The contribution of reflex inhibition to arthrogenous muscle weakness

This Editorial Review is based on Dr Young's essay 'The pathophysiology of arthrogenous muscle weakness: lessons for rehabilitation', winner of the 1983 Eli Lilly Prize of the Medical Research Society.

MARIA STOKES AND ARCHIE YOUNG
Nuffield Departments of Orthopaedic Surgery and Clinical Medicine, University of Oxford, Nuffield Orthopaedic Centre, Oxford, U.K.

'Arthrogenous muscle weakness' is weakness of muscles acting about an injured or inflamed joint. The weakness may be due to loss of muscle or to inability to activate the muscle (Fig. 1). Weakness of the thigh muscles, and of the quadriceps in particular, is a common and important consequence of knee trauma, surgery or arthritis. Muscle weakness contributes significantly to disability and probably also renders the joint vulnerable to further damage (Fig. 1). This review starts with a brief discussion of the contribution of atrophy to weakness. It concentrates, however, on inhibition of quadriceps activation and suggests some therapeutic implications. It does not deal with the reduced oxidative capacity and increased fatiguability of disused muscle since, although important, these have not been part of our programme of work.

Quadriceps wasting

Measurement

Traditionally, thigh muscle wasting is assessed from measurements of thigh circumference. The tape measure is too insensitive and inaccurate for measuring the selective wasting of the quadriceps which occurs with knee damage because it also encloses a large bulk of other muscles and a layer of subcutaneous fat. Transverse imaging techniques, such as computerized axial tomography [1, 2] and ultrasonic compound B-scanning [3], allow accurate measurement of the cross-sectional area of the quadriceps itself and should be used for any studies involving changes in quadriceps size. The inadequacy of the tape measure has been demonstrated by ultrasonic studies of selective quadriceps wasting [3] and growth [4].

Selective wasting of heads of quadriceps

It is commonly believed that vastus medialis wastes more than the other three heads of the quadriceps. However, the few direct data that are available are more suggestive of a uniform atrophy [5, 6].

Fibre atrophy or fibre loss?

Studies of human muscle, using the needle biopsy technique [7], suggest that quadriceps wasting due to injury and/or immobilization of the
knee is caused by atrophy of fibres [6]. This differs from the wasting seen in elderly muscle which is thought to involve both loss in fibre size and fibre number [8], with the latter perhaps predominating [9].

**Selective atrophy of fibre types**

Fibre-typing according to alkali-stable myosin ATPase activity may reveal striking changes in the relative sizes of type I and type II fibres. Atrophy of type II fibres occurs in a wide variety of conditions [7]. Since it is the high-threshold motor units that comprise type II fibres, it is generally held that selective type II fibre atrophy reflects a sick patient's general inactivity. It is no surprise, therefore, that some patients with arthrogenous quadriceps atrophy show preferential atrophy of their type II fibres [e.g. 6, 10]. Preferential atrophy of type I fibres is not a common feature in muscle histopathology. Nevertheless, in the context of arthrogenous wasting, it is as common as type II atrophy [11].

It is far from clear which clinical features determine whether there is selective atrophy of one or other fibre type [11, 12]. An understanding of the mechanisms responsible for preferential fibre-type atrophy would allow the prediction of the likely pattern of atrophy in any given clinical situation and the individual patient to be given the most appropriate treatment. For example, treatment might involve removing the cause of the selective atrophy and then performing specific exercises tailored to stimulate growth of the more atrophic type of fibre [7, 12]. The possibility that selective atrophy might result from selective inhibition is discussed later.

Irrespective of which fibre type is more atrophic, it seems that arthrogenous atrophy may be associated with an increase in the frequency of fibres with a high activity of alkali-stable myosin ATPase (type II fibres) [6, 13]. Whatever its physiological interest, the difference between healthy and atrophic muscles in type II frequency is small and seems unlikely to be of major clinical importance except, perhaps, for the injured endurance athlete [14] whose athletic performance depends on his muscles' high proportion of type I fibres.

**Reflex inhibition**

Even in the absence of pain, joint pathology can inhibit muscle activity and so cause both weakness and wasting (Fig. 1). The dependence of arthrogenous weakness on afferent stimuli from the joint and its dissociation from pain were documented last century, and the mechanism was judged to be a reflex [e.g. 15]. Reflex inhibition has been observed in different clinical situations, e.g. in the quadriceps after minor knee trauma [16], in the elbow flexors after elbow dislocation [17]. It is commonly seen in the quadriceps after knee surgery; patients often describe their inability to contract their quadriceps as a lack of 'control' over the muscle. Although the existence of reflex inhibition is still recognized [e.g. 18], few appreciate its potency. It is often ascribed to pain [19] and there has been little attempt to find methods for its removal other than by the relief of pain.

**Measurement**

**Strength/cross-sectional area.** Healthy women in their twenties and in their seventies show the same close relationship between the quadriceps' isometric strength and its cross-sectional area (CSA) but the older women are 35-40% weaker and their quadriceps' CSA is 35-40% less [20]. The strength of a young female patient's wasted quadriceps can therefore be judged against that of a similarly sized muscle in a healthy elderly woman. 'Excessive' weakness, whether due to pain, reflex inhibition or an intrinsic defect of muscle contractility, can therefore be quantified. Although this approach may be helpful, it has its limitations. Firstly, it cannot be used in young men; although the relationship between quadriceps size and strength in old men is similar to that in both young and old women, the quadriceps strength of some young men is substantially greater than would be expected from the size of the muscle [21]. Perhaps, even in young men, there might be a place for comparing the quadriceps strength/CSA of the injured with that of the uninjured limb (rather than with a normal range). Secondly, many patients with knee pathology are unable to flex the joint to 90°, the angle at which the standardized strength measurements were made. Thirdly, as discussed below, the severity of quadriceps inhibition may be less when the knee is in flexion than when it is in extension [22]. Finally, if type II fibres have a greater isometric specific strength than type I fibres [23, 24] severe selective atrophy of type II fibres would result in a disproportionate loss of strength/CSA.

**Maximal voluntary activation.** The level of quadriceps activation achieved during maximal voluntary isometric contractions can be measured by integration of the rectified electromyogram, recorded with surface electrodes at a fixed site over the quadriceps. In a patient with unilateral
quadriceps wasting, the maximal voluntary activation (MVA) recorded for the two quadriceps should be almost the same. There may be a small difference in MVA due to the unequal recording conditions but major differences can be considered a measure of inhibition.

Meniscectomy as a model for investigating quadriceps inhibition

We have used arthrotomy and meniscectomy as a model of controlled knee injury, studying the magnitude and duration of postoperative quadriceps inhibition and seeking methods for its reduction or prevention.

Bilateral measurements of MVA of quadriceps were recorded over rectus femoris (at full knee extension) before surgery. All subsequent measurements were then expressed as ‘percentage inhibition’ (i.e. percentage reduction in MVA). Knee pain experienced during each contraction was recorded on a linear analogue scale (horizontal line without word cues) and expressed as a percentage of the length of the line.

Magnitude and duration. Inhibition in the immediate postoperative period is severe (typically 50–70%), tends to become even more pronounced over the first 24 h (80%), and by 3–4 days postoperatively is still very severe (typically 70–80%) (Fig. 2). Even 10–15 days postoperatively there is still some 35–40% inhibition despite the fact that patients have been discharged from hospital and are fully weight-bearing.

Role of pain. Dorsal root section prevents muscle atrophy secondary to experimental arthritis [15, 25] but not secondary to disuse [25]. Harding observed that her experimental animals with artificially induced arthritis did not seem to be in pain and so argued that dorsal root section was blocking an inhibitory afferent stimulus other than pain [25].

During the first 24 h after meniscectomy, pain during contraction may be quite severe (typically 50–70%) but, unlike inhibition, it is usually only

Fig. 2. Quadriceps inhibition (median and range, in both legs) and knee pain (median, in the operated leg) recorded during maximal voluntary isometric contractions (in extension), after medial meniscectomy. In the one patient who developed an effusion, recordings were made after its aspiration.
mild by 3-4 days (1-15%) [26]. Ten to 15 days postoperatively pain is mild or absent (0-10%) (Fig. 2). Another example of a clear dissociation between pain and inhibition was seen in a study in which we attempted to block the inhibitory afferent stimuli. Pre-operative infiltration of the meniscal bed and surrounding tissues with 15 ml of 0.5% (75 mg) bupivacaine temporarily prevented most of the pain and most of the inhibition. If only 10 ml were used, however, there was no change in the severity of inhibition although most of the pain was still prevented [27].

**Role of ischaemia.** It has been suggested that the period of tourniquet ischaemia during knee surgery contributes to postoperative quadriceps weakness [28, 29]. If this were true, our findings with the meniscectomy 'model' would be less relevant to patients with, for example, rheumatoid arthritis (i.e. with joint pathology but without tourniquet ischaemia). We therefore studied the quadriceps of four normal subjects before and after the maximal tolerable periods of unilateral tourniquet ischaemia [30]. The tourniquets were applied exactly as for meniscectomy and the durations of ischaemia (37-50 min) were comparable with those of our meniscectomy patients. Quadriceps MVA was unaltered after voluntary ischaemia so we can conclude that the reduced MVA in our meniscectomy patients was not caused by the tourniquet alone.

**Role of effusion.** Normal subjects and patients given a large experimental knee effusion (>55 ml approx.) lose the ability to make an effective quadriceps contraction, even in the absence of pain [31, 32]. In patients who developed an effusion post-meniscectomy, although aspiration of the effusion always reduced the severity of inhibition, it rarely abolished it (Fig. 3). Indeed, all the measurements of inhibition reported in Fig. 2 were made in the absence of any clinically apparent effusion. Perhaps congestion and inflammation of the synovium or of the capsule are also important. Nevertheless, it is clear that there are strong grounds for a less tolerant attitude to the presence of an effusion in the pathological knee.

**Fig. 3.** Effect of aspirating a knee effusion on quadriceps inhibition, 3-5 days after meniscectomy.

**Peri-articular pathology.** Stimuli from peri-articular tissues have been shown to cause quadriceps inhibition [e.g. 33]. We have seen this in a patient with profound quadriceps wasting and weakness 2 years after the excision of a calcified prepatellar haematoma (Fig. 4, and below). Perhaps inflammation around the incision causes inhibition after meniscectomy. In decerebrate cats, pinching the anterior aspect of the knee joint capsule inhibited the quadriceps stretch reflex and also inhibited quadriceps activity in the crossed extensor response [34]. Perhaps tight suturing of the capsular incision has a similar inhibitory effect. This suggestion is compatible with some preliminary studies of patients who have undergone either arthroscopy or arthroscopic meniscectomy. The capsular incision for arthroscopy is small and so is not sutured after surgery. Patients who have had arthroscopy (with or without meniscectomy) do not appear to develop the severe and prolonged quadriceps inhibition observed in patients who have undergone arthroscopy (with or without meniscectomy) (M. Stokes, K. Sherman, D. Shakespeare & A. Young, unpublished data).

**Afferent block.** Quadriceps inhibition is associated with afferent stimuli from the knee joint. Thus, dorsal root section prevents atrophy secondary to experimental arthritis [15, 25], the quadriceps inhibition which results from filling a normal knee with a large volume of fluid can be partially prevented by previous intra-articular injection of local anaesthetic [31], and quadriceps weakness did not occur in a patient with Charcot's arthropathy of the knee when the joint was distended at high pressure [31]. In the patient whose prepatellar haematoma had been excised, infiltration of the prepatellar scar with local anaesthetic substantially reduced her quadriceps inhibition, confirming that the source of the afferent stimuli was outside the joint proper (Fig. 4).

In clinical practice, if the afferent stimuli from a damaged knee could be blocked effectively by local anaesthetic (or some other method) for long periods, the patient would be able to achieve maximal quadriceps activation in this therapeutic
Arthrogenous muscle weakness

exercise and perhaps atrophy would be prevented. After meniscectomy, however, the protective effect of 15 ml of bupivacaine has already been lost by 5 h postoperatively [27]. Although local anaesthesia is useful for identifying inhibition and for localizing the source of the inhibitory afferent stimuli, its effect seems too short-lived to be of clinical value. I. Arvidsson, E. Eriksson & E. Knutsson (unpublished work, [19]) have described how voluntary quadriceps activation is increased, by epidural injection of a dilute local anaesthetic, in patients who have had knee surgery. They assumed that the inhibition was pain-induced because pain was blocked by the injection and because the anaesthetic was sufficiently dilute so as not to block the large motor fibres [19]. The strength of the anaesthetic may have been such, however, that other afferent fibres were also blocked. If effective in the absence of pain, light epidural anaesthesia might be useful, allowing the afferent block to be maintained for several days postoperatively.

Joint angle. An effusion inhibits quadriceps contractions less in 30° of flexion than in full extension [35]. This is probably because, in both effused and normal knees, intra-articular pressure is less with the knee in about 30° of flexion than in full extension [32,36-38]. After meniscectomy, however, it is striking that without any clinically apparent effusion, MVA is greater during isometric quadriceps contractions in flexion than in extension [22] (Fig. 5). This also occurred in the patient with the prepatellar scar (Fig. 4). The quadriceps activation increased to similar extents at 10° and 90° (angles of high intra-articular pressure) and 40° (angle of low pressure). This exercise and perhaps atrophy would be prevented. After meniscectomy, however, the protective effect of 15 ml of bupivacaine has already been lost by 5 h postoperatively [27]. Although local anaesthesia is useful for identifying inhibition and for localizing the source of the inhibitory afferent stimuli, its effect seems too short-lived to be of clinical value. I. Arvidsson, E. Eriksson & E. Knutsson (unpublished work, [19]) have described how voluntary quadriceps activation is increased, by epidural injection of a dilute local anaesthetic, in patients who have had knee surgery. They assumed that the inhibition was pain-induced because pain was blocked by the injection and because the anaesthetic was sufficiently dilute so as not to block the large motor fibres [19]. The strength of the anaesthetic may have been such, however, that other afferent fibres were also blocked. If effective in the absence of pain, light epidural anaesthesia might be useful, allowing the afferent block to be maintained for several days postoperatively.

Joint angle. An effusion inhibits quadriceps contractions less in 30° of flexion than in full extension [35]. This is probably because, in both effused and normal knees, intra-articular pressure is less with the knee in about 30° of flexion than in full extension [32,36-38]. After meniscectomy, however, it is striking that without any clinically apparent effusion, MVA is greater during isometric quadriceps contractions in flexion than in extension [22] (Fig. 5). This also occurred in the patient with the prepatellar scar (Fig. 4). The quadriceps activation increased to similar extents at 10° and 90° (angles of high intra-articular pressure) and 40° (angle of low pressure). This
suggests that in patients with intra- or peri-articular joint pathology without apparent effusion, a cause other than intra-articular pressure must be responsible for the reduced MVA in extension.

Although this phenomenon cannot reduce the immediate disability caused by quadriceps inhibition, it seems likely that quadriceps exercises might well be more effective (by achieving greater activation) when performed in flexion rather than in the conventional, fully extended position. It may also have important implications for the position in which an injured or inflamed joint is immobilized because involuntary activity might also be more severely inhibited in extension.

**Reflex inhibition of involuntary muscle activity**

It seems likely that involuntary, reflex, activation of muscle may also be inhibited. In the decerebrate cat, increasing intra-articular tension or pinching the knee capsule inhibits the mono-synaptic reflex from the quadriceps [34]. The H-reflex is the muscle activation elicited, via this reflex, by electrical stimulation of 1a afferents of the femoral nerve. Reduction of the H-reflex implies reduced excitability of the motor neurone pool. In man, it has been claimed that an experimental knee effusion reduces the quadriceps’ H-reflex and that intra-articular anaesthesia blocks this effect [39], but the complete data are still unpublished.

Various effects of immobilization on neural and muscular excitability have been studied but some studies fail to distinguish between immobilization alone and immobilization plus a source of inhibitory afferent stimuli. For example, group 1a excitatory postsynaptic potentials were reduced in gastrocnemius motor neurones of cats whose knee and ankle joints were immobilized by pinning [40]. Voluntary activation of motor units in human quadriceps was reduced after knee immobilization for treatment of collateral ligament injuries [41]. In a study which involved immobilization alone, of human thenar muscles, there was a reduction in reflex potentiation (i.e. the enhancement of reflex responses by voluntary effort, which is considered a function of motor neurone excitability) [42].

**Selective inhibition of heads of quadriceps**

Just as there is no evidence to support the concept of selective wasting of individual heads of the quadriceps, there is little published evidence to indicate that activity of a single head of the muscle can be selectively inhibited. The claim that distending a normal knee reduces the H-reflex more in vastus medialis (VM) than in vastus lateralis (VL) or rectus femoris (RF) [39] is not, as yet, supported by adequate data.

Stener’s patient with a tender subperiosteal tumour proximal to the lateral femoral epicondyle had almost no inhibition of RF despite severe inhibition of VL and VM [33]. In this case, however, the inhibition might have been part of a nociceptive flexor response, thus explaining the continuing activity in RF (a hip flexor) when the tumour was palpated during a quadriceps contraction.

**Selective inhibition of fibre types**

A possible explanation for the selective atrophy of type I or type II fibres is selective inhibition of their motor neurones. There is, as yet, very little evidence to support this, other than the demonstration that ‘painful’ stimulation of the sural nerve caused selective inhibition of low-threshold motor units (presumably type I fibres) in the human biceps femoris, whereas ‘tactile’ stimulation caused facilitation [43]. New electrophysiological techniques [e.g. 44, 45], however, offer the exciting prospect of distinguishing changes in voluntary activity (and therefore changes in inhibition) of type I fibres from changes in activity of type II fibres. This could provide a key to understanding the clinical correlates of selective atrophy of type I or type II fibres.

**Implications for rehabilitation**

In the previous sections we have highlighted ways in which inhibition might be reduced in rehabilitation practice. In addition, some techniques in current use, e.g. ice, transcutaneous sensory nerve stimulation (TNS), transcutaneous motor nerve stimulation (faradic stimulation), may have an effect on reflex inhibition. Ice and TNS are used for pain relief to allow exercises to be performed comfortably but perhaps they might also be influencing inhibition. It is known that certain sensory stimuli can block other afferent sensory stimuli in the spinal cord [46]. Cutaneous sensory nerve stimulation can increase motor neurone excitability in humans [47]. Perhaps TNS might reduce quadriceps inhibition by one of these mechanisms, i.e. by preventing activation of inhibitory synapses (disinhibition), or by increasing the excitability of the anterior horn cells. We are currently testing the effect of TNS on post-meniscectomy quadriceps inhibition.

Training of the quadriceps by transcutaneous motor nerve stimulation has produced voluntary
Arthrogenous muscle weakness

strength increases in normal subjects [48]. Although it is difficult to stimulate the whole quadriceps, this might still be a worthwhile way of bypassing reflex inhibition. The effects of transcutaneous motor nerve stimulation on the prevention or reversal of atrophy have not yet been objectively tested.

Therapeutic resources today are too scarce for the prescription of ineffective physiotherapy. The contribution of atrophy to arthrogenous weakness has been reviewed elsewhere and some recommendations for rehabilitation were proposed [11]. This present discussion of investigations into another aspect of the pathophysiology of arthrogenous muscle weakness has included further recommendations, concerning the prevention and/or reduction of reflex inhibition, and concerning the investigative techniques which might be used for further work in this area. Such studies will ensure that the rehabilitation of patients with joint damage is more scientifically based and more effective.

Acknowledgments

We are grateful to all the patients, normal subjects and co-authors who have contributed to our research programme. In particular, we are pleased to acknowledge the collaboration, at different stages, of Professor R. H. T. Edwards, Dr J. M. Round, Miss I. Hughes, Dr M. Crowe, Mr D. T. Shakespeare and Mr K. P. Sherman. We thank the Department of Health and Social Security for financial support.

References


