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Delayed Onset Muscle Soreness

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DELAYED ONSET MUSCLE SORENESS

by

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This Independent Study, submitted by Bryan L. Guthmiller, in partial fulfillment of the requirements for the Degree of Master of Physical Therapy from the University of North Dakota, has been read by the Faculty Preceptor, Advisor, and Chairperson of Physical Therapy under whom the work has been done and is hereby approved.

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ABSTRACT

Delayed-onset muscular soreness (DOMS), the sensation of pain and stiffness in the muscles that occurs from 1-5 days following unaccustomed exercise, can adversely affect muscle performance, both from voluntary reduction of effort and from inherent loss of capacity of the muscles to produce force. This exercise-induced muscle damage causes a response that can be characterized by a cascade of metabolic events. Increased circulating neutrophils and interleukin-1 occurs within 24 hours after the exercise, with skeletal muscle levels remaining elevated for a much longer time. Several theories underlying the physiological mechanisms of DOMS have been proposed. The majority of evidence contradicts the 'spasm' and 'lactic acid' theories. Recent evidence indicates that ultrastructural damage to skeletal muscle may be the primary mechanism contributing to muscle soreness. The best treatment for DOMS appears to be muscular activity. Training for the specific contractile activity that causes DOMS reduces the soreness response.

CHAPTER 1

INTRODUCTION

Numerous studies in applied physiology, sports medicine, and nutrition have been dedicated to a search for the mechanisms underlying delayed onset muscle soreness (DOMS), a phenomenon first studied by Hough[1] beginning early this century. Hough described many of the signs and symptoms of DOMS and distinguished the pain of delayed onset muscle soreness from that of muscular fatigue, noting that this delayed pain was more likely to be associated with rhythmic contractions marked by high intensity with relatively little associated fatigue.[1] Later research has verified Hough's initial findings, concluding that the soreness represents a type of pain which follows the strenuous use of skeletal muscle not accustomed to such activity, especially if the target activity has a primary eccentric (lengthening) component. Studies show that DOMS typically appears within 24 hours, reaches a peak at approximately 48 hours, and gradually declines over an additional 2-5 days.[2] While current literature favors microtrauma of connective tissue and/or myofibers as the pain mechanism behind DOMS, a precise

understanding of its chemical and physical basis is largely unknown.

DOMS has wide-ranging implications for the human population, as everyone from the professional athlete to the occasional weekend jogger can be affected by its painful exacerbations. Despite the expanse of literature on the subject, recent research on the prevention or attenuation of this phenomenon has generally been lacking. Due to its transient nature, a majority of researchers have failed to address the importance of prevention and management of this disorder. Studies that have been performed in this area have generally focused on the modalities of ultrasound and iontophoresis, as well as drug therapy and the adoption of alternative training methods.[2] Integration of these methods as well as the discovery of other treatments based on sound physiological principles should be the priority of future research.

The purpose of this literature review is to provide a comprehensive overview of the mechanisms, physiological basis, nutritional concerns, and management of delayed onset muscle soreness.

CHAPTER 2

METABOLIC EFFECTS

Muscle contraction and shortening produces a concentric action; however, when skeletal muscle lengthens as it produces force, the result is an eccentric muscle action. An example of this is lifting a weight (concentric action) and lowering it (eccentric action). At the same power output, the oxygen cost of eccentric exercise is lower than that of concentric exercise.[3] Despite the lower oxygen cost, eccentric exercise has been demonstrated to be a potent cause of muscle damage, DOMS, and increased creatine kinase (CK) activity.[3] The reason why eccentric exercise causes far greater amounts of muscle damage than concentric exercise may be due to different fiber recruitment patterns.

Newham et al.[4] measured the integrated EMG (IEMG) during chair stepping exercise. They asked their subjects to perform the exercise with one leg raising the body and the contralateral leg lowering the body. Fewer motor units were recruited during eccentric exercise and, unlike the concentric leg, the IEMG rose progressively during the eccentric exercise. They concluded that the fact that the

greater tension per muscle fiber is generated under eccentric contraction conditions provides a situation where relatively few fibers are recruited and are producing relatively large forces. It thus appears that when an individual performs eccentric exercise that he or she is not accustomed to, there is far greater force/fiber than during concentric exercise producing similar amounts of force.

MYOCELLULAR ENZYME RELEASE

The appearance of myocellular enzymes, primarily creatine kinase, in the circulation is generally taken as an indication of "muscle damage." The extent of the post-exercise rise in circulating skeletal muscle enzymes appears to be most closely related to the type and intensity of the exercise and the previous activity of the subjects.

Type and Intensity of Exercise

Friden et al.[5] examined serum muscle enzyme activities (glutamic oxalocetic transaminase [SGOT], lactic dehydrogenase [LDH], and creatine kinase [CK]) in young subjects performing eccentric, concentric, or isometric exercise of the lower-leg anterior compartment. The SGOT and circulating CK activities increased significantly 48 hours after the eccentric exercise only. Serum LDH levels were not affected by any of the exercise interventions. The increases in serum enzyme activities were relatively small for this study (36% and 17% for CK and SGOT, respectively) probably

because of the low intensity of the exercise and the small mass of muscle during the exercise. Much larger increases in circulating CK have been seen following other eccentric exercise protocols. A 351% increase in circulating CK activity was seen following downhill running but no change was seen following running on the level.[6] Newham et al.[4] examined circulating CK after stepping exercise and found a remarkably variable response: some subjects showed only a small two-to threefold increase 24 hours after the exercise, whereas others displayed a 70-to 100-fold increase peaking up to 6 days following the exercise. They found no relationship between peak-circulating CK and body weight, but neither the aerobic capacity or the activity patterns of the subjects were described.

Training

Hunter et al.[7] demonstrated that a single maximal exercise test elicited increases in circulating CK, SGOT, and LDH activities in previously sedentary men. After 10 weeks of endurance training, however, the exercise-induced changes in these enzymes were attenuated. This same training phenomenon has been seen in rats. Schwane and Armstrong[8] showed that training by downhill running or level running greatly reduced or eliminated the post-exercise rise in circulating CK activity, but that uphill training did not effect the increase. Byrnes et al.[6] found that a single bout of downhill running diminished or eliminated the amount of

delayed onset muscle soreness and circulating CK activity following subsequent bouts of downhill running up to 6 weeks later. Evans et al.[9] found that in previously sedentary men, 45 minutes of eccentric exercise caused an average 33-fold increase in circulating CK activity which did not return to pre-exercise levels for 10 days. In the same study, a group of endurance athletes performing the same exercise had a mild twofold increase that was only significant 24 hours after the exercise. The endurance athletes in this study also had higher resting circulating CK activity than did the sedentary men.

The large intersubject variability reported by many investigators in the rise in circulating CK activity following exercise is an indication that CK is not an accurate predictor of skeletal muscle damage.[10] It is likely that the post-exercise rise in circulating CK activity is a manifestation of skeletal muscle damage but not a direct indicator of it.[10]

Mechanisms of Enzyme Release

Is the release of myocellular enzymes following severe exercise analogous to myocardial infarction? Armstrong et al.[11] postulated that the enzyme efflux following an initial exposure to high-intensity eccentric exercise does in fact indicate irreversible destruction of muscle fibers. Based on this hypothesis, Newham et al.[4] proposed that the "training effect" (the dramatically reduced enzyme efflux in response

to a second exposure to eccentric exercise) is attributable to the elimination of weak or susceptible fibers by the first exposure.

One possible mechanism of cellular destruction could be physical shearing of membranes or filaments by excessive loads experienced during exercise.[10] Eccentric exercise can easily expose muscles to excessive loads, which may explain why it is particularly damaging. During concentric exercise, aerobic capacity may limit the length of time a person can develop forces sufficiently high to cause damage. In contrast, the external forces imposed on a person's muscles during eccentric exercise are not strictly limited by aerobic capacity, thus increasing the risk of overload.

Cellular destruction could also stem from transient ischemia caused by compression of vasculature during force development.[10] Again, eccentric exercise attenuates this potential mechanism for damage. Friden et al.[5] determined that eccentric contractions caused 50% higher intra-muscular pressures than concentric contractions at the same loads. Evidence has shown, however, that muscle blood flow is not different between the two modes of exercise.[10] The mass of muscle tissue likely to become ischemic is therefore small, which is consistent with the focal damage observed immediately after exercise. In most tissues, ischemia and subsequent reperfusion cause a conversion of xanthine dehydrogenase to xanthine oxidase, leading to the

production of superoxide and hydrogen peroxide.[10]

Other investigators[10] have suggested that enzyme leakage is a consequence of disturbances in cell volume or in energy state or both. One possibility is that a reduced metabolic state inhibits sarcolemmal Na-K-ATPase, resulting in swelling from intracelluar accumulation of sodium and water.[10] The swelling then leads to stretching and ultimate rupture of the membrane, allowing intracellular enzymes to escape. Jones et al.[12] also found an association between adenosine triphosphate (ATP) depletion by muscle and the efflux of enzymes. Edema and swelling following exercise-induced muscle damage has been seen by a number of investigators.[10] The evidence for this swelling has ranged from increased circumference of exercised muscle 24-48 hours after exercise, to ultrastructural evidence of post-exercise muscle edema, to direct measurement of intramuscular resting pressure.[10] Friden et al.[5] used a slit catheter placed in the leg anterior compartments to measure pressure during and following eccentric exercise in one leg and concentric exercise in the other. Average peak muscle pressure was greater during eccentric than concentric exercise and resting pressure was elevated for a prolonged period in the eccentrically, but not the concentrically, exercised leg. Friden et al.[5] also saw an increase in the water content of muscles following eccentric exercise. This increase in intramuscular pressure is thought to occur as a result of

the release of protein-bound ions in damaged muscle cells. The release of intracellular proteins into the circulation most likely results from an increase in intracellular pressure.

Exercise that results in muscle damage also initiates a well-orchestrated response that ultimately results in the repair of the damaged tissue. Indeed, exercise that may result in a great deal of muscle damage, such as lifting and lowering a heavy weight, also has the capability of producing skeletal muscle hypertrophy, which ultimately decreases the risk of future muscle damage from that particular exercise.

THE ACUTE PHASE RESPONSE

Tissue damage and infection initiate a stereotyped sequence of host defense reactions, known as the acute phase response. Although the acute phase response generally is recognized for its antibacterial and antiviral actions, it also promotes clearance of damaged tissue and sets the stage for repair and growth. These latter activities may be an explanation for why an acute phase response is initiated by exercise. The generation of an acute phase response depends on the duration, and possibly to a lesser extent, the intensity of exercise. Running a 42-kilometer marathon is an adequate stimulus of an acute phase response, but as the duration decreases, acute phase reactions are less clear.[10] Experimental complications arise because the facets of the acute phase of the response are transient and sequential.

Some are very rapid in onset (within minutes) because the elements are preformed (complement, neutrophils). Others require hours or days to become maximal owing to time-dependent transport processes (trace metals) or protein synthesis (acute phase proteins).[10] Reports indicating no changes in acute phase reactants following exercise can sometimes be attributed to sampling that was done too early, measuring trace metals immediately after short-duration exercise, or too late, sampling for circulating neutrophils 24 hours after exercise.[10] The following brief overview will focus on the aspects of the acute phase response that are associated with tissue damage and repair, and present the evidence that these occur following exercise.

Complement System

An early manifestation of the acute phase response after exercise is activation of complement.[10] Researchers have observed up to a two-fold increase in plasma anaphylatoxins immediately after a 2.5 hour running protocol.[10] Exercise of this magnitude may have caused damage to contractile or connective elements, releasing fragments that activate complement through the alternate pathway (by foreign pathogens and damaged host cells). In addition, a 10% increase was found in circulating immune complexes one hour after a similar running protocol, raising the possibility that complement may be activated by the classical pathway (antigen-antibody complexes) following exercise as well.[10]

Neutrophils

Within hours of injury or infection, the number of circulating neutrophils can increase several fold. This rapid increase is possible because only about half of the mature neutrophils released from the bone marrow usually circulate, the other half adhere to vessel walls (margination).[10] Neutrophils phagocytize pathogens and tissue debris, and release an array of cytotoxic factors, including elastase, lysozome, and oxygen radicals.[13] These factors affect intact host tissue with adaptive and maladaptive consequences. For example, elastase, collagenase, and oxygen radicals increase vascular permeability by breaking down basement membranes of the microvasculature near a site of injury, thus promoting migration of leukocytes.[10] If released in an uncontrolled manner, however, these agents also can break down healthy surrounding tissue and are the basis of several inflammatory diseases.

The number of circulating neutrophils increases during exercise and can continue to increase for several hours afterwards, depending on the duration and intensity of exercise.[3] The mechanism responsible for the increase in circulating neutrophils is not settled. It has been proposed that the increased blood flow during exercise shears marginated neutrophils free of vessel walls, but it is not clear how this mechanism can account for the continued increase in circulating neutrophils for several hours after

extended periods of exercise.

Greater neutrophil increases have been observed after eccentric exercise than after concentric exercise in the same subjects at similar levels of oxygen consumption.[3] These data raise the possibility that other factors, possibly tissue damage, may contribute to the increase in circulating neutrophils.

High intramuscular pressures, especially during eccentric exercise, may cause transient, localized interruptions of blood flow.[10] On a whole-muscle scale, experimental ischemia and subsequent reperfusion result in reduced function, increased histological evidence of cellular damage, and increased release of CK and other cytoplasmic enzymes. Neutrophils have been observed in muscle tissue following a marathon, but have not been mentioned in reports of leukocytic infiltration following eccentric exercise.[3]

Several lines of evidence suggest that neutrophils are activated following exercise. Degranulation of neutrophils apparently occurs, based on increased plasma concentrations of lactoferrin (100% increase immediately after a triathalon) and elastase (50% increase immediately after a 10 km run).[10] In addition, post-exercise plasma lysozome concentrations increases with concurrent decreases in neutrophil lysozome content.[10]

Monocytes

Monocytes circulate with a half-life of about 3 days,

and their life span is thought to be on the order of months after egress into tissue.[14] Within tissue, monocytes undergo morphological and functional differentiation, becoming macrophages. During inflammation, monocytes accumulate at the site of injury by chemotaxis. Like neutrophils, monocytes and macrophages are capable of phagocytosis and secretion of cytotoxic factors, but in addition, these cells are prime sources of cytokines that mediate most of the physiological and inflammatory reactions accompanying injury and infection.[10]

Substantial numbers of mononuclear cells were found in muscle interstitium 24 hours after completion of a marathon.[3] In some studies of eccentric exercise in humans, 4 to 7 days elapsed before significant accumulations of mononuclear cells were observed.[13] These cells bring with them not only phagocytic and clearance capabilities, but also the capacity to promote repair.

Evidence has shown that pentose phosphate pathway enzyme activity attributable to macrophages and fibroblasts was increased sevenfold by 7 days, and remained for at least 21 days, following muscle overload by removal of synergists.[10] This elevated pentose phosphate activity in damaged or overloaded muscle may contribute to the prolonged state of glycogen depletion observed after eccentric exercise.

Cytokines and Acute Phase Proteins

Although exceedingly diverse, cytokine-mediated

reactions are functionally related. At the site of injury, cytokines potentiate cytotoxic and inflammatory mechanisms. For example, the cytokine TNF induces production of oxygen radicals and release of proteolytic enzymes from neutrophils. Both the cytokines IL-1 and TNF alter endothelial permeability, leading to leukocyte infiltration and edema. Systemically, cytokines promote adaptations that protect the organism as a whole. Injection of IL-1 or TNF into laboratory animals causes liberation of branched-chain amino acids from skeletal muscle.[15] This proteolysis is thought to provide a pool of free amino acids needed to support cytokine-accelerated rates of hepatic protein synthesis.

Acute phase plasma protein concentrations are sometimes elevated immediately after unusually long-duration exercise, such as a 100 km run, but normally these concentrations are not significantly increased until approximately 24 hours after exercise. The investigations cited above, along with more recent investigations, have shown that C-reactive protein (CRP), antitrypsin, a_2 macroglobulin, ceruloplasmin, and transferrin concentrations all increase significantly following long-duration (> 2 hours) exercise, whereas albumin concentrations decrease.[10]

Trace Metals

Inflammation, or systemic administration of IL-1 or TNF, causes a redistribution of trace metals within the body: plasma iron and zinc concentrations fall and plasma copper

concentrations rise.[10] The ability to sequester iron in intracellular depots during infection reduces the availability of this nutrient to bacteria that require it for growth and replication. The adaptive value of the redistribution of the other metals is not understood.

Physical training is associated with reductions in hematocrit, blood hemoglobin concentration, and plasma iron concentration.[10] These changes have sometimes been mistaken for an iron deficiency and termed "runner's anemia." In fact, hematocrit and hemoglobin concentrations are lower because of the increases in plasma volume that are a part of the training response. Total red cell numbers and hemoglobin mass in the circulation are usually increased, and erythropoiesis is normal in highly trained individuals. The chronically lower plasma iron concentration in trained subjects is accompanied by lower plasma zinc and higher plasma copper concentrations and is most likely another manifestation of the acute phase response. Furthermore, acute changes in plasma iron, zinc, and copper have been observed after long-duration exercise. These changes in plasma iron concentrations may have adaptive value in reducing oxidative stress. As exercise is associated with increases in oxygen radical-induced lipid peroxidation, lowering plasma iron and subsequent formation of deleterious oxygen radicals may reduce damage to tissues during exercise.

SUMMARY

Exercise-induced skeletal muscle damage results in a remarkable number of localized and systemic changes, including release of intracellular proteins, delayed onset muscle soreness, the acute-phase response, and an increase in skeletal muscle protein turnover.[10] These exercise-induced adaptations appear to be integral to the repair of the damaged muscle and may be essential for hypertrophy. Chronic exercise produces adaptations in skeletal muscle, resulting in increased capacity of oxidative metabolism; the repair of damaged muscle resulting in hypertrophy may be an important mechanism for protection against further exercise-induced damage. Although the release of CK from skeletal muscle following damage is a commonly observed phenomenon, circulating CK activity is not a quantitative and, in some cases, even a qualitative indicator of skeletal muscle damage. Eccentric exercise-induced skeletal muscle damage offers an opportunity to investigate the signals and modulators of the repair of muscle damage, a process that may be central to the adaptations in muscle as a result of chronic activity.

CHAPTER 3

MECHANISMS/ETIOLOGY

The most elemental principle underlying the mechanisms of DOMS is the basic premise that delayed muscle soreness results from overuse of the muscle. In other words, any activity in which the muscle produces higher forces than normal, or produces forces over a longer period of time than usual, is capable of producing DOMS. Although the degree of soreness is related to both the intensity of the muscular contractions and the duration of the exercise, intensity seems to be the more important factor.[16] Because higher torques are normally generated by maximal or high-velocity or high-intensity, eccentric activity, these are the situations in which maximal soreness and damage seem to occur.[16] Tiidus and Ianuzzo[17] attempted to quantify the effects of intensity and duration of exercise in DOMS and muscle damage using serum enzyme markers. The intensity of exercise was defined as the percentage of 10 repetition maximum (10RM) of the dead-weight resistance lifted, and defined duration of exercise as the number of contractions performed.[17] Results demonstrated that DOMS and enzyme levels were significantly

elevated by increased intensity and increased duration of exercise, with intensity having the more pronounced effect.

The fact that eccentric muscle work results in a greater degree of DOMS than isometric or concentric contractions has been extensively discussed in the literature. Exercise employing eccentric or concentric actions induces distinct physiological responses. In order to produce the same tensions, the muscles utilize a much smaller volume of oxygen in eccentric work and the accompanying circulatory and respiratory responses are correspondingly smaller.[16] At comparable velocities, eccentric contractions result in far greater external force development at a lower metabolic cost than similar concentric contractions, and the highest force that can be developed is in a fast eccentric contraction.[18] Also, at equivalent submaximal force developments, far fewer motor units need to be recruited for eccentric as compared to concentric contractions.[18] Stauber[19] reported that, during eccentric contraction, the cross-bridges which form after the binding of myosin and actin has taken place must be forcibly separated. This requires more force than for normal concentric cross-bridge cycling and thus greater tension is developed per active motor unit during submaximal and maximal eccentric contractions.

THEORIES OF DELAYED MUSCLE SORENESS

There has not been general agreement about which of the factors associated with increased muscle force production is

specifically responsible for DOMS. Elevated muscle activity could be accompanied by 1) increased tension in the contractile and elastic elements that causes physical damage to the structural components; 2) increased metabolism that results in accumulation of waste products toxic to the tissues; 3) increased muscle temperature that causes structural injury to the tissues; 4) altered neural control of the muscles, producing spasms that elicit pain; or 5) inflammation caused by tissue damage. Each of these mechanisms has been hypothesized to be a causative factor in the etiology of DOMS.

Structural Damage

Hough[1] reported that delayed pain was closely associated with mechanical tensions in the muscles, which led him to suggest that soreness had its origin in 'some sort of rupture within the muscle itself.' Recent evidence indicates that skeletal muscle damage may be the primary mechanism contributing to muscle soreness.[4,11]

Exercise involving eccentric muscle contractions results in greater disruption or injury to the muscle tissues than concentric exercise, as evidenced by histological and electron microscopic examination and elevations in serum enzymes of muscular origin.[20] This is true even though the perceived exertion is less and fewer motor units are activated in an eccentric contraction. Thus, in eccentric contractions the force is distributed over a smaller cross-

sectional area of muscle, i.e., the tension per active cross-sectional area is greater. It seems probable that this increased tension per unit area could cause mechanical disruption of structural elements in the muscle fibers themselves or in the connective tissue that is in series with the contractile elements.[21] Friden et al.[5] were the first to demonstrate ultrastructural changes within skeletal muscle fibers following an exercise protocol of repeated stair descents which caused severe DOMS. Post-exercise samples showed myofibrillar disturbances consisting of Z-band disruption and streaming. Armstrong et al.[20] utilized an animal model and found similar changes in histological appearance except that damage was predominately in type I fibers, as opposed to type II fiber damage found in human subjects.

In addition to morphological evidence of ultrastructural damage to muscle tissue, various blood enzymes have also been used as evidence of muscle damage. The presence in the blood of enzymes that are normally localized in muscle fibers is taken as evidence of disruption, or increased permeability of the muscle cell membranes.

Despite evidence to the contrary (chapter 2), creatine kinase is considered the best indicator of muscle damage, since this enzyme is found almost exclusively in muscle. Other substances normally contained within muscle fibers also appear in the blood in the period following exercise (e.g.

myoglobin). Appearance of this substance in the urine is one of the primary clinical signs of rhabdomyolysis (dissolution of muscle).

That structural damage occurs in muscles that are not trained for the particular exercise is evident. Verification of muscle injury comes from studies employing histological, electron microscopic, plasma enzyme, biochemical, and metabolite excretion analyses.[20] The damage may occur in the muscle fibers per se, in the connective tissue element in the muscle, or both. Nonetheless, it has not been proven that injury to muscle cells or connective tissue is the causative factor in DOMS.

Metabolic Waste

Undoubtedly, the most popular concept in the lay exercise community is that delayed soreness is a result of lactic acid accumulation in the muscles. This is a seemingly logical conclusion from the apparent relationship between exercise intensity and the extent of soreness. However, there is considerable research that argues against the metabolic hypothesis. The most convincing evidence is that the muscle contractions that cause the greatest degree of soreness, i.e., eccentric contractions, require relatively low energy expenditure.[22] Exercise involving eccentric contractions requires lower oxygen consumption and produces less lactate than exercise with concentric contractions at the same power output.[21] Furthermore, energy use per unit

area of active muscle appears to be less in eccentric exercise than in equivalent concentric exercise.[23]

Temperature

Elevated temperatures in the muscles resulting from exercise could conceivably damage the structural element in the muscle, resulting in necrosis of muscle fibers and breakdown of connective tissues. Eccentric muscle exercise, whose delayed soreness effects have been readily discussed, may generate higher local temperatures than concentric contractions.[21] Finally, complete dissolution of the muscle is more prevalent in untrained subjects during exercise in the heat and the myopathy resulting from hyperthermia resembles that present during DOMS.

Spasm

The spasm theory, originally described by de Vries,[24] proposed that exercise could cause ischemia in the active muscle, which in turn would result in the production of a pain substance. If too much of this substance accumulated, pain endings would be stimulated and the resulting pain would, in turn, produce more reflex spasms that would prolong the ischemia and initiate the pain-spasm-pain cycle. These hypotheses were made following experiments in which de Vries observed that subjects with DOMS had higher electrical activity of the muscle as recorded by surface EMG.[25] Other researchers have found increased EMG activity in muscles

following eccentric exercise, but the magnitude of activity was not related to the perception of soreness.[26]

Inflammation

There is some evidence to suggest that delayed onset muscle damage involves inflammation. Researchers have reported significant elevations in white blood cell count 12 hours post-exercise.[16] In addition, evidence has revealed ultrastructural changes of inflammatory response associated with necrotic changes occurring in the muscles of 10 male runners throughout the week of post-marathon recovery, with both pain and inflammatory ranges peaking 1-3 days after the event.[16] Because the inflammatory process began immediately after the marathon, when pain was not a feature, they suggested that the inflammation may have served as a stimulus to surrounding free nerve endings, and that when the inflammatory process reaches a certain level, the nerve endings for the pain then respond.

Thus, it was reasoned that DOMS is caused by inflammation. However, the investigators did not explain how inflammation was measured or how the magnitude and time-course of this inflammatory response was measured. Schwane et al.[27] found that increases in neutrophil and total white blood cell counts, which usually accompany inflammation, did not occur in association with soreness following downhill running. Bobbert et al.[28] also found no difference between pre- and post-exercise means of white blood cell count. They

proposed that the soreness was related to edema, which did not reflect classical muscle inflammation. Although no statistical evidence was presented, they hypothesized that edema was caused by Z-band disruption leading to the formation of protein-bound enzymes, which would exert an osmotic pressure.

PAIN MECHANISMS

It is widely accepted by the medical profession that a major function of pain is to protect the organism by signalling injurious infringement on the tissues. However, DOMS does not seem to fulfill this role. Because the soreness appears some time after the exercise, it presumably does not function to prevent overuse during the exercise bout in which the injury occurs. It could be argued that DOMS discourages use of the muscle at a time when it requires rest, but exercising a sore muscle appears to provide the most effective way of reducing soreness. Also, at the time the muscle develops maximal soreness following exertion (24-48 hours), it has regained its ability to produce maximal force. Thus, the potential benefit of the delayed pain is not clear.

No studies have been published to determine the specific chemical or physical agents that serve as the stimuli to mediate DOMS. Similarly, the neurons and receptors in the muscles that sense and initiate this type of pain have not specifically been sought or identified. In fact, mechanisms

of pain sensation in general are not well understood, even though a considerable amount of research has been directed toward eliciting the primary noxious agents, the receptors, and the neural pathways.

The sensation of pain in skeletal muscle is transmitted by myelinated group III and unmyelinated group IV afferent fibers.[21] Both group III and IV sensory neurons terminate in free nerve endings that are primarily distributed in the muscle connective tissue between fibers, particularly in the regions of arterioles and at the myotendinous junctions.[21] The larger myelinated group III fibers are believed to transmit "sharp," localized pain, whereas the group IV fibers carry dull, diffuse pain.[21] It therefore seems probable that the sensation of DOMS is primarily carried over group IV afferent neurons. The population of free nerve endings of group IV afferent neurons in muscles are sensitive to a variety of stimuli, including chemical, mechanical, and thermal.[21] Any one, or all three, of these stimuli could conceivably be involved in producing pain in muscles following exercise.

Chemical substances that elicit action potentials in muscle group IV fibers in order of effectiveness are bradykinin, serotonin, histamine, and potassium.[21] There appear to be separate receptor sites on the free nerve endings for these various noxious substances. Any or all of these could potentially accumulate in a region of damaged

muscle and contribute to the sensation of pain. The length of time between the occurrence of the injury and the sensation of pain may be explained by the time required for the cells to die and the noxious agents to accumulate.[21] Serotonin is released from platelets during clotting, histamine is released from mast cells in damaged tissue, and potassium is released locally in injured muscle tissue. Thus, all of these substances potentially could accumulate locally in necrotic muscle tissue and stimulate pain receptors.

Similarly, elevated pressure and mechanical distortion of the tissue which accompanies edema or elevated local temperatures associated with inflammation-like processes could activate the nociceptors in the muscles and elicit the sensation of DOMS. Therefore, although the precise stimuli that act to cause delayed pain are not known, it is possible that a combination of chemical, mechanical, or thermal factors are involved.

PROPOSED MODEL OF DOMS

As stated previously, the causative factors in DOMS are not known at this time. The same holds true for the cellular mechanisms. However, a possible sequence of events in the production of delayed soreness has been proposed, starting with the assumption that high local tensions in the muscles cause structural injury. Following is a condensed model of DOMS proposed by Armstrong[21] that best fits the available

data:

1. High mechanical forces produced during muscular exercise, particularly in eccentric exercise when forces are distributed over relatively small cross-sectional areas of the muscles, cause disruption of structural proteins in muscle fibers and connective tissue in series between the active cross-bridges and the bony attachments.

2. Structural damage to the sarcolemma, or alterations in permeability of the cell membrane, resulting from the high mechanical forces is accompanied by net influx of Ca^{++} from the interstitium. This abnormal influx of Ca^{++} has several deleterious effects on the muscle fiber. High Ca^{++} concentrations in the muscle cells have been shown to activate a calcium-dependent proteolytic enzyme that preferentially degrades Z-discs and troponin and tropomyosin.

3. The progressive deterioration of the sarcolemma in the post-exercise period would be accompanied by diffusion of intracellular components into the interstitium and plasma. These substances, as well as the products of collagen breakdown, would serve to attract monocytes that convert to macrophages, and to activate mast cells and histocytes

in the areas of injury.

4. Accumulation of histamine, kinins, and potassium in the interstitium in the regions of group IV free nerve endings resulting from phagocytosis and cellular necrosis, as well as elevated pressure from the tissue edema and increased local temperature, could then activate the nociceptors and result in the sensation of DOMS.

CHAPTER 4

TREATMENT/MANAGEMENT

Although the pathophysiological processes underlying DOMS are not completely understood, many researchers have investigated various treatments in an attempt to reduce the soreness. These treatments have focused on reducing the inflammation, or edema, consequent to tissue damage, and/or breaking up the cycle which is thought to provoke tonic muscle spasms or pain.

STRETCHING

de Vries'[24] examination of the ability of static stretch to reduce soreness led to the proposal of his spasm theory. In one study, de Vries[24] reported that stretching exercises helped to relieve the pain in seven of nine subjects. de Vries' method was to have the subject lock the limb, using body weight, in such a position that the muscle in question was held at its maximum length for 1-3 minutes, but no details were given of the timing, frequency, and duration of the treatment. In addition, there was no controlled trial to produce DOMS: accidentally induced muscle pain was the criterion, and the subjects included in the study had varying

degrees of soreness in a variety of muscle groups, making comparisons difficult. It was stated that resting EMG and soreness were reduced after stretching, but there are no details of how soreness was measured or whether the effects were significant. In a further study by de Vries,[25] static stretching for two minutes reduced resting EMG activity and soreness 48 hours post-exercise.

The effectiveness of stretch EMG biofeedback was examined by McGlynn et al.[26] Following eccentric exercise at 80% MVC to fatigue, their subjects received 15-minute sessions of either biofeedback, static stretch, or neither, over a time-course of 6, 25, 30, 49, and 54 hours. The stretch protocol was as used by de Vries.[24] Although there was no increase in EMG immediately after exercise, there was a significant increase at 24 hours. Both biofeedback and stretch significantly decreased EMG activity but had no effect on perceived pain as measured on a 30-point scale. Also measured was the effect of static stretching upon soreness induced by eccentric hamstring activity. There was no change in EMG activity, but a marked (although not statistically significant) decrease in pain, which was temporary in nature and returned the following day. Buroker and Schwane[29] found that post-exercise static stretching did not alleviate DOMS, either on a temporary or longer-term basis, in subjects who performed an eccentric hamstring step-test protocol for 30 minutes.

Smith et al.[30] studied the effects of static and ballistic stretching on DOMS and creatine kinase levels. The purpose of their study was to determine if a bout of static and/or ballistic stretching, of a similar intensity and duration, would induce significant amounts of DOMS and increases in serum CK. Results indicated that both types of stretching resulted in a significant increase in DOMS, which peaked at 24 hours after stretching. However, static stretching resulted in significantly higher levels of DOMS than did ballistic stretching.

CRYOTHERAPY

Following acute soft tissue injury, the application of cold is known to decrease inflammation and pain as well as decrease muscle spasm via suppression of the monosynaptic stretch reflex. Ice massage causes the greatest reduction in intramuscular temperature when compared to other cryotherapy techniques.[16] This led Yackzan et al.[31] to investigate the effects of cold application on soreness. They suggested that if muscle spasm occurred, the resultant muscle shortening would create a decreased range of motion. The subjects received ice massage for either 15 minutes immediately after the exercise or at 24 or 48 hours post-exercise. Although the investigators found a decrease in ROM that was proportional to an increase in muscle soreness, cold application did not relieve soreness or improve ROM in any of the three groups. Also examined was the effect of ice bath

immersion of the arm for 25 minutes prior to 70 maximum voluntary eccentric contractions in seven female subjects, who also wore a cold pack during the exercise.[16] The cold treatment did not reduce the damage response to eccentric exercise as measured by isometric strength, CK levels, relaxed elbow angle and flexed elbow angle, which were assessed pre-exercise, immediately post-exercise and for 6 days following exercise. All measures showed significant changes which had still not returned to baseline day 6 post-exercise.

ULTRASOUND/PHONOPHORESIS

In one study, pulsed ultrasound was found to be effective in reducing DOMS.[32] The experimental group of six subjects was compared to placebo treatment and control groups of the same size, after 10 minutes of bench-stepping involving eccentric exercise only for the left leg. Ultrasound treatment, given 24 hours later, was applied to the proximal area of the vastus lateralis and the distal vastus medialis, which were found to be areas that were sore. The dosage was 20 minutes pulsed at a ratio of 1:4, an intensity of .8 W/cm^2 and a frequency of 1 MHz. Significant reductions in soreness were found among the members of the experimental group after 48 hours compared to the placebo and control groups.

Ciccone et al.[33] designed a study to determine the effectiveness of ultrasound and trolamine salicylate

phonophoresis in decreasing pain and stiffness associated with DOMS. Repeated eccentric contractions were used to induce DOMS bilaterally in the elbow flexors. The authors concluded that ultrasound enhanced the development of DOMS but that this enhancement was offset by the anti-inflammatory-analgesic action of salicylate phonophoresis. These findings suggest that salicylate phonophoresis may be useful in clinical situations in which it is desirable to administer ultrasound without increasing inflammation.

IONTOPHORESIS

Hasson et al.[34] evaluated the pain alleviating effects of dexamethasone iontophoresis on delayed onset muscle soreness and muscle function. Single treatment application of dexamethasone iontophoresis has not been suggested for acute inflammatory conditions. Hasson's[34] study concluded that a single treatment of dexamethasone iontophoresis following muscle soreness development is effective for slowing the progression of muscle soreness from 24-48 hours, but does not eliminate muscle soreness or normalize muscle performance.

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

Denegar et al.[35] researched the effects of transcutaneous electrical nerve stimulation (TENS) on pain, range of motion, and serum cortisol concentrations in females experiencing delayed onset muscle soreness. Low-frequency

TENS of pulse width 300 microseconds was applied to the upper arm in eight female subjects who experienced DOMS of the elbow flexors. Results demonstrated a significant reduction in pain perception and an increased range of elbow extension. Treatment using TENS of low frequency and a pulse width of 300 microseconds was also applied at four sites associated with the relief of upper arm pain. The range of movement improved significantly immediately after treatment, as well as at 20 and 40 minutes post-treatment. As there was no control group, the passage of time could also have been responsible for the results.

PHARMACOLOGICAL AGENTS

Various pharmacological agents have been administered in order to alleviate DOMS. One of the main functions of vitamin C is the synthesis of collagen, an important component of connective tissue. Vitamin C supplementation might increase collagen synthesis in normal muscle, and so increase its resistance to damage. In one study, following administration of 500 mg of vitamin C twice daily for 34 days, no difference in soreness response was observed between treatment and placebo groups.[16] Kaminski and Boal,[36] however, suggested that ascorbic acid may significantly reduce the delayed soreness typically seen following the strenuous use of muscles in an unaccustomed manner. Supplementation appeared to blunt the reported soreness, showing the greatest effect when DOMS was at its peak.

Evans[3] recently examined the effects of vitamin E on exercise-induced muscle damage in old and young men. It was his hypothesis that eccentric exercise results in an increase in the production of neutrophil-generated oxygen radicals and causes the exercise-induced increase in lipid peroxidation. Because of the well-known properties of vitamin E as an antioxidant and oxygen radical scavenger, Evans hypothesized that it might reduce the eccentric-exercise-induced increase in circulating creatine kinase activity. Results showed that vitamin E supplementation has specific effects on older subjects after eccentric exercise that were not seen in young men, indicating that vitamin E may affect the rate of muscle repair after exercise that results in muscle damage in old, but not young, individuals.[3]

Various non-steroidal anti-inflammatory agents have also been used to alleviate DOMS without success.[16] Headley et al.[37] examined the effects of prednisolone in human subjects in a double-blind cross-over design and found no significant difference in either pain scores or CK levels between the experimental and placebo groups. Donnelly et al.[38] studied the effects of ibuprofen on exercise-induced muscle soreness. They found that ibuprofen was not effective in reducing DOMS after downhill running. In contrast, Francis and Hoobler[39] observed that aspirin, also an anti-inflammatory agent, significantly reduced DOMS 48 hours after eccentric exercise when compared to a control group.

Topical analgesic anti-inflammatory creams have also been found to reduce DOMS. Politino et al.[40] used 10% triethanolamine salicylate on a very large sample, but then positive results are highly questionable due to the massive variation in types of exercise used to produce DOMS. These ranged from marathon dancing to weightlifting, and for unspecified durations or intensities.

EXERCISE

Exercise is thought to reduce the effects of DOMS. Donnelly et al.[41] investigated the effect of a light bout of eccentric exercise one day after heavy eccentric exercise consisting of 70 maximum eccentric contractions of the forearm flexor and extensor muscles of the non-dominant arm. The experimental group of nine subjects performed 25 submaximal contractions with the same arm. Although there was no difference in delayed soreness between the two groups 19 days after exercise, there was a significant reduction in CK enzyme efflux on days 2-6 for the experimental group.

A study by Hunter et al.[7] found that a high-velocity concentric isokinetic exercise performed 24 hours after DOMS-producing stepping exercise, significantly reduced DOMS and facilitated the return of strength after 48 hours in 5 subjects when compared with a control group. Nevertheless, the results demonstrated that the soreness and strength deficits were still significantly above baseline levels at 48 hours, justifying the need for further research in this

particular area.

MASSAGE

Massage has also been used in an attempt to reduce delayed onset muscle soreness. Smith et al.[42] proposed that vigorous sports massage rendered 2 hours after termination of unaccustomed eccentric exercise reduces the intensity of DOMS and reduces serum creatine kinase levels. This may be due to interference with neutrophil activity ascribed to the mechanical action of vigorous massage and/or higher levels of serum cortisol. In contrast, Wenos et al.[43] did not find any significant differences in soreness or in strength loss, post-exercise, in the quadriceps muscles of the treatment leg when compared with the control leg in a group of 9 subjects.

TRAINING

Hough[1] observed that DOMS did not occur when a trained muscle was exercised. Other workers have since described the effect of training, not just in alleviating the soreness response, but also in reducing morphological changes, performance changes and CK activity in the blood.[16] It seems that DOMS resulting from eccentric exercise is reduced by training that specifically involves eccentric contractions. In contrast, other research has shown that concentric training did not reduce DOMS in subsequent eccentric exercise.[16] The protective effect of a prior bout of exercise, that in itself may produce only minimal soreness,

has been found to last for prolonged periods. Byrnes et al.[6] observed that the muscle soreness response to downhill running was reduced by up to 6 weeks following an initial bout of downhill running. Some studies have used a number of weeks of training to produce an effect. Friden et al.[5] used 8 weeks of training on a cycle ergometer and Komi and Buskirk[44] used 7 weeks of eccentric forearm flexor work. However, a number of recent investigations have shown that the prophylactic effect of training may be due to the performance of a single initial exercise bout.[16] Clarkson and Tremblay[45] found that as few as 24 maximum voluntary eccentric contractions produced a training effect and resulted in no CK response, less soreness and smaller strength decrements when 70 maximum voluntary eccentric contractions were performed two weeks later. Clarkson et al.[46] indicated that this protective effect is specific to the muscle which is exercised at the first bout. This may mean that the 'repeated bout effect' occurs at the level of the muscle exercised, and is not a central effect. One study found that as little as two 12-minute bouts of downhill running at a gradient of 10% were sufficient to protect against the occurrence of DOMS in a subsequent downhill run 3 days later, which had produced DOMS in the control group.[16] Interestingly, they found the training was insufficient to prevent a 2-to 3-day loss of muscular strength, suggesting that strength loss and DOMS may have different physiological

causes.

In treating muscle soreness, 'prevention is better than cure' would seem to be the best approach, and prior exercise utilizing the 'repeated bout effect' seems to offer considerable protection against further damage to muscle and the related soreness. Other treatments employed show varying results but, on the whole, few seem to reduce DOMS effectively.

CONCLUSION

A wide variety of protocols involving intense eccentric exercise has been found to produce DOMS in both upper and lower extremity muscle groups. Greater soreness tends to be produced by increasing intensities and durations of exercise.

The majority of evidence contradicts the 'spasm' and 'lactic acid' theories of DOMS. There is also little evidence to support the torn muscle or connective tissue theories as causes for DOMS. Some studies suggest that inflammation subsequent to damage may be more closely associated with DOMS, however, further study is needed.

Although some success has been reported by a few authors using stretch, ultrasound, TENS, or topical anti-inflammatory creams to alleviate DOMS, the majority of studies indicate that no effective treatment protocol has yet been found to reduce soreness once it has occurred. Prevention seems to be better than cure, and a number of studies show that training using submaximal eccentric exercise protocols may prevent DOMS in subsequent maximal bouts using the same muscle groups. The training effect may last for up to several weeks.

Further study is essential to clarify the exact nature and direct causes of delayed onset muscle soreness as well as to ascertain the best overall treatment plan to attenuate the effects of DOMS.

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