - 9	7	4 - ?	9
" below elbow	4	1 - 5	5	0 - 9	8
Continuity	3	3	3	3	1
Facial Nerve:					
Section	9	6 - ?	2	0 - ?	11
Continuity	9	5 - ?	2	0 - ?	4

The mumber of examples in several of the groups is too small to make the results significant. We can, however make the following generalizations from these results. 1. There is a definite "advance /

"advance information" to be got from careful V-T curve reading; the actual interval is of the order of a few weeks, and appears undoubtedly longer in the radial and facial nerves than in the more mixed median and ulnar. 2. After the establishment of voluntary power, faradic response, as usually tested, definitely is delayed (as in the traditional teaching on the point) and this delay is again of the order of a few weeks, but very variable, and indeed in certain instances faradic response does not seem to re-appear. This is usually in the cases where full regeneration fails to occur. 3. In certain cases, notably these of facial nerve injury, V-T improvement may not imply ultimate recovery, though improved tone always followed improved excitability. In other nerves, recovery of excitability and voluntary movement is no guide whatsoever to ultimate recovery of strength. 4. The interval between excitability improvement and active recovery is probably not significantly different in cases of complete nerve section and these of "lesions in continuity". The evidence on this point is inadequate. 5. There is some indication that the interval increases as the distance of the muscle from the site of nerve injury increases. This is probably not significant. Grouping the results /

results in another way, we see this tendency again, though not conclusively:

Radial nerve - anatomical section above elbow.

Muscle name	V-T-Vol.M Interval		Vol.M. to Faradic Resp.		No. of cases.
	Mean	Limits	Mean	Limits	
Brachio-radialis	4	3 - 5	2	1 - 6	15
Ext. carp radialis	6	2 - 7	2	1 - 6	15
Ext. dig. communis	6½	2 - 11	3	0 - ?	17
Abd. pollicis	5	3 - 9	3½	2 - 6	12
Ext. brevis poll.	6½	2 - 11	3	2 - ?	12

In the above table many of the cases overlap. On the whole the more distal muscles, in any one individual patient, show a week or two longer in the "advance information" interval. This is of little practical importance, unfortunately. 6. In no instance have we detected a significant alteration in excitability which has not been followed within a period of 11 weeks by signs of active movement. In other words the technique as described seems to be reliable. 7. In seven cases the irregularity of the variation of normal and denervated curves was such that no prognosis was given and these seven did in fact recover. There was no apparent reason for the failure of the method in these cases, and the V-T curve record was some weeks in advance of the faradic response, though of no value from the practical point of view because of the voluntary improvement.

5.8. Wallerian Degeneration.

During the first few days after a nerve injury which is severe enough to cause axon degeneration, the excitability of the muscle changes from normal to denervated. This process takes some little time, for although function is lost immediately on interruption of the nerve fibres, the muscle remains "innervated", with the normal anatomical and chemical arrangements at the neuro-muscular junction until degeneration has extended from the site of injury right down to the fibre terminations in the motor end-plates. This has been recognized since the time of Erb, who described in 1876 the retention of faradic response for an average period of ten days in muscle where nerve had been sectioned; he further pointed out that during this period the neuro-muscular mechanism was commonly hyper-excitable, and responded to less current than usual.

This retention of faradic response in the early days after injury is a source of difficulty in electro-diagnosis. It so happens that the geographical situation of the Gogarburn Unit, and the military arrangements for immediate disposal of casualties, have prevented us from examining many cases in the first /

first few days of injury, and those who have been injured in the neighbourhood and seen early have had wounds interfering with muscle testing. We can therefore only show two cases followed completely from the first day or two. Conversation with physiotherapists from centres receiving fresh nerve injuries reveals that this early stage of Wallerian degeneration is not too well understood, and that too much is expected from electro-diagnostic measures; their complaint being that they are frequently asked to perform a muscle test on a patient within a few days of nerve injury, and that information regarding muscle denervation is expected from such a test, whereas the usual finding of faradic response present is no guide to the actual condition. The general opinion seems to be that faradic response is retained in fore-arm muscles for a period of about ten days after nerve section in the upper arm, and for about three weeks in the small muscles of the hand, to reach which the degenerative process has considerably further to descend.

Case A.H., Fig. 42, sustained a knife wound in a brawl, and developed a complete ulnar nerve paralysis below the elbow, with typical ulnar sensory and autonomic defect. From the position and size of the /

the wound just above the elbow, it seemed almost certain that the ulnar nerve had been completely severed above the supply to flexor carpi ulnaris muscle. 8 days after injury faradic response was still reported in all the ulnar muscles, and the V-T curves were practically normal. On the 13th day the faradic response disappeared from flexor carpi ulnaris and from flexor digitorum profundus and the V-T curves revealed the rising chronaxie and Lassalle Index. The curves from the dorsal interossei muscles were still in the normal range; faradic response was lost there on the 16th day. 23 days after the nerve section all the ulnar muscles give typically denervated responses and curves. Fig. 42 represents the curve of degeneration in flexor digitorum profundus, and that in flexor carpi ulnaris was identical. The small ulna muscles ran a very similar course several days later.

The table below shows the course of the degeneration.

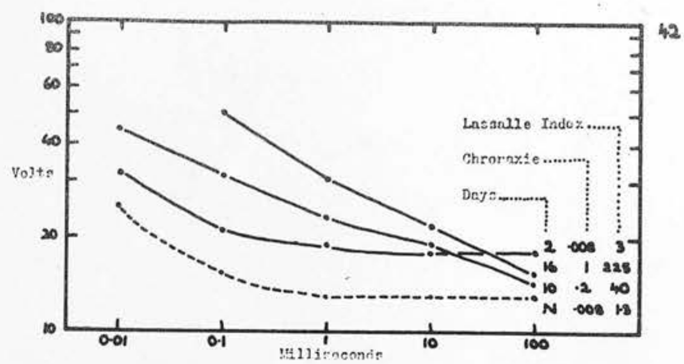
<u>Muscle</u> /

Muscle	First increase of chronaxie	Disappearance of faradic response	Complete Denervation
Fl. carpi ulnaris	8	13	21
Fl. dig. profundus	9	13	21
Abd. dig. minimi	12	15	23
Dors. int. I	13	16	23

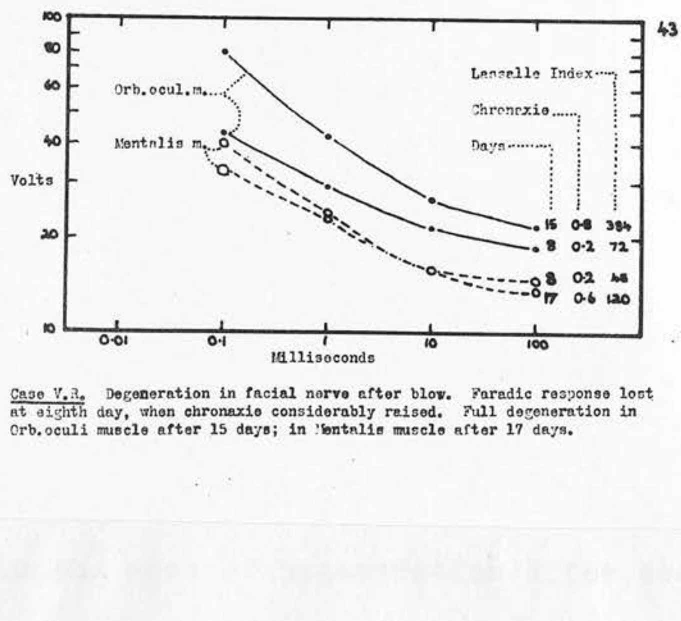
Figures represent days after ulnar nerve section.

Another most interesting case was that of V.R., Fig. 43, a girl of 8 years, who ruptured her facial nerve with an apparently very mild blow while at play. The history given was that the child, playing under the table on all fours, became unbalanced and fell over sideways striking the side of her head on the square-sectioned table-leg. "She rose from the ground with her face squint," to quote the mother's own words, and did in fact sustain a complete facial nerve paralysis without complete division of the nerve, although the soft tissue damage was limited to bruising. This patient was examined through the kindness of Mr Norman Dott, and has not yet completed recovery. The facial muscles on the 8th day after injury showed absence of faradic response (faradism is not well tolerated in that region /

Figs.42 & 43.



Case A.H. Records from Fl.dig.prof.m. during degeneration of ulnar nerve after complete knife section at elbow. Figures are days after injury. Faradic response weak at 5 days; absent at 10 days. Curve typical of complete nerve degeneration after 16 days.



Case V.R. Degeneration in facial nerve after blow. Faradic response lost at eighth day, when chronaxie considerably raised. Full degeneration in Orb.oculi muscle after 15 days; in Mentalis muscle after 17 days.

region, especially in a child), but complete degeneration was not definite until the 17th day after the nerve injury. There was not a great deal of difference in time of degeneration; the mentalis muscle was the last to show total denervation, 2 days after the others.

The results of quantitative stimulation of muscles during the process of degeneration are very important from the point of view of interpreting excitability records during recovery, for we have the whole course run through from normal activity to total denervation in a few days as compared with the many weeks of recovery. It is to be regretted that we have not been able to see more cases. However, there seems little doubt that after nerve section the muscles exhibit a gradual lengthening of chronaxie and rise of Lassalle index, and that the intermediate values are similar to those found in the process of recovery. Yet the two circumstances are not identical. In the case of degeneration after section there can be no partial innervation of the muscle in the sense that some nerve fibres are intact and the others severed, for in such section all the fibres are divided simultaneously, and we must assume that they degenerate at roughly the same rate. In muscle re-innervation /

re-innervation, however, we have some normal completed fibres, and some not as yet re-grown and matured. The intervening values of V-T curve between normality and denervation must therefore be connected with changes in the peripheral neuro-muscular complex alone, and this will be considered in more detail in the Disunion section to follow.

5.9. Anomalous Innervation of Muscles.

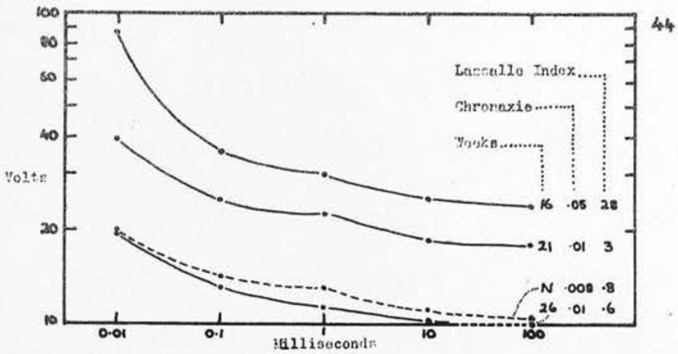
In the course of examining a large number of muscles by stimulation, various anomalies and unusual findings turn up from time to time. The diagnosis and prognosis from results of stimulation alone should never be regarded as more than a valuable adjunct to thorough clinical examination. One of the relatively common anomalies encountered is that of anatomical innervation of a given muscle by a nerve other than the usual motor supply; such abnormal innervation may be complete, but is more usually partial, and this is a possible source of confusion.

Case W.T., Fig. 44, presented several features of unusual interest. He sustained two wounds of his ulnar nerve, one above and one below the elbow joint, with complete anatomical division at both ends. There was therefore an intermediate length of nerve completely detached at both ends which might be regarded as a "graft" composed of the subject's own nerve, exactly the right size, lying in an undisturbed and natural bed, and merely requiring apposition and suture at upper and lower ends to provide a control experiment of the efficacy of nerve grafting under the most ideal conditions! This was actually done, but the final results cannot yet be assessed /

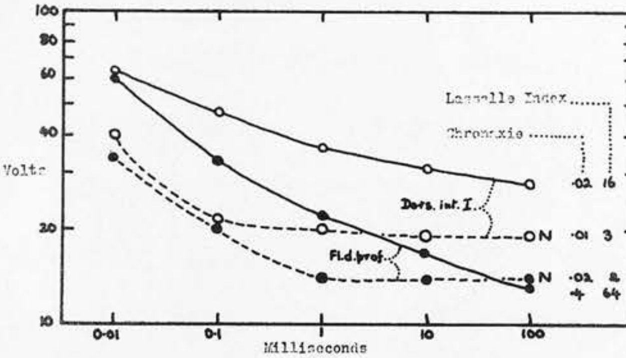
assessed, as time for final recovery has not elapsed. In the course of measuring muscle excitability on this patient we observed after operation total paralysis of the flexor digitorum profundus muscle to the little and ring fingers, and this gradually recovered voluntary power and increased excitability. The operation notes, however, state that all the ulnar motor nerve branches to the profundus muscle were deliberately sacrificed during the operation. In view of the suture line above the sacrificed branches and the fact that no recovery in any other muscles was detectable at the time, or for long after, the possibility of true regeneration seems unlikely; and we may speculate whether in a muscle like flexor digitorum profundus, which has a nerve supply both from median and ulnar (although the two muscle sections are usually clearly defined) a certain amount of function can be regained in a denervated position from extension, anatomical or chemical, of the activity of the other normal part. This is not an isolated example, for we have V-T records of three muscles which improved both in excitability and power after complete division at operation their motor branches. All three muscles were flexor digitorum profundus anatomically, but this is inconclusive, as it /

as it happens to be that muscle which is most commonly deliberately denervated as far as the ulnar motor component is concerned during the operation of anterior transplantation of the ulnar nerve. It is possible that all motor branches are not cut at the operation, but this is unlikely in view of the good exposure of the nerve and its branches and because of the total denervation which is indicated soon after operation. The true reason is not therefore exactly known, and one must bear in mind that recovery of a partially denervated muscle such as flexor profundus after ulnar section is not an absolute sign of true ulnar regeneration, and must be confirmed by indications of re-innervation in other muscles supplied by the ulnar nerve before being used as a definite prognostic sign.

Case M.M., Fig. 45, is a more common and simpler instance of anomalous innervation. This patient had an ulnar nerve suture performed in the upper arm for a missile injury, but did not lose weak active movement in the interosseous muscles of the hand. The graph shows the V-T curves for Flexor profundus and for the first dorsal interosseus muscle, and the corresponding normal muscles; profundus was initially denervated, and remained so for 22 weeks, and /



Case W.T. Re-innervation of Fl.dig.prof.m. after surgical division of the motor nerve branches. Re-innervation in this instance was accidental, as the nerves were divided to mobilize the main trunk for other reasons. N = normal contralateral m. Possible accessory innervation?



Case H.H. Anomalous innervation of ulnar hand muscles. Records 8 weeks after ulnar nerve suture in upper arm. Fl.dig.prof.m.denervated, but Dors. int.1.m.has partial innervation and weak voluntary movement in spite of known ulnar nerve section. Solid circles = Fl.dig.prof.m. Clear circles = Dors.int.1.m. N = normal contralateral in both cases.

and in spite of an unusually low rheobase and an accordingly low Lassalle Index has denervated excitability. Dorsal interosseus I, however, weakly active before and after the ulnar nerve suture, had a chronaxie of 0·02 milliseconds, Lassalle index of 16, and was evidently partially innervated by the median nerve.

Innervation of the small muscles of the hypothenar eminence and of the interossei by the median nerve is fairly common, and we have recorded 7 such cases; it does not as a rule cause confusion, and is usually detectable clinically. The problem arises in connection with ulnar nerve injuries where the weak activity of muscles which are normally ulnar-supplied leads to doubt as to the condition of the ulnar nerve. Usually the total denervation of proximal ulnar muscles gives a pointer to ulnar nerve section; in cases of ulnar nerve injury at the wrist level median nerve block by local anaesthesia may be necessary to determine the function of the ulnar. In such circumstances the V-T curves are of little help; they may be of value where the anomalous median component is very small, and only capable of doubtful voluntary movement if any at all. In such cases the V-T curves will reveal the partial innervation /

innervation, but this is of largely academic interest because of the very considerable defect due to ulnar loss requiring repair in any case. The most confusing circumstance is that where the anomalous component is small, undetected clinically, and yet giving some evidence of innervation to the stimulator shocks. The muscle tester is then apt to give a report of re-innervation when such is not the true state of affairs, the innervation being there in truth, but original and anomalous, and not regenerated.

We have three times fallen into this trap and given an erroneous report of recovery which was not borne out later on. This should not happen if careful records of the small muscle V-T curves are kept, and if these records are made before and after operation. In the cases which mislead us, the examination was conducted for the first time sufficiently long after operation for recovery to have been a reasonable possibility; had we examined the cases before and shortly after operation we should have known that the partially innervated muscles could not have been so by process of regeneration. The possibility of being misled by anomalous innervation is always present, and especially in dealing with ulnar-supplied /

ulnar-supplied muscles very careful regular examination from the early stages, supplemented with due consideration of other clinical details such as sensory loss and recovery, is essential if the report is to have any real worth.

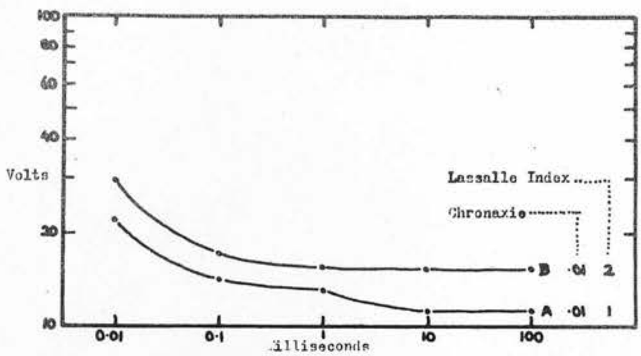
Finally, we have encountered a few cases where some glaring anomaly in the V-T curves as compared with clinical examination had no obvious explanation. Fortunately, these were rare; only in 4 cases out of 370 examined was the stimulation method an obvious failure. One such case, G.R., Fig. 46, showed every clinical sign of complete radial denervation from wounds in the upper arm, yet on stimulating the radial muscles, their V-T curves were perfectly normal. This provoked a diagnosis of hysterical paralysis (the patient was a German storm-trooper, prisoner-of-war, and a very nervous subject), but the weight of clinical evidence decided for operative exploration. No nerve injury was found at the operation, but the muscles did not respond to stimulation of the exposed nerve. Nothing was done at the operation, and the patient was transferred elsewhere soon after, with normal excitability and complete clinical paralysis. There is no satisfactory explanation for these findings.

Hysterical /

Hysterical paralysis would have revealed response to the nerve stimulation at operation; and so would a high pressure palsy without resulting denervation. A possible explanation would be an anomalous innervation of the radial muscles together with a functional paralysis, for in such a case high damage and degeneration of the radial nerve would account for the lack of nerve activity on stimulation, and a relatively small accessory innervation might give normal V-T records to the muscles, but either from inadequacy or hysteria might not be able to cause active movement of them. This explanation is perhaps far-fetched. As the patient has been lost track of, the course of recovery, if any, is unknown. Only one such case has been encountered.

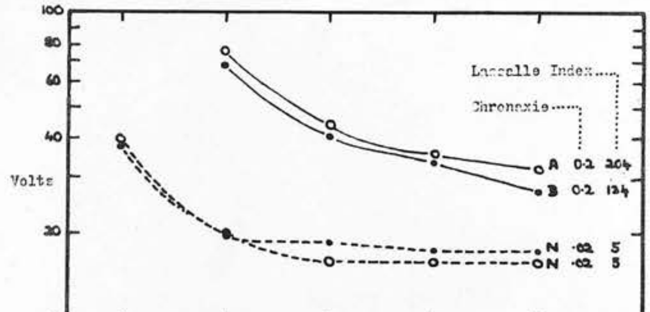
Three cases have been examined who demonstrated the reverse anomaly, namely good muscular power accompanied by a denervated type of V-T curve. Fig. 47 shows the records from two of these cases. Both had recovered from an organic radial nerve lesion, and had recovered almost normal power in the finger extensors, and yet persistently exhibited a "denervated" curve until discharged! The third case showed the same features in the triceps muscle, and /

46



Case G.R. Radial palsy from high lesion. Clinically complete paralysis below br.-radialis m. Curve A = Ext.dig.com.m. on admission, of normal type. Operation disclosed no nerve damage. B = same muscle 2 weeks after operation. Diagnosis - query functional paralysis?

47



Case H.T. (clear circles) and Case J.S. (full circles). Apparent curves of denervation from Ext.dig.com.m. after high radial injury. In both cases the muscles were strongly active voluntarily, though not responding to faradism. No known explanation of this anomalous finding.

and was indeed operated upon partly on the strength of the report of triceps denervation; the muscle contracted well when the radial nerve was stimulated on the operating table. All these three cases had faradic response absent, so that the discrepancy is between electrical excitation and voluntary activity, and not between V-T curve recording and all other methods of examination. The most likely suggestion is that the muscle had so re-innervated anatomically that, by chance, the effective normal active portion was that in the deepest part, overlain by a layer of denervated muscle next the skin. To confirm this, the notes made at the time remark that the contraction observed was the sluggish type characteristic of denervated muscle. It must happen now and again, by accident of nerve regeneration, or possibly of funicular arrangement of the nerve cross-section, that one part of a muscle becomes or remains innervated, and that that part is occasionally located remote from the skin surface. However that may be, these three instances have all been found in the larger muscles, and no such finding has been noted from small muscles where no part could be very remote from the stimulus. Four major discrepancies in examination of nearly four hundred patients, and several thousands /

thousands of muscles, are not unexpected in any method of examining biological material. We must again stress the point that muscle stimulation is an adjunct to general clinical examination, and can never replace any part of such examination.

5.10. Discussion of Results.

In considering the results and value of excitability measurements on these cases of peripheral nerve injury we are faced with two rather different aspects of the research, one severely practical, and another of more academic physiological interest. Considering the practical aspect first, we have reasonably successfully worked out a technique for percutaneous stimulation of nerve and muscle in man which gives reproducible results without extremes of experimental variation. What information can be obtained from using such a method as alternative to classical methods of electrical stimulation? In the first place, a rapid qualitative assessment of denervation is possible with less time, trouble and discomfort than the double mechanism of galvanic and faradic current testing involves. This in itself is no more than a technical improvement of the apparatus used for muscle testing, and contributes nothing fresh. In the second place, if the operator is prepared to take the necessary precautions in working and in assessing the results, the earliest sign of clinical recovery can be anticipated in most cases by a few weeks, and as a rule this anticipation is quite reliable /

reliable. The interval is never longer than eleven weeks, and usually averages about four to five weeks. But the working-out of results is laborious and yet essential if prognosis from such a technique is to be reliable within the ordinary standards of ancillary clinical procedures. The V-T curve method cannot be worked alone and without taking into account all the other circumstances involved, and it therefore requires a good deal of thought and attention.

Recovery of nerve supply to a muscle can be followed up to the stage of weak voluntary power in that muscle; as the excitability is then normal, it can be of no further help in prognosis, and testing should be abandoned at that stage.

In a number of other circumstances such as certain degrees of muscle fibrosis, hysterical paralyses, and anomalous innervation cases, useful information is to be had, but must be interpreted with clinical commonsense. The method is in this respect always superior to galvanic-faradic testing, as at the worst it is capable of being quantitatively checked against normal muscles. It may be said from the practical aspect that the V-T curve recording method as described is a great advance in convenience /

convenience, and a minor advance in certain odd cases where the extra information is valuable. We have here naturally shown the patients' records who were systematically followed, as in-patients, for considerable periods, but in addition to these, scores of out-patients have been tested under circumstances where the actual readings are not required, and where the rapid and simple identification of denervation is all that is wanted. It must again be emphasized that a single record at one examination, if not either typically normal, or typically denervated, means nothing, as an intermediate V-T curve between the two extremes mentioned may imply degeneration, regeneration, anomalous innervation, or even partial fibrosis. In conjunction with clinical findings it may be suggestive, but little more.

From the academic view-point of physiology, the case-records present us with a number of very interesting problems. We have to enquire to what are these excitability variations due, and how do intermediate values come about, and what light do these experiments throw on the process of nerve regeneration? The very great difference in excitability between innervated and denervated muscle is well understood. The nerve fibre is readily depolarized /

depolarized, and the arrival of the impulse so initiated causes the appearance of acetyl choline at the neuro-muscular junction; this chemical transmitter depolarizes the muscle fibre membrane in turn and contraction follows. The normal innervated muscle, then, is being stimulated indirectly through the normal channels of axon and motor end-plate. The totally denervated muscle is stimulated directly, and the artificial application of current takes the place of the chemical transmitter, and depolarizes the muscle fibre membrane. The resultant sluggish and prolonged contraction is due to the failure of "accommodation" in denervated muscle, as is described in Section 4.3.6. The amount and duration of electric currents to bring this about are greater than those necessary for nerve. We have already pointed out that the actual values of chronaxie by means of a voltage-time technique differ from those obtained from current-time technique. This is an important appreciation, because much of the argument amongst physiologists about reliability of chronaxie measurement has arisen from the employment of mixtures of the two techniques. However, in both cases, the difference between nerve chronaxie and that of muscle itself is of the order of 100 times, and our records verify /

verify this. Bourguignon (1923) found that the chronaxie of human flexor muscles was slightly shorter than that of the extensors of the same joint, and this fact is also apparent in our measurements; it is not very noticeable for any single examination, but the mean chronaxie for the extensor muscles in our series is 0·01 milliseconds, for flexor muscles 0·008 milliseconds. We also find a difference between flexor and extensor chronaxie in respect of denervated muscle; that of denervated flexor muscle having a mean value of 0·6 msec. as compared with 0·8 msec. for extensor muscles.

Now with regard to the occurrence of V-T curves and chronaxie values intermediate between denervated and normal muscle, we find such in the following circumstances; certain stages of degeneration, certain stages of re-innervation, and partial innervation (as pressure palsy or anomalous innervation). Ischaemic stages are characterized by normal chronaxie and very high rheobase (if excitable at all) presumably due to admixture of normal nerve-muscle complex with inert and non-conducting fibrous tissue. The three conditions in which intermediate V-T curves are found correspond to three quite different physiological circumstances; during Wallerian degeneration /

degeneration we have all motor nerve fibres inactive and degenerating; during re-innervation we have a few active motor unit muscle groups in a bulk of denervated fibres; while in the partially innervated muscle we have a number of perfectly normal uninjured motor units with a denervated portion. One important clue to the physiology of the excitability of such complexes is given by examining the actual figures themselves, for those from pressure palsies or double-innervated muscles are never so high as the chronaxies from degenerating or re-innervating muscle. The highest recorded chronaxie from an anomalous innervated muscle is 0·06 msec., or about six times the normal. Although this is well without the range of variation for normal muscle chronaxie, it is probably not an extreme value for normal motor units which lie in or behind a block of denervated fibres; the necessity for the current to traverse these will reduce its strength, and the presence of the inactive fibres may impede the response of the normal group. The truly denervated fibres will not, of course, respond to the shocks which excite the normals. This is not altogether a satisfactory explanation, and the whole point is obscure. In general, we must bear in mind the words of Davis and Forbes (1936) "the important /

important question is whether one is ever able to measure the absolute time factor in the excitation process itself when the depolarizing current is not applied directly at the seat of this process but through tissues which may alter considerably the effective duration and intensity of a given stimulus." We shall show in a later section that the tissues do in fact very greatly "alter . . . the effective duration and intensity of a given stimulus," and prefer to put forward these results on an empirical basis backed up by statistical examination and practical usefulness rather than by theoretical explanations.

From a consideration of excitability during degeneration and re-innervation we can, however, make some physiological deduction. There appears to be no doubt, in practice, that intermediate excitability states exist, and there appears an equal certainty that excitability alters before voluntary activity re-commences. There are several possible reasons for this "electrical recovery - active recovery" interval. The first is that the disorganization of intra-neural pattern inevitably resulting from nerve section and suture causes the muscle to re-innervate at random in such a way that voluntary activity lags behind muscle innervation; voluntary movement being a /

a co-ordinated activity of certain anterior horn cell groups, such central re-organization must take place to some extent after every nerve suture. That this is almost certainly not the explanation of the excitability - voluntary recovery interval can be deduced from our records. In lesions in continuity which do not involve nerve section, and therefore do not cause any great degree of axon shuffling, the same interval is detected, and is of the same order of time. The number of cases examined as lesions in continuity is not large, but if disturbance of neural pattern were the main cause of the interval, they should reveal no such interval, or a very much shorter one.

The second possibility is that the number of muscle fibres required to give a muscle twitch when stimulated artificially is much less than that necessary to show a voluntary flicker of movement; so that in the early stages of re-innervation not the co-ordination of the motor units but their total strength is at fault. This is probably true, for we have already described the observation that an almost normal V-T curve can be recorded from muscles incapable of voluntary movement, and this particularly so in the case of the facial nerve muscles which are flat and thin, and wherein a few normal fibres might be /

be expected to be the less masked by bulk of denervated fibres. The only evidence against this explanation is statistical, and is that if in fact normal fibres masked by inactive ones show a decreased excitability (from the outside of the muscle) then one would expect to find a range of chronaxie figures so spread out that little significance could be attached to them. This would be so because the innervated "patch", postulated to be so small as to be incapable of active, visible or palpable contraction, might occur anywhere in the bulk of a muscle; therefore, the course of recovery in a large muscle such as extensor digitorum communis would be much more variable from one patient to another than the same course of recovery in say the interosseus muscles, where small bulk would prevent them "hiding" an innervated patch. But in practice, as our records have shown, the variability, the actual V-T figures, and the time course of recovery is almost identical in all muscles; one could not tell from a family of curves whether a large thick or a small flat muscle was involved. We believe that in practice electrical stimulation can give a twitch involving less fibres than the weakest detectable active movement (this is a matter of clinical observation during muscle-testing) /

testing) but that the excitability - voluntary recovery interval is only very partially due to this.

The third possibility, and that which we believe to be the most likely explanation of the interval, is connected with the process of maturation of newly-grown axons on arrival at their functional termination in muscle. Young (1942) has reviewed the histological appearances of newly-grown nerve fibres in experimental re-innervation of mammalian muscle, and has shown that the process of maturation in regenerating nerve fibres sweeps down the nerve some time after the histological advance of the axon tips. Such newly arrived axons may not be capable of impulse propagation from above downwards, but may contain stores of the depolarizing chemical acetyl choline which may be released by artificial means. There appears little doubt, after the researches published by Nachmansohn (1939), Feldberg (1943) and Fulton and Nachmansohn (1943), that acetyl choline is an essential part of the mechanism of impulse propagation, and that its appearance at the neuro-muscular junction as "chemical transmitter" is one aspect of this.

Guttmann (1942) and Guttmann and Young (1944) have detected electrical excitability in re-innervating /

re-innervating muscle of rabbits preceding active movement by two or three weeks, and the histological study of the muscles at various periods suggests that the excitability appears with the arrival of the new-grown axon tips, and the voluntary movement after the maturation of these axons to a certain size capable of impulse propagation. Moreover, Weddell, Feinstein and Pattle (1944), in the extensive survey of electro-myography already referred to, have observed that in the earliest stages of re-innervation of human muscle normal polyphasic action potentials can be provoked in muscle by insertion of the needle, although they cannot be produced or sustained by volitional activity. Such "insertion potentials" are the earliest signs of re-innervation, and may very readily be overlooked or missed in a bulky muscle. We have made three experiments on these lines before being informed of the results of Weddell and his collaborators. Three cases who had undergone radial nerve suture were examined by the electromyogram technique as soon as the V-T curve indicated the probability of incipient re-innervation. In each case the extensor digitorum communis was used as test muscle, having the most reliable V-T records, and being also convenient for needle insertion. No voluntary movement nor volitional action potentials could be detected on the first /

first examination; but in all three cases "insertion potentials" were identified, though only after eleven needle insertions in one case, six and five insertions in the other two. Three weeks later, still in the absence of voluntary activity, "insertion potentials" were obtained in all three cases after two insertions. This is of course a very crude estimate, for on the second examination the site at which potentials had been previously discovered was known beforehand. In one of the cases, voluntary action potentials were detected for a few seconds, and were very localized; they were not identified after several needlings in either of the other two subjects.

We may summarize the evidence in the following way. First sign of muscle re-innervation is lowering of V-T curve and appearance of insertion potentials; in animals this is the stage of first arrival of new but non-propagative axon tips. The second stage consists of more numerous and readily detectable insertion potentials accompanied by an obviously lowered V-T curve; in this stage a few normal active motor units (insufficient to cause detectable clinical movement) may be identified by careful search. In the third stage maturation of the axons has completed in sufficient degree to allow of /

of detectable voluntary movement, V-T excitability is approaching normal, and both insertion and volitional action potentials are readily picked up. Finally, as voluntary power increases (as it may not necessarily do) the number of mature motor units increases, and faradic response returns, having been previously absent because of the intolerance of the subject to the amount of faradic current required for excitation of scattered or deep-seated motor units. It will be seen that the story from excitability recording tallies well with that from action potential study and from mammalian histology, and we believe that the interval between excitability improvement and voluntary recovery, which we have described, and which is of practical importance for prognosis, is due to the maturation of regenerating nerve fibres after reaching muscle. If this is accepted, then we can say that the experiments yield the physiological information that the time of maturation of motor fibres re-innervating muscle in man is on the average about five weeks, from arrival to the stage of full nerve impulse propagation.

There is a further point of discussion with regard to strength-duration curves from re-innervating muscle. The only other published records /

records of complete strength-duration excitability curves during nerve regeneration in man are due to Adrian (1917), Marble, Hamlin and Watkins (1942) and Pollock, Golseth and Arieff (1944). In 1917 Adrian made a thorough investigation of a limited number of nerve injury cases using a laboratory mechanical contact-breaker to provide shocks of known duration. Each individual S-D curve was plotted on a base of twelve or more different durations, and he came to the conclusion that in the degenerative period following nerve section the excitability curve consisted of two components, and exhibited a "kink" or discontinuity. As the transformation from normal to denervated muscle takes place, Adrian says, "the curves are made up of a steep sharply bent curve where the current strength is high and the duration short, and a slower and more gradual curve when the duration is longer and the strength less. The time-constants of these two components of the curve are found to agree very closely with the average values for muscle with intact and with degenerated nerve supply." He identifies the rapid mechanism with the nerve fibre, and the slow mechanism with the muscle itself. These observations of the 1914-18 War period have been neglected (they appear in a journal which under present /

present conditions is rare and inaccessible) and have recently been confirmed by a series of records published by Pollock, Golseth, and Arieff (1944). These workers, using a square-wave current stimulator of precision, using a series of duration shocks of 33 different time-intervals, have shown that these kinks or discontinuities are a feature of degenerating or re-innervating nerve-muscle complex. These C-T curve discontinuities have been demonstrated on a series of experimental animals, and on a few cases of nerve injury, and Pollock believes the appearance of such a kink in the curve to be a reliable sign of re-innervation. On the other hand, the Voltage-capacity curves recorded by Marble, Hamlin and Watkins, again on a few cases only of nerve injury recovery, show no such discontinuity, and re-innervation is assessed by a general lowering of the whole curve. Details of technique and number of plot points used are not given, and cannot be read from their records.

We are somewhat undecided as to our own belief in the matter. Although we have examined and reported a far greater number of cases than any of the previous authorities, we are not in a position to make a definite statement about these discontinuities in strength-duration curves, for our technique, designed /

designed as a routine procedure, employs too few points to identify such kinks with certainty. We regret very much that until latterly we were not conversant with Adrian's paper, or an attempt to detect such kinks would have been made on a large series of cases. Going over our records with the possibility of this dual mechanism in mind, our opinion is that such discontinuities are a common finding in the intermediate stages of innervation, and might well be a constant one if the technique had been designed to reveal them by using a greater number of duration points. Reference to the graphs in sections 5.3. and 5.7., and especially Figs. 23, 32, 36, 37 and 44 suggests that the kinks are present, and may readily be overlooked or drawn out in the plotting of the V-T curve from five points only. The lack of evidence makes our confirmation of such discontinuities an impression only. Theoretically, the occurrence of kinks is liable to various interpretations. Although Rushton (1935) has established the appearance of two excitability components in frog nerve-muscle complex stimulated through large fluid electrodes, Doupe (1943) has recently questioned whether in man these are due to this cause, and suggests on a basis of human experiment that two methods of response rather than of excitability are present. He /

He has shown that C-T curve kinks can be recorded from perfectly normal human muscle if cooled by immersion in water at 20°C . We are strongly inclined to accept Doupe's conclusions, which are deduced from most carefully controlled experiments.

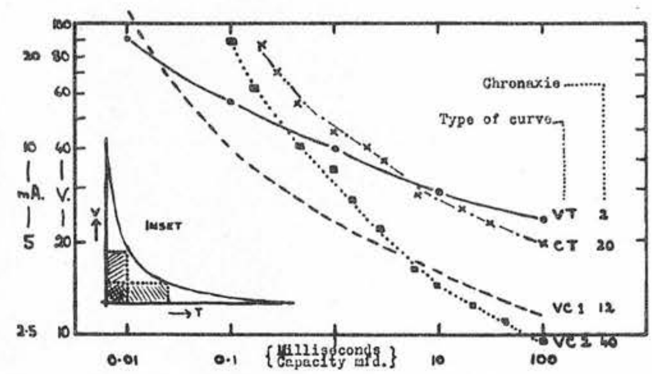
We have already quoted the opinion of Davis and Forbes (1936) that such indices as chronaxie are probably not wisely regarded as of supreme biological significance, and that a practical basis of assessment is essential for any method of excitability measurement. As none of the authors already mentioned have examined an extensive series of cases, and have made no attempt to relate the appearance of discontinuities to the practical facts of voluntary recovery and faradic response, we feel that our results must rest on a purely practical and empirical basis. In this respect, the sacrifice of discontinuity detection for the ability to examine a larger number of disabled persons cannot be regretted. It is true and right that many fascinating side-issues arise and should be investigated under laboratory conditions; the reason for the difference between V-T and C-T chronaxies, the greater toleration of subjects to square voltage pulses as compared with square current ones, and the significance of discontinuities and chronaxie variations are all lines of /

of research which now, as the War closes, can claim more attention. But the original intention to assess the value of excitation methods on a practical basis, to help with the diagnosis and the treatment of scores of war casualties, has had a prior claim hitherto.

We have made one further calculation with a view to demonstrating the similarities and differences between strength-duration curves obtained by different methods, and this is shown in Fig. 48. We have extracted mean curves for denervated human muscle from the papers of the authors referred to, and plotted them on a common scale with our own. Chronaxie figures are also given, though it should be noted that the chronaxie figures cannot be read off the scale direct in this case. The actual chronaxie figure depends upon the method used for delivering the known-duration stimuli; for our V-T method it is 2, for the square-current shocks used by Pollock, and by Doupe, it averages 20, and varies between 12 and 40 for the two voltage-capacity curves given. In these latter cases, as the time of discharge is reckoned in condenser capacity and not in absolute time units, the actual chronaxie figure is not exactly comparable. By using an abscissa scaled in logarithmic decades, time and capacity units can be plotted /

Fig.48.

48



<u>The correspondence between various types of Strength-Duration curves.</u>

All of the above curves are mean values for denervated human muscle.
VT - Square voltage curves by Ritchie technique; chronaxie 2 msec.
CT - square current pulses as used by Pollock; chronaxie 20 msec.
VC1 - voltage-capacity curves after Marble, Hamlin and Watkins.
VC2 - " " " " Pollock.

The actual figures differ with the exact technique, but the general trend of the curve remains the same. The ordinate and abscissa numbers can be read for the appropriate curve; it will be noticed that the ordinate scale implies that the tissues and electrodes used had an effective ohmic resistance of 4000 ohms. The actual durations of the condenser discharges cannot be given, as they depend on the absolute value of the circuit resistance.

<u>Inset</u>: diagram of Bauwens' explanation of the possible inadequacy of condenser discharges in precise diagnosis; the exponential condenser discharge inevitably contains "square" components of several values.

plotted together, but are not necessarily equivalent, as the electrode and patient's resistance will govern the absolute value of the condenser discharge time. With respect to the ordinate scale, the curves can be equated by assuming that a given voltage will force a corresponding current through electrodes and tissues, and this again implies that electrode size and position is constant. The scale of Fig. 48 implies that the average resistance of electrodes and tissues is about 4000 ohms, for 20 volts is equivalent in excitatory effect to 4 milliamperes. As we shall show, this is not strictly true, for the patient does not present a true or constant resistance to electric pulses of the types used for S-D curve determination, and this fact accounts for the difference in chronaxie values given by the several techniques. The point is, however, that the general nature of the curves is very similar, and there is no reason to suppose that any one method has theoretical superiority over the other. Bauwens (1941) has attempted to account for the apparently greater efficiency of rectangular shocks as compared with condenser discharges in terms of the shape of the condenser discharge (inset: Fig. 48) which he points out must contain several rectangular components of different durations /

durations and amplitudes; for this reason, he suggests that testing with condenser shocks will fail to reveal certain excitability characters as separate figures. Accepting Bauwen's explanation as sound in theory, we nevertheless feel that in practice it is inadequate, for the shape of the currents through living tissues is so greatly distorted by tissue reactance that such mathematical considerations do not hold. We shall demonstrate this in due course. If the testing with rectangular pulses yields more information than that with condenser discharges, and it is by no means sure that this is so, we believe that it is due to a combination of circumstances; the greater precision of square-wave generators (which is not intrinsic, but happens to be so in the work so far done) and the fact that in our records voltage waves are well-tolerated are the two main factors. Although the V-T technique gives chronaxie figures which appear very low in comparison with other methods, they are consistent amongst themselves, as we have shown, and the fact that the method is simple and comfortable means that it can be of more general application than the others. Having no particular theoretical superiority, it has nevertheless this practical advantage over the alternatives.

6. SUMMARY - PART I.

(1) The main physiological and clinical features of peripheral nerve injury are described and reviewed with especial reference to these which lend themselves to measurement by relatively simple methods. Measurement of peripheral nerve activity is important not only for itself but as an adjunct to clinical examination.

(2) Autonomic tests of vasomotor, sudomotor and pilomotor activity are reviewed; their usefulness in practice is necessarily limited by the facts of anatomy, and in high-level nerve injuries autonomic tests will not provide the first signs of recovery. The reflex levels of autonomic activity are outlined, and their significance as regards preganglionic and post-ganglionic fibre integrity demonstrated. A series of measurements of skin resistance on nerve injury subjects is included, showing that autonomic denervation greatly increases the resistance of the skin if tested with dry electrodes, but makes little difference with the more commonly used saline-pad type.

(3) The assessment of sensory defect is outlined briefly, and the entirely clinical nature of this side of peripheral nerve injury examination emphasized /

emphasized. No adequate quantitative method of sensation estimation has yet been devised, though the possibility is now a reasonable one.

(4) Examination of motor defect is probably the most important side of ancillary examination in nerve injury work, because of the practical importance of muscular power recovery and the anatomical situation of muscles nearer to the site of most injuries than superficial manifestations such as autonomic and sensory defect. The three main lines of attack are reviewed - clinical examination, electromyography, and stimulation of muscles by electric currents.

(5) The various methods of electrical stimulation of muscle in man are described and reviewed in detail, with original observations on their comparative value. The drawbacks and fallacies of galvanic/faradic testing, and condenser set stimulation are considered in detail; the validity of various methods of chronaxie measurement and of strength-duration curve recording is discussed. Methods of accommodation measurement and alternating-current excitation are reviewed and tested. As far as possible, an estimate of the relative worth of these several methods is made, and the practical conclusion come to that strength-duration curve measurement combines the maximum /

maximum simplicity with maximum practical value.

(6) The electromyogram technique for recording human action potentials from muscle is described, with a critical review of its value in examination of nerve injury cases.

(7) A new technique for the recording of strength-duration curves is described, and the results from some 10,000 records on nearly 400 patients are analysed in detail. A method of stimulation which uses rectangular shocks measured in volts is more comfortable and simple than the alternatives, and has been developed. For purely qualitative routine testing the V-T curve method is more reliable than galvanic/faradic testing, is quicker to perform, requires a less bulky and erratic apparatus, and is more comfortable for the subject. Quantitative V-T curve recording is a more laborious procedure and requires fairly rigid adherence to a set technique, some use of simple statistical method, and considerable care and experience in accurate interpretation. Granted these, we believe we have shown the following advantages of such a method of muscle testing. Normal innervation and complete denervation can be distinguished with certainty; pressure palsy and hysterical paralysis with almost complete certainty, and /

and certain stages of muscle ischaemia can be distinguished from other causes of muscular weakness. During Wallerian degeneration the excitability gradually changes from that of normal muscle to that typical of denervated muscle; and the reverse process occurs when denervated muscle re-innervates after degeneration.

(8) The alteration of excitability with re-innervation is of some value in prognosis; it appears some weeks before voluntary power is regained, and is a reliable sign. In high injuries such excitability alteration is the first sign of any sort of regeneration, and is thereby valuable in practice, although the period of "advance information" is not very long. We believe that this interval corresponds to the period of maturation of new regenerated fibres from first arrival in the muscle to the mature state capable of impulse propagation in the normal way. The evidence for this is discussed.

(9) Chronaxie figures are given for each V-T curve, and also the Lassalle Index which takes the rheobase into account. The chronaxie figures for a Voltage-Time method are much lower than those for a Current-Time method because of distention of stimulus in the tissue layers. Voltage-Time chronaxies /

chronaxies average 0·01 msec. for normal muscle and 0·8 - 1·0 msec. for denervated muscle. They bear the same relation to one another as the more usual Current-Time figures of 0·1 and 10 msec. respectively. This being so, the Voltage-Time method offers great advantages of comfort and simplicity of apparatus, and is as reliable.

(10) Neither chronaxie nor Lassalle Index figures can satisfactorily express V-T curves, and graphic methods are almost essential. Fig. 49 is a simple schematic representation of the types of curve found in normal muscle, denervated muscle, and in certain stages of ischaemia and re-innervation.

(11) The method is claimed as being original, simple for routine use, convenient in practice, and capable of yielding valuable information if systematically used. It has been in regular use for three years at a Nerve Injuries Unit, and has only very rarely provided misleading information.

Fig.49.

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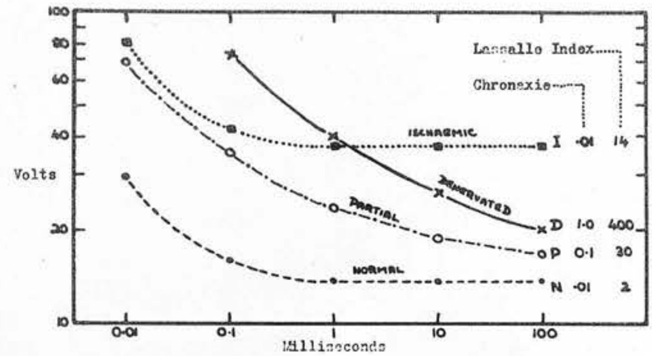

SUMMARY. The typical Voltage-Time curves for various muscle states. Normal muscle has flat curve with chronaxie around 0.01 msec., and L.I. under 10. Denervated muscle has steep curve, chronaxie about 1.0 msec., and L.I. over 100. Intermediate curves are found in conditions of partial innervation and during the period of degeneration and re-innervation when the neuro-muscular junction is abnormal and the nerve axon cannot transmit impulses but has not entirely disappeared.

The above curves are taken from examples of the same anatomical muscle, but represent average values only - see text.