Clinical assessment of skeletal muscle function

Autor(en): **Edwards, Richard H.T.**

Objekttyp: **Article**

Zeitschrift: **Bulletin der Schweizerischen Akademie der Medizinischen Wissenschaften = Bulletin de l'Académie Suisse des Sciences Medicales = Bollettino dell' Accademia Svizzera delle Scienze Mediche**

Band (Jahr): **34 (1978)**

PDF erstellt am: **01.06.2024**

Persistenter Link: https://doi.org/10.5169/seals-308137

Bull. Schweiz. Akad. Med. Wiss. 34, 7-23 (1978)

University College Hospital Medical School, London

CLINICAL ASSESSMENT OF SKELETAL MUSCLE FUNCTION

RICHARD H. T. EDWARDS

Summary

A systematic clinical analysis of skeletal muscle function is presented. Tests range from assessment of muscle weakness with a new hand-held dynamometer (the "Hammersmith Myometer") to studies of the contractile properties of the quadriceps and adductor pollicis muscles described in terms of the force generated at different frequencies of stimulation of the motor nerve, the force-sustaining capability and the time course of relaxation following a brief tetanus. A new measure of the energy-exchanging capacity of muscle is given by the Myothermogram (MTG - so named by analogy with the Electromyogram - EMG). The technique measures metabolic heat production in muscles when maximally activated by voluntary effort or electrical stimulation and the heat changes during sustained contractions. The MTG offers a practical means for assessing in normal and diseased human muscle the metabolic capacity, economy of force maintenance and fatigue mechanisms. Needle biopsy provides safe, rapid and repeatable access to muscle for diagnosis, studies of chemical energy exchange and the correlation of function and metabolism with constituent muscle fibre types.

This approach provides a possible basis for recognising the functional disorder and for evaluating the effects of physiotherapy and drug treatments in patients with neuromuscular disorders.

Zusammenfassung

Eine systematische Uebersicht über die klinischen Untersuchungsmöglichkeiten der Skelettmuskelfunktion wird vermittelt. Das Spektrum reicht vom "Hammersmith-Myometer" zur Bestimmung von Muskelschwäche der Hand bis zu Studien über die kontraktilen Eigenschaften der Mm. Quadriceps und adductor pollicis auf Grund der Korrelation zwischen Spannungs-

ablauf und Reizfrequenz sowie zwischen Haltetonus und Entspannung bei kurzer tetanischer Reizung. Eine neue Methode zur Bestimmung des Energieverbrauchs des Muskels ist das Myothermogramm (MTG, so genannt in Analogie zum Elektromyogramm, EMG). Diese Technik beruht auf der Bestimmung der metabolischen Wärmeproduktion der Muskeln bei willkürlicher Innervation, elektrischer Stimulation oder während anhaltender Kontraktionen. Das MTG ermöglicht die Beurteilung der Stoffwechselkapazität beim normalen und erkrankten Skeletmuskel mit Bezug auf die Oekonomie der Kraftentfaltung und die Ermüdbarkeit. Nadelbiopsien bedeuten einen risikolosen, schnellen und wiederholbaren Eingriff für die Muskeldiagnostik, wobei die thermischen Daten mit den übrigen Eigenschaften der einzelnen Typen von Muskelfasern korreliert werden können. Dieses Vorgehen vermittelt eine Grundlage für die Erkennung der Funktionsstörungen sowie für die Beurteilung der Behandlungserfolge bei neuromuskulären Erkrankungen.

Introduction

The clinical assessment of skeletal muscle function is usually made on the basis of the conventional neurological examination supplemented as required by performance tests, e.g., measurement of the stride length in observations of gait patterns. Further investigations have usually included examination of muscle action potentials by various electromyographic (EMG) techniques and the pathological examination of muscle obtained by open biopsy. Such approaches to the investigation of patients are of proven value but new possibilities are now available for assessing the function of the muscle when viewed as a biological machine designed to generate force by the metabolism of energy-producing substrates. In this account I propose to draw attention to the recent progress made in studies of normal subjects and patient volunteers in developing a series of tests which help describe the force generating characteristics of human muscle in a way which may prove helpful in the diagnosis and management of patients presenting with complaints of weakness or fatigue. These detailed tests have been applied to a large proximal muscle (quadriceps femoris) often involved in myopathies and in a small distal muscle (adductor pollicis). Simple force measurements have also been made in a variety of muscle groups with the aid of a hand-held dynamometer (the Hammersmith Myometer - EDWARDS and McDONNELL, 1974; EDWARDS and HYDE, 1977; HOSKING, BHAT, DUBOWITZ and EDWARDS, 1976).

Measurement of force

This would appear to be a logical necessity in the investigation of weakness or fatigue, symptoms which both arise from a real or apparent failure of the muscle machine to generate the required force. An indication of the force of voluntary contractions made by the patient in the course of a clinical examination of the neuromuscular system may be made with the Myometer but this approach, though perhaps useful in the management of the patient, also serves to indicate the limitations of the subjective assessment of contraction force. Once a number is available to describe the response which happens to be elicited by the examiner it soon becomes clear how variable and potentially open to misinterpretation the clinical assessment of force can be. The patient may not have the will-power or for some other reason be unable to make a maximum voluntary effort, or he may be examined in such a way that it is physically impossible for him to maximally use his muscles, e.g., by testing the strength of the soleus/gastrocnemious muscles when the patient is supine.

Measured force depends on the size of the muscle and on the dimensions of the skeletal levers on which the muscles act. Only if the measuring technique is standardised can comparisons be made between normal individuals (TORNVALL, 1976). The provision of normal data as a yardstick for interpreting results in patients is difficult since the tests to be described are more appropriate for assessing weakness and fatigue than strength which, though the other side of the same coin, is subject to a large numer of physiological influences due to many causes from occupational usage to athletic aspirations. It is easier to seek normal data in children (HOSKING, BATH, DUBOWITZ and EDWARDS, 1976) since they are probably less subject to variation than adults. The myometer may also be used to assess changes in muscle weakness in adult patients (EDWARDS and HYDE, 1977). However the investigation must not be rendered totally inert by such reservations, and must employ the best method of standardisation available to him.

A systematic series of muscle function tests is now available (EDWARDS, 1975; EDWARDS, YOUNG, HOSKING and JONES, 1977; HOSKING, YOUNG, DUBOWITZ and EDWARDS, 1977; YOUNG and EDWARDS, 1977). The force of a maximum voluntary contraction (MVC) of the quadriceps has been determined with a strain gauge in a normal population of males and females of different ages. Body weight has proved to be a clinically useful standard for comparison between different individuals. A patient may for practical purposes be considered weak if quadriceps MVC is less (in kg force) than half body weight (in kg). Though this measurement depends on the cooperation of the subject or patient, it is found that the best two of three of four consecutive efforts normally agree within 3 %. This procedure may be

considered to be analogous to determination of well established measures of lung function (e.g., peak expiratory flow rate, vital capacity). To obtain a more precise basis for comparing the contraction force between individuals and possibly between different muscle groups, it would be desirable to measure force per unit cross-sectional area of the muscle. Although attempts have been made to determine this in human muscle (MORRIS, 1948; ALEXANDER and VERNON, 1975), there are formidable difficulties not only in determining the cross-sectional area of the muscle (though these may partly be overcome by modern radiological or ultrasonic scanning techniques (IKAI and FUKUNAGA, 1968; 1970)) but also in calculating the moments of the skeletal lever system through which the muscle force acts. The series of muscle function tests which are described below do not solve the difficulty about the meaning of measured force but they do offer alternative approaches which give a quantitative indication of muscle function which is not affected by the absence of information about muscle size, lever moments etc. They have the added advantage that, owing to their being based on electrical stimulation rather than voluntary contractions, they do not depend for their precision on the patient's consistent motivation or effort.

Electrical stimulation

Though used in many muscle groups by DUCHENNE (1867) physiological studies involving electrical stimulation have more recently been limited to peripheral muscles with accessible motor nerves (BURKE, SKUSE and LETHLEAN, 1974; DESMEDT, EMERYK, RENOIRTE and HAINAUT, 1968). Unfortunately, these peripheral muscles are not typically affected in myopathies. A practical recent finding (EDWARDS et al., 1977) has been that the contractile characteristics (described below) of a part of the quadriceps is essentially the same as for the muscle as a whole. Several physiological features of such a portion of quadriceps muscle are similar to those of the adductor pollicis, e.g., the frequency: force relationship (Fig. 1). Table 1 summarises the frequency: force relationship as a ratio of the force at 20 Hz (a force on the steep part of the curve) to that at 50 Hz (a tetanic force on the plateau of the curve) for adductor pollicis and quadriceps. For comparison are shown the responses of an isolated human muscle preparation (a variety of muscle samples obtained at surgery and studied in vitro by MOULDS, YOUNG, JONES and EDWARDS, 1977). The frequency: force curve is a valid description of the characteristics of the muscle itself only if the tetanic tension achieved at high frequencies (Fig. 1) is sustained. Rapid loss of force (fatigue) with repetitive nerve stimulation is well known to occur in myasthenia gravis and is due to impaired neuromuscular transmission but can also occur in some myotonic syndromes because

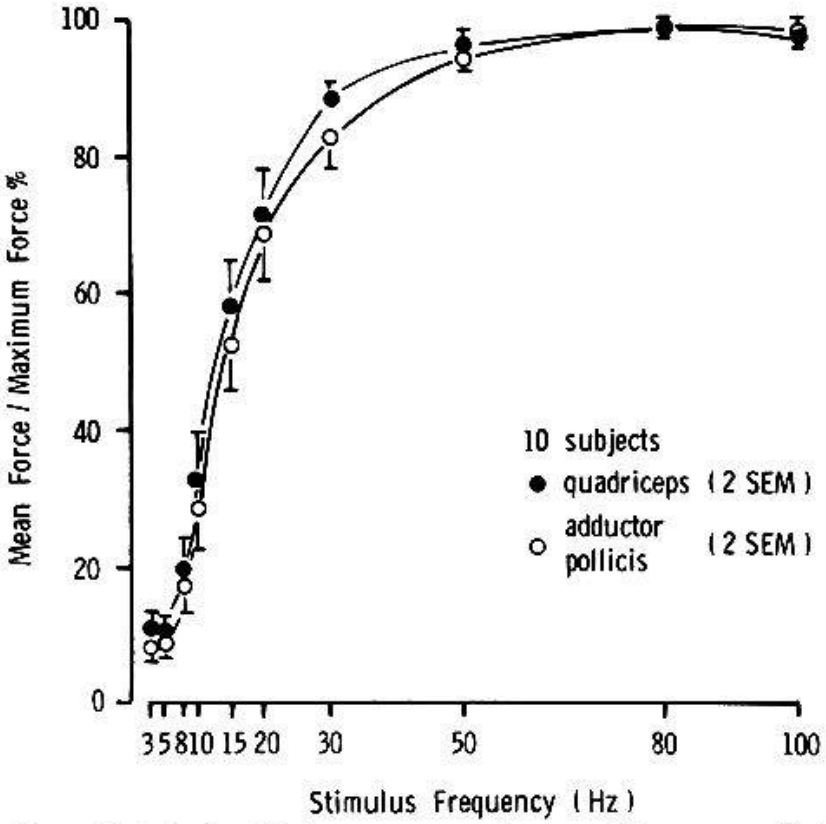

Figure 1. Relationship between mean force and frequency of stimulation of motor nerve in quadriceps and adductor pollicis in normal subjects. As a simple description of the electromechanical activation it is convenient to give the ratio of the force developed when stimulated at a low frequency (e.g., 20 Hz) to that at a high frequency (e.g. 50 Hz).

Table 1. Contractile properties of human muscle in vitro and in vivo.

	In vitro	In vivo	
	Isolated muscle preparation	Adductor pollicis	Quadriceps
Force $\frac{\text{tetanus 20 Hz}}{\text{tetanus 50 Hz}}$ %	71,7 (2,8)	73,1 (2,8)	75,6 (2,0)
Relaxation time msec (SF_{50})	104,8 (5,9)	95,8 (3,4)	103,3 (3,9)
	Mean values (SEM) shown		

Notes:
1. These results summarise those previously published by Edwards et al. (1977) and Moulds et al. (1977).
2. For the definition of SF_{50} see Fig. 2.

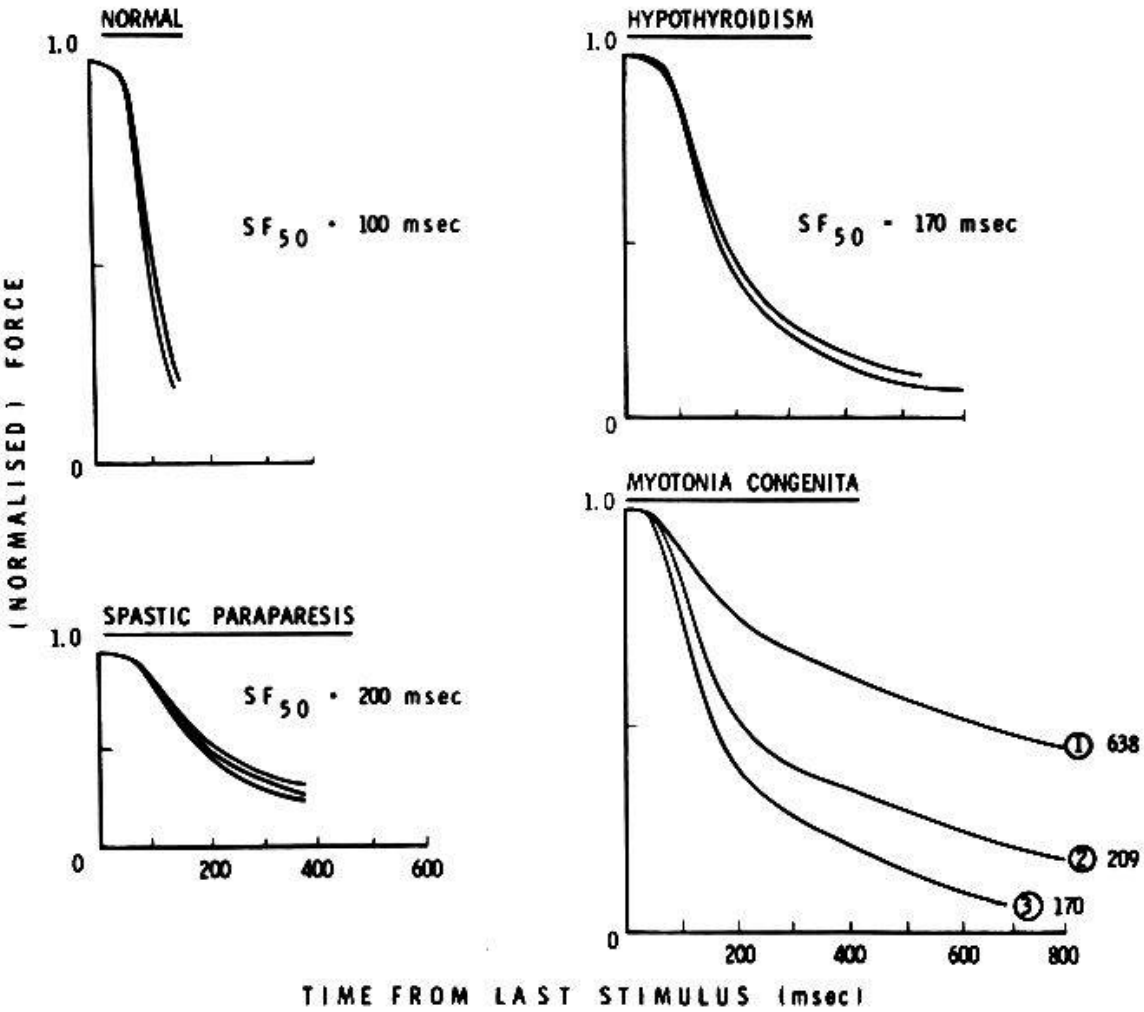

Figure 2. Time course of relaxation from 3 successive tetani at 30 Hz in quadriceps. The index SF_{50} is defined as the time from the last stimulus to 50 % loss of force. Shown also are examples of slow relaxations in hypothyroidism, spastic paraparesis and myotonia congenita (in these last two the slow relaxation is due to continuing electrical excitation). (Reproduced from Hosking, Young, Dubowitz, and Edwards, 1977 by permission of the Editor of Archives of Disease in Childhood.)

of fading of the action potential or impaired excitation-contraction coupling (WILES and EDWARDS, 1977). Fatigue occurring with high frequency stimulation must be elucidated by other means, such as electromyography or a test dose of an anticholinesterase. The time course of relaxation from a brief tetanus also serves as a characteristic index of muscle function which can be altered by physiological and pathological factors (Fig. 2).

The Myothermogram (MTG)

Muscle temperature measurements have been made many times since first made by BECQUEREL and BRESCHET (1825) (Fig. 3) but there have been only a few attempts to measure the rate of metabolic heat production in human muscle (BARCROFT and MILLEN, 1947; BUCH-

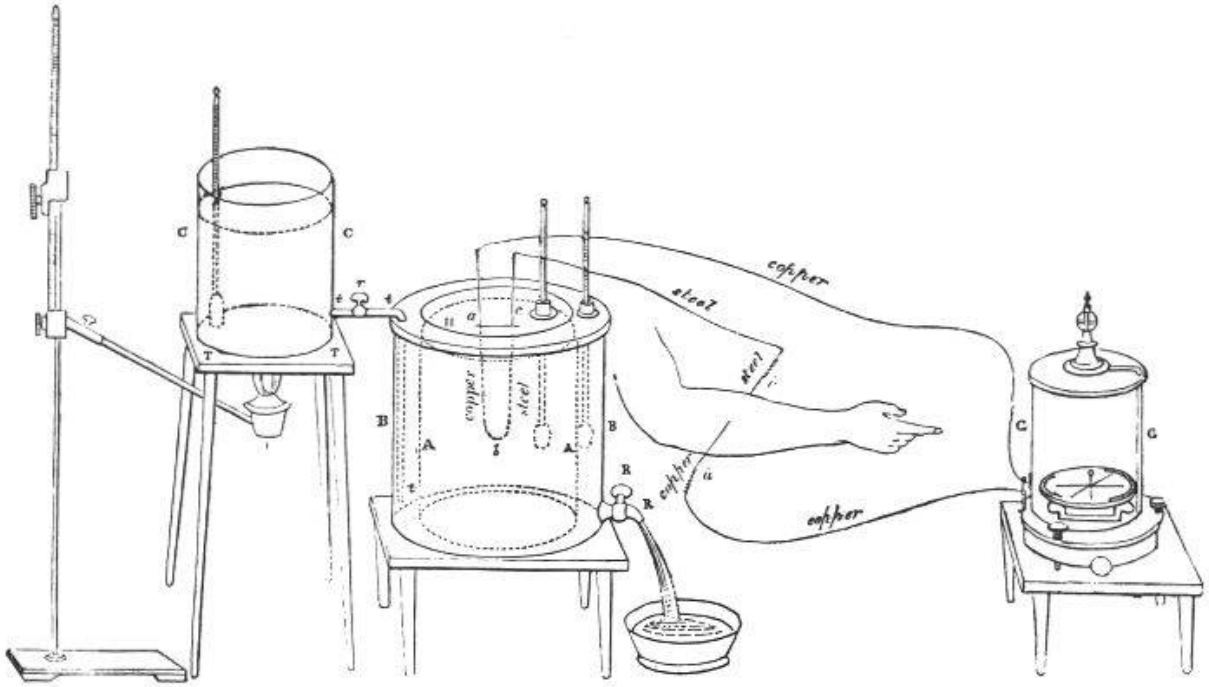

Figure 3. The first measurement of muscle temperature in man with a copper-steel thermocouple by Becquerel and Breschet (1835). These early workers made realistic temperature measurements and recognized that muscle temperature is greatly dependent on local circulation. The apparatus was not sensitive enough however to recognize metabolic heat production.

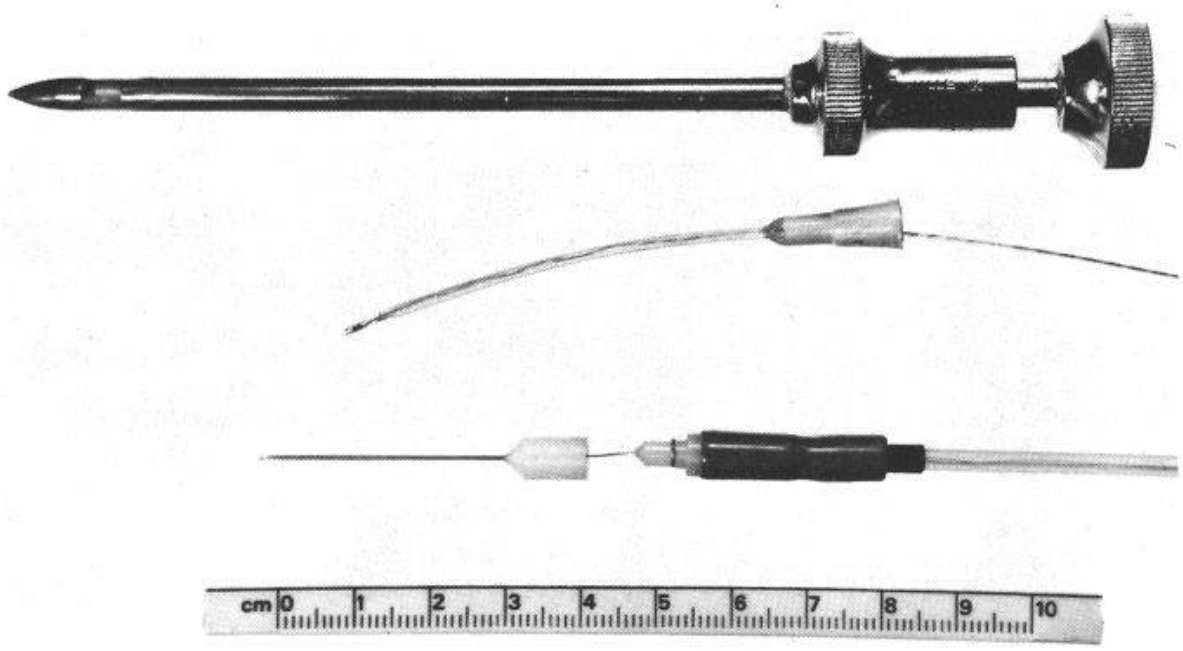

Figure 4. The essential "tools" for studying muscle energy metabolism in man. Above is shown the Bergström muscle biopsy needle. In the middle is the thermistor probe which is inserted into the muscle down a canula. Below is the thermocouple needle (SIEREX). The fine copper-constantan wires pass down a needle with a blocked-off tip. Apart from the protecting the fine couple this arrangement allows metabolic heat production to be quickly assessed at different depths in the muscle.

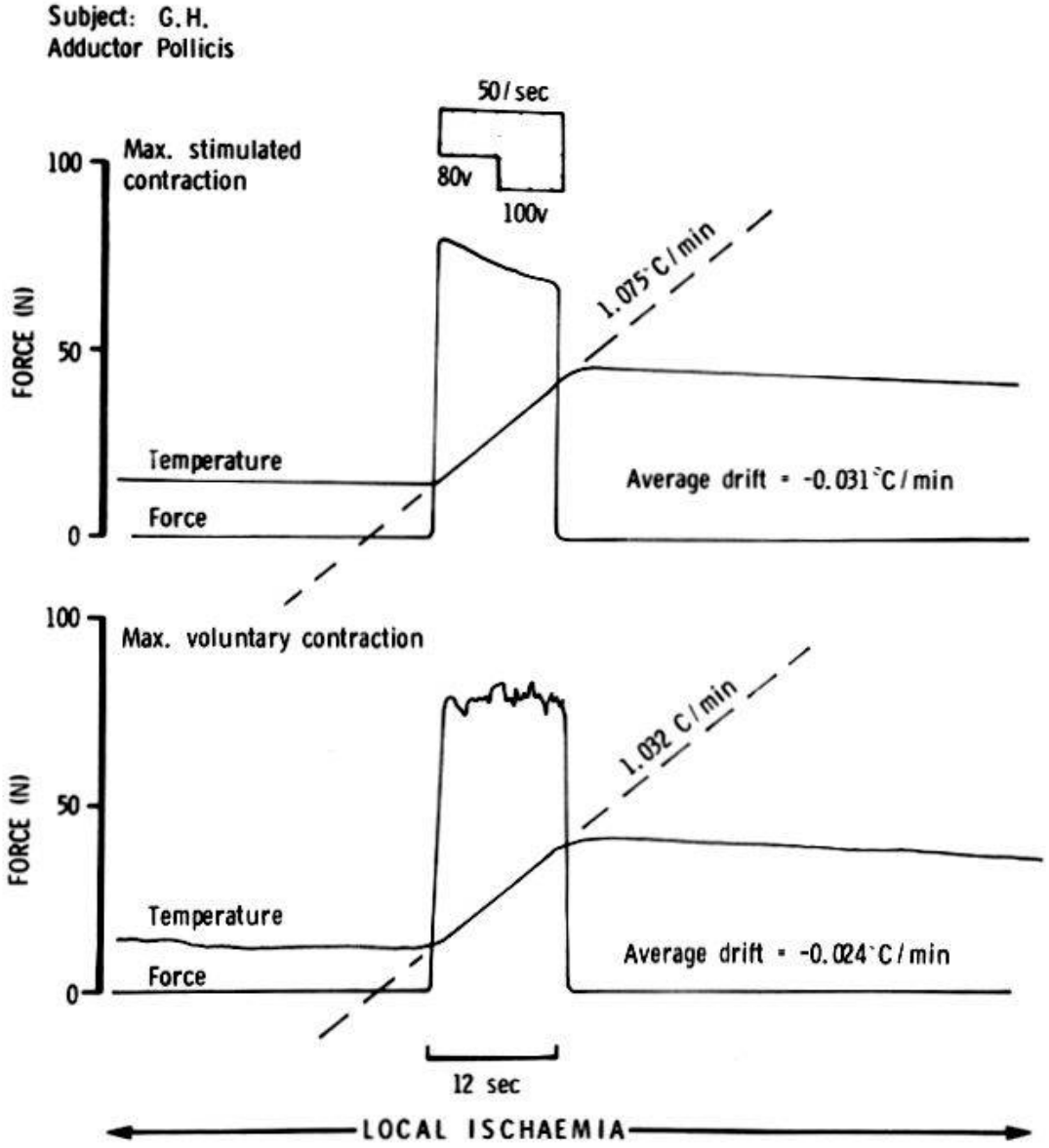

Figure 5. Myothermal measurements in the normal adductor pollicis muscle. During a period of ischaemia there was a fall in muscle temperature of about 0.03 °C/min. During the 12 sec period of supramaximal stimulation of the ulnar nerve at the wrist at 50 Hz temperature deep in the adductor pollicis increased at 1.075 °C/min. A similar rate of temperature rise was found with a maximal voluntary contraction which followed after an interval of a minute.

THAL, HØNKE and LINDHARD, 1944; AKRE and AUKLAND, 1970; EDWARDS, HILL and McDONNELL, 1972). New tools (Fig. 4) have made possible the first quantitative assessment of metabolic heat production in human muscle in terms of the changes in local energy exchanges in the contracting quadriceps (EDWARDS, HILL and JONES, 1975a). Metabolic heat production during isometric contractions was measured with a thermistor probe (EDWARDS, McDONNELL and HILL, 1974). The changes in muscle ATP, phosphorylcreatine and lactate were determined by enzymatic analysis of muscle samples obtained by the BERG-

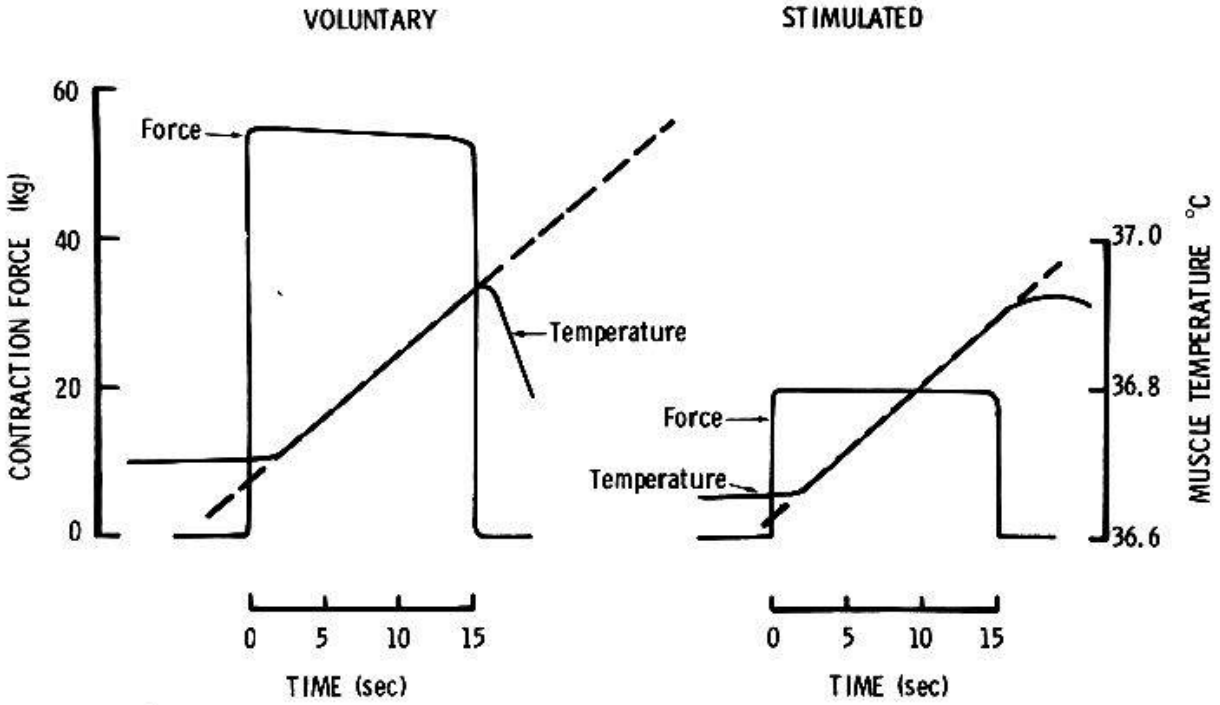

Figure 6. Illustration of the MTG measurement in the quadriceps. In a maximum voluntary contraction all fibres are made to work maximally and this is reflected in the overall contraction force and rate of muscle temperature rise. In the stimulated contraction only a small part of the muscle is fully activated, giving a large rate of rise of temperature, but a much smaller overall contraction force.

STRÖM needle biopsy technique (see below). It was found that measured heat production was equal to that expected from the known heats of reaction of the chemical constituents. Heat production fell as the muscle became fatigued (also illustrated by new data given in Table 2). Closer examination in the adductor pollicis revealed that the heat rate fell more than the fall in force indicating increased metabolic "economy" of force maintenance (EDWARDS and HILL, 1975) as had been shown to occur in frog muscle (FENG, 1931) and by the reduced ATP turnover with fatigue in mouse muscle (EDWARDS, HILL and JONES, 1975b). When contractions showed this improved metabolic economy, there was also slowing of relaxation (EDWARDS, HILL and JONES, 1975a, b). This has led to a way of interpreting myothermal measurements in terms of the relaxation speed of the muscle (EDWARDS, 1977) since there is an analogous correlation of mechanical and metabolic characteristics in "fast" and "slow" animal muscles (CLOSE, 1972).

Myothermal measurements are made only under conditions of local ischaemia to avoid overriding heat exchanges with the circulating blood. Illustrations of the records obtained are shown (Figs. 5, 6 and 7) and their interpretation (Fig. 8).

Such measurements are made with a thermistor probe (EDWARDS, McDONNELL and HILL, 1974) or a fine thermocouple needle (MK 19, SIEREX LTD., LONDON) which with its recor-

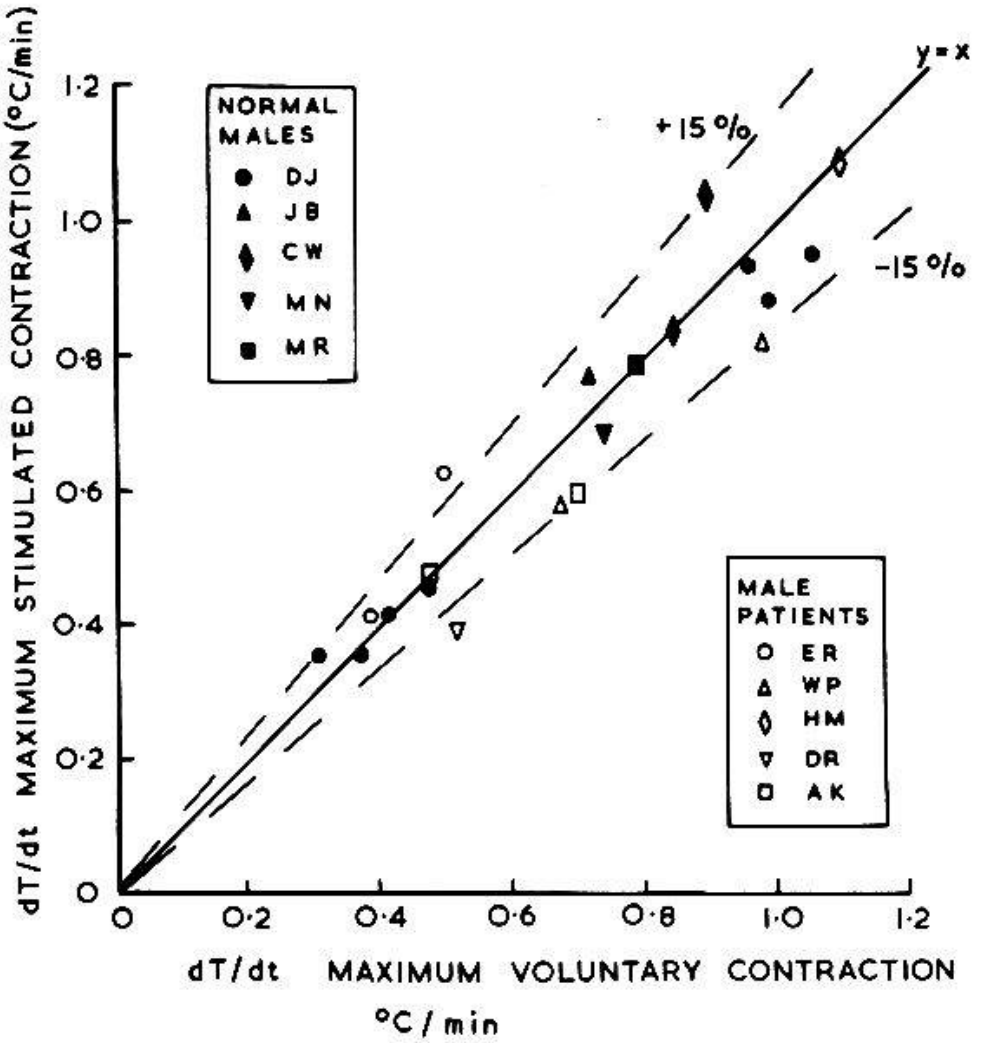

Figure 7. Comparison between the maximum rate of muscle temperature rise (dT/dt) in voluntary contractions compared with stimulated contractions in a portion of the quadriceps. Measurements were made in a series of alternate stimulated and voluntary contractions. The absolute temperature fell as the muscle fatigued but there was good agreement between maximum voluntary and stimulated contractions indicating that the muscle could be maximally activated by voluntary effort in normal subjects and well motivated patient volunteers.

ding equipment is sensitive to a temperature change of 1/1000°C. In general the thermistor probe has been found to be the more satisfactory for use in the quadriceps muscle whereas the adductor pollicis is studied with a thermocouple needle while the hand is attached to a strain gauge dynamometer (EDWARDS et al., 1977) based on that of MERTON (1954).

Clinical application of the MTG

The MTG is conceived as being complementary to the electromyogram (EMG) in the investigation of muscle symptoms. With the fine thermocouple needle the procedure is little more troublesome to subject or observer than conventional electromyography with a concentric

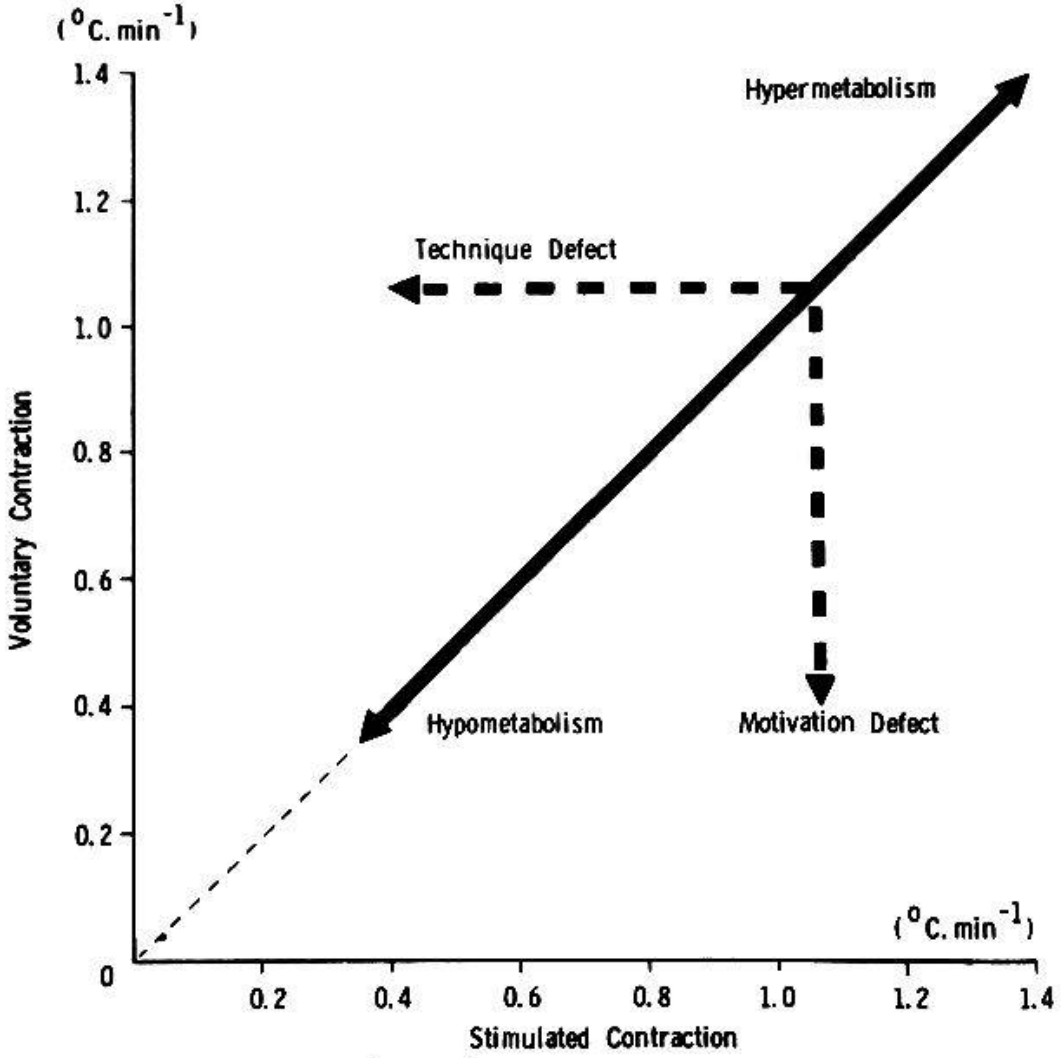

Figure 8. Interpretation of the myothermogram. By measuring the maximum rate of temperature rise in a stimulated contraction (checking for an error in placing the thermal probe in active tissue and/or full electrical stimulation by comparing with a voluntary effort) a guide can be obtained to the metabolic capacity of the muscle. Finding a lower maximum rise in voluntary effect compared with a stimulated contraction indicates that the subject cannot or will not activate the muscle maximally.

needle electrode. Studies have been carried out in patients with a variety of myopathies (EDWARDS, 1977). Three patients with muscle symptoms but in whom no abnormality was found on examination of serum creatine phosphokinase, EMG or muscle histology or histochemistry had a maximum rise in temperature in the normal range as did a patient with mild polymyositis. Three patients with muscle symptoms but in whom no abnormality was found on examination of serum creatine phosphokinase, EMG or muscle histology or histochemistry had a maximum rise in temperature in the normal range as did a patient with mild polymyositis. Three patients with hypothyroidism and one with chronic alcoholism had maximum rises just below normal but the rise was much reduced in a patient with myotonic dystrophy and

Table 2. Effect of fatigue on relaxation and metabolism in adductor pollicis (Mean±SEM, n = 10)

	Fresh	Fatigue
Relaxation time SF_{50} msec	90.8±1.7	186.3±10,2
Relaxation speed $1/SF_{50} \times 10^{-2}$ $msec^{-1}$	1.106±0.021	0.554±0.037
Max. Rate of muscle temperature rise $^{o}C.min^{-1}$	1.078±0.019	0.281±0.038

Subjects voluntarily sustained an isometric contraction at half maximum voluntary force as long as possible (60-100 sec) under ischaemic conditions. Muscle temperature was recorded continuously with thermocouple needle (Fig. 4) and relaxation measured after a brief tetanus at 30 Hz before and at the end of the fatiguing contraction before restoration of the circulation. Such contractions resulted in fatigue equivalent to a 50 % loss of MVC.

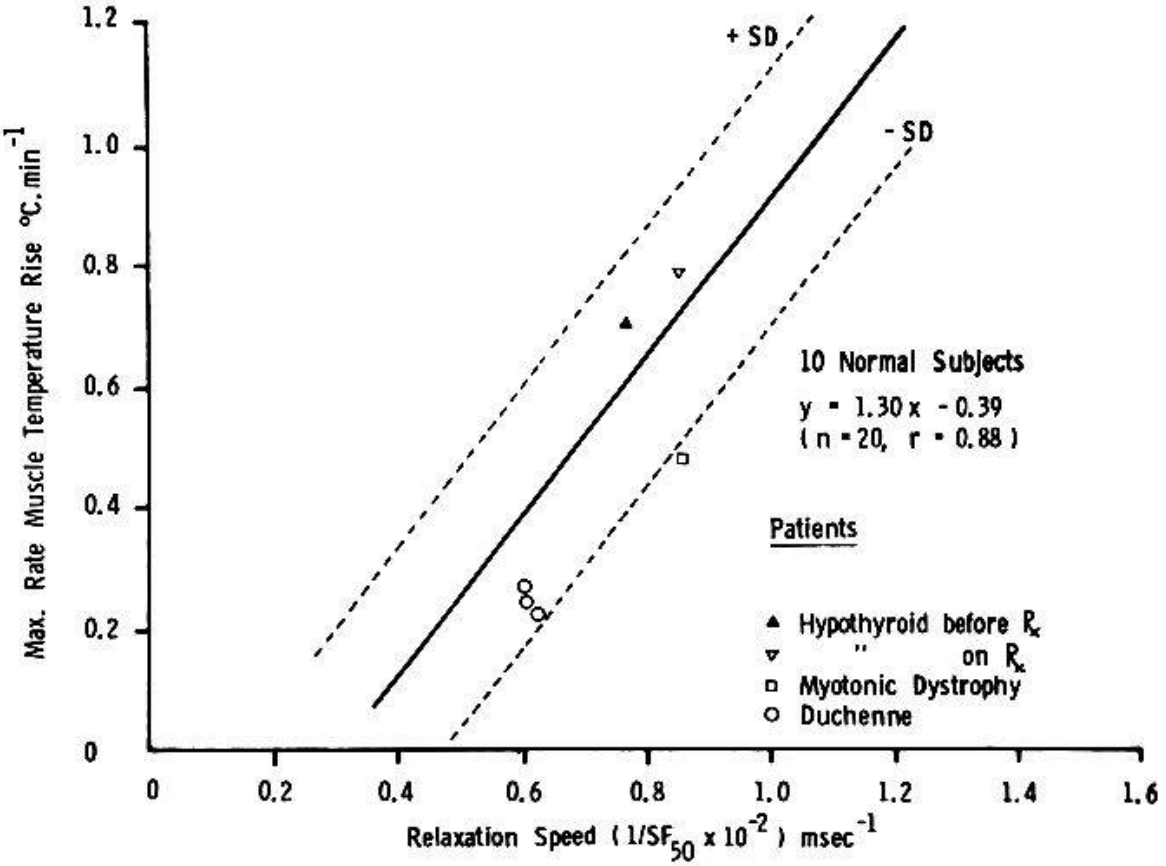

Figure 9. Relation between maximum rate of muscle temperature rise and relaxation speed. The regression line has been calculated through the range of results in normal subjects in whom muscle was fatigued by a 60 - 90 sec contraction at 50 % MVC made under ischaemic conditions. In such a contraction both relaxation speed and maximum rate of muscle temperature rise are reduced (Table 2). Preliminary results are shown for patients having a reduced maximum rate of muscle temperature rise and relaxation speed.

three with Duchenne muscular dystrophy. The interpretation of the low maximum metabolic rates has been greatly helped by consideration of the relaxation speed of the muscles, here measured as the reciprocal of the relaxation time for 50 % loss of tetanic force (SF_{50}) (Table 2). It would appear that the maximum rate of heat production in unfatigued muscles of patients is related to the relaxation speed (Fig. 9) in the same way as has been found in the studies of fatigue in normal subjects, i.e., the lower the maximum rate of temperature rise, the slower the relaxation speed. A patient's muscle may behave as if it were fatigued. Clearly there are several technical problems which might lead to an incorrect interpretation such as the inadvertent placing of the tip of the thermal probe in an area of fat or fibrous tissue, or failure to electrically excite the muscle adequately but the practical correlation with relaxation speed, as well as the comparisons between voluntary and electrically stimulated contractions (Figs. 7 & 8) help to check against such errors.

Needle biopsy

DUCHENNE (1872) described a "harpoon" biopsy needle for obtaining muscle samples from his patients with muscular dystrophy. Nearly a century later, BERGSTRÖM (1962) reintroduced the technique for studying muscle electrolytes and subsequently energy metabolites. His technique was then shown to be a practical means for investigating muscle chemistry, histology, histochemistry and ultrastructure in patients with muscle disorders (EDWARDS, 1971; EDWARDS, JONES, MAUNDER and BATRA, 1975; EDWARDS, MAUNDER, LEWIS and PEARSE, 1973; EDWARDS and MAUNDER, 1977). Providing care is taken with the orientation of the fibres in the biopsy specimen; needle biopsy provides an effective alternative to open biopsy and has the advantages that it is safe, simple, rapid and repeatable. Virtually all patients with muscle weakness referred for routine electromyography might benefit from a diagnostic needle biopsy. A needle biopsy is also an essential to the interpretation of physiological measurements of muscle function since a number of features (e.g., relaxation speed, MOULDS et al., 1977; and maximum rate of metabolic heat production; BOLSTAD and ERSLAND, 1975) are dependent on the relative contributions of the slow oxidative and fast glycolytic fibres as revealed by myosin ATPase staining (DUBOWITZ and BROOKE, 1973).

Clinical applications

Over a century ago Dr GEORGES DUCHENNE of Boulogne mapped out the field of scientific and clinical research in human muscle disease (DUCHENNE, 1872). By his careful clini-

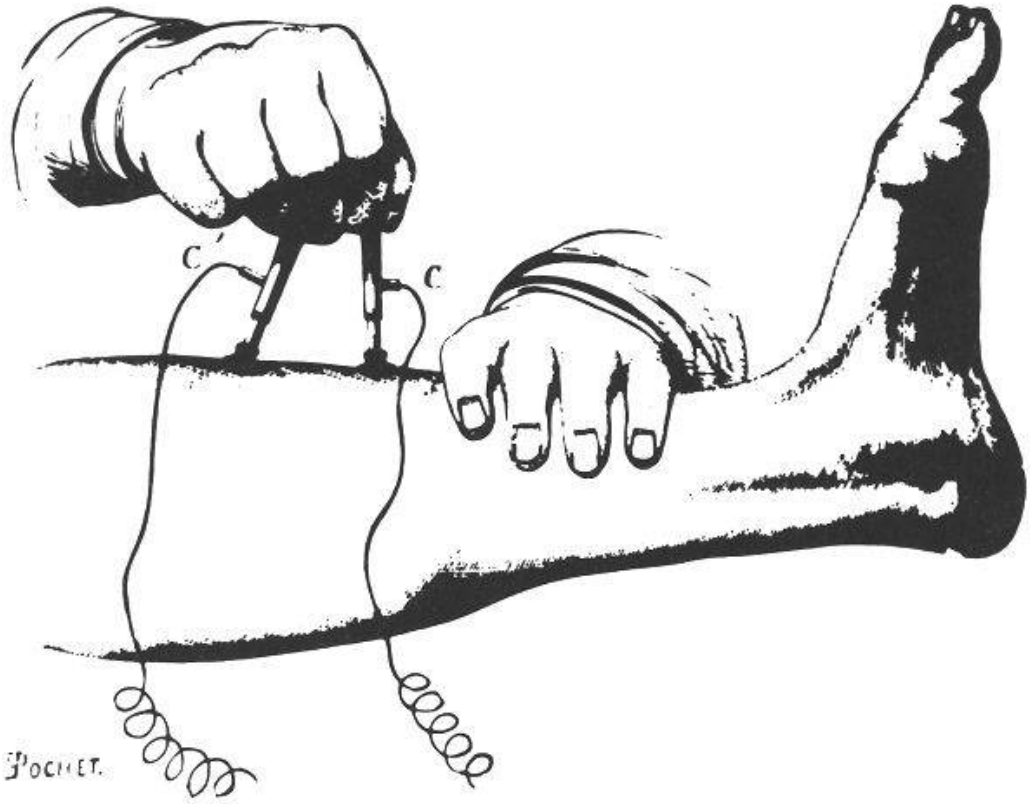

Figure 10. Duchenne's method for demonstrating the physiological action of the anterior tibial muscle in response to maximum Faradic stimulation applied by electrodes C´, C (Duchenne, 1867).

cal descriptions of muscle disorders (including the muscular dystrophy which bears his name), introduction of a needle biopsy technique for histological studies and detailed investigations of muscle action by electrical stimulation (Fig. 10), Duchenne is justly regarded as the founder of myology and clinical electrophysiology. But today there are still no accepted means for quantitatively evaluating the function of human skeletal muscle. Perhaps, by analogy with the rebirth of interest in lung function after the second world war, and the subsequent great developments in respiratory physiology, it seems to me that the means are becoming available (Table 3 and Fig. 4) for the systematic study of human skeletal muscle function and that this can be used as a basis in determining the physiological disturbance in neuromuscular disorders. Though some of the ideas are a hundred years old, the problems of human muscle disease are so intractable as to remain largely unsolved both in respect of diagnosis and even more so as to treatment. It is hoped that the application to clinical problems of new and fundamental studies of normal human muscle will lead to a greater understanding of how the machinery of human muscle works and how its function is disturbed in patients with neuromuscular disorders. Armed with this greater understanding we may, hopefully, make new progress in the search for effective treatments in these disorders.

Table 3. Clinical assessment of skeletal muscle function

Total muscle (motivation dependent)	Force	Clinical performance tests Strain gauge } measurements Myometer }
Local muscle characteristics	Chemistry	Needle biopsy
	Structure	Needle biopsy
	Contractile properties	Electrical stimulation
	Energy turnover	Myothermogram

Acknowledgements

I am grateful to Professor D.K. Hill, F.R.S., Dr D.A. Jones and Mr M. McDonnell, Dr A. Young, Dr G.P. Hosking and Mrs C.A. Maunder for their collaboration in different stages of the research described. Support from the Wellcome Trust and Muscular Dystrophy Group of Great Britain is also gratefully acknowledged.

Akre, S. and Aukland, K. (1970): Energy turnover in contracting human muscle. Acta physiol. scand. 79: 20-21A.

Alexander, R.McM. and Vernon, A. (1975): The dimensions of knee and ankle muscles and the forces they exert. J. Human Movement Studies, I: 115-123.

Barcroft, H. and Millen, J. (1947): On the heat production in human muscle during voluntary contraction. J. Physiol., 106: 13-14P.

Becquerel and Breschet (1835): Premier Memoire sur la Chaleur animale. Anal. de Phys. et Chimie, 59: 113-136.

Bergström, J. (1962): Muscle electrolytes in man. Determined by neutron activation analysis on needle biopsy specimens. A study in normal subjects, kidney patients and patients with chronic diarrhoea. Scand. J. clin. Lab. Invest., Supp. 68.

Bolstad, G. and Ersland, A. (1975): Energy metabolism in different human skeletal muscles during voluntary isometric contraction. Acta physiol. scand., 95: 73A.

Buchthal, F., Høncke, P. and Lindhard, J. (1944): Temperature measurements in human muscles in situ at rest and during muscular work. Acta physiol. scand., 8: 230-288.

Burke, D., Skuse, N.F. and Lethlean, A.K. (1974): Isometric contraction of the abductor digiti minimi muscle in man. J. Neurol. Neurosurg. Psychiat. 37: 825-834.

Close, R.I. (1972): Dynamic properties of mammalian skeletal muscles. Physiol. Rev., 52: 129-197.

Desmedt, J.E., Emeryk, B., Renoirte, P. and Hainaut, K. (1968): Disorder of muscle contraction processes in sex-linked (Duchenne) muscular dystrophy, with correlative electromyographic study of myopathic involvement in small hand muscles. Amer. J. Med., 48: 853-872.

Dubowitz, V. and Brooke, M. (1973): Muscle Biopsy: A Modern Approach. London: Saunders.

Duchenne, G.B. (1867): Physiologie des mouvements demontrée à l'aide de l'expérimentation électrique et de l'observation clinique et applicable à l'étude des paralysies et déformation. (English translation. Physiology of Motion by Kaplan, E.B. (1959) Philadelphia: Saunders.)

Duchenne, G.B. (1872): De l'électisation localisée et de son application à la pathologie et à la thérapeutique par courants induits et par courants galvaniques interrompus et continus. 3e édition. Paris: Ballière.

Edwards, R.H.T. (1975): Muscle fatigue. Postgrad. Med. J., 51: 137-143.
Edwards, R.H.T. (1977): Energy metabolism in normal and dystrophic human muscle. In: Pathogenesis of Human Muscular Dystrophies. Ed. L.P. Rowland. pp. 415-418. Amsterdam: Excerpta Medica.
Edwards, R.H.T. and Hill, D.K. (1975): "Economy" of force maintenance during electrically stimulated isometric contractions of human muscle. J. Physiol., 250: 13-14P.
Edwards, R.H.T., Hill, D.K. and Jones, D.A. (1975a): Heat production and chemical changes during isometric contractions of the human quadriceps muscle. J. Physiol., 251: 303-315.
Edwards, R.H.T., Hill, D.K. and Jones, D.A. (1975b): Metabolic changes associated with the slowing of relaxation in fatigued mouse muscle. J. Physiol., 251: 287-301.
Edwards, R.H.T., Hill, D.K. and McDonnell, M. (1972): Myothermal and intramuscular pressure measurements during isometric contractions of the human quadriceps muscle. J. Physiol., 224: 58-59P.
Edwards, R.H.T. and Hyde, S. (1977): Methods of measuring muscle strength and fatigue. Physiotherapy, 63: 51-55.
Edwards, R.H.T., Jones, D.A., Maunder, C. and Batra, G.J. (1975): Needle biopsy for muscle chemistry. Lancet, i: 736-740.
Edwards, R.H.T., Maunder, C., Lewis, P.D. and Pearse, A.G.E. (1973): Percutaneous needle-biopsy in the diagnosis of muscle diseases. Lancet, ii: 1070-1071.
Edwards, R.H.T. and Maunder, C.A. (1977): Review. Muscle biopsy. Hospital Update (in Press).
Edwards, R.H.T. and McDonnell, M. (1974): Hand-held dynamometer for evaluating voluntary-muscle function. Lancet, ii: 757-758.
Edwards, R.H.T., McDonnell, M.J. and Hill, D.K. (1974): A thermistor probe for myothermal measurements in man. J. Appl. Physiol., 36: 511-513.
Edwards, R.H.T., Young, A., Hosking, G.P. and Jones, D.A. (1977): Human skeletal muscle function: description of tests and normal values. Clin. Sci. molec. Med., 52: 283-290.
Feng, T.P. (1931): The heat tension ratio in prolonged tetanic contractions. Proc. R. Soc. B., 108: 522-537.
Hosking, G.P., Bhat, U.S., Dubowitz, V. and Edwards, R.H.T. (1976): Measurements of muscle strength and performance in children with normal and diseased muscle. Arch. Dis. Childh., 51: 957-963.
Hosking, G.P., Young, A., Dubowitz, V. and Edwards, R.H.T. (1977): Tests of skeletal muscle function in children. Arch. Dis. Childh., (In Press).
Ikai, M. and Fukunaga, T. (1968): Calculation of muscle strength per unit cross-sectional area of human muscle by means of ultrasonic measurement. Int. Z. angew.Physiol. einschl. Arbeitsphysiol., 26: 26-32.
Ikai, M. and Fukunaga, T. (1970): A study on training effect on strength per unit cross-sectional area of muscle by means of ultrasonic measurement. Int. Z. angew. Physiol., 28: 173-180.
Merton, P.A. (1954): Voluntary strength and fatigue. J. Physiol., 128: 553-564.
Morris, C.B. (1948): The measurement of the strength of muscle relative to the cross-section. Res. Quart. Amer. Ass. Hlth. phys. Educ., 19: 295-303.
Moulds, R.F.W., Young, A., Jones, D.A., and Edwards, R.H.T. (1977): A study of the contractility, biochemistry and morphology of an isolated preparation of human skeletal muscle. Clin. Sci. molec. Med., 52: 291-297.
Tornvall, G. (1963): Assessment of physical capabilities with special reference to the evaluation of maximal voluntary isometric muscle strength and maximal working capacity. Acta physiol. scand., 58: Suppl. 201.
Wiles, C.M. and Edwards, R.H.T. (1977): Weakness in myotonic syndromes. Lancet, ii: 598-601.

Young, A. and Edwards, R.H.T. (1977): Clinical investigations of muscle contractility. Rheumatol. & Rehab., 16: (In Press).

Author's address: Professor R.H.T. Edwards, Department of Human Metabolism, University College Hospital Medical School, University Street, London WC1E 6JJ