Musculoskeletal pain

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ABSTRACT Acute pain within the various components of the musculoskeletal system is a cardinal symptom of the pathophysiological processes involved with tissue damage, disease, or dysfunction. These disorders are generally well-characterised and management usually associated with good symptomatic and functional outcomes. Immediate activation of an inbuilt and hard-wired basic pain system serves a primary protective function to the host. Another system, perhaps best described as an advanced pain system, augments, amplifies, and extends the role of the pain system to other functions. Emotional distress has a potent effect on this process and drives a series of events that results in altered 'downstream' musculoskeletal symptoms and function. Under these circumstances chronic pain states may arise and may particularly involve the musculoskeletal tissues.

Fibromyalgia syndrome is used here as an example of a common chronic musculoskeletal pain syndrome, characterised by widespread pain and tenderness, in order to allow for discussion of the biopsychosocial inputs that must be addressed to provide the best clinical outcome. Emphasis is placed on understanding the nature of these problems, particularly to enhance reversibility and hence improve outcomes.

KEYWORDS Distress, fibromyalgia, injury, musculoskeletal pain, regional pain

LIST OF ABBREVIATIONS Adrenocorticotrophin hormone (ACTH), anti-nuclear antibodies (ANA), fibromyalgia syndrome (FMS), selective serotonin reuptake inhibitors (SSRIs)

DECLARATION OF INTERESTS No conflict of interests declared.

PAIN AS A SYMPTOM OF MUSCULOSKELETAL DISEASE

Pain due to damage, dysfunction, or disease of any of the components of the so-called muscle–tendon unit (see Figure 1) is very common. For instance, acute tissue injury will rapidly activate free nerve endings of the Aδ and C-fibre types, known as nociceptors (see Figure 2). The musculoskeletal system has an abundance of nociceptors with thresholds set to respond to injury stimuli that activate the pain system before significant tissue damage ensues. This allows for immediate reflex withdrawal of the threatened part, as well as activation of pain sensations with cognitive appraisal of the threat. This basic pain system therefore provides warning and subsequent protection from potential tissue damage.

Continued nociceptor stimulation, through ongoing injury for example, can lead to a decrease in the stimulation threshold in the neurones that receive the pain message in the dorsal horn of the spinal cord. This important neurobiological process is called sensitisation and since it involves central nervous system processes, the term central sensitisation is applied. In this situation, otherwise innocuous sensory inputs that have links to the sensitised dorsal horn pain-transmitting cells, particularly those coming from mechanoreceptor Aβ fibres, will have their input translated into pain sensations. Thus, with central sensitisation, touch and movement in the region of the injury will be painful. Through other mechanisms, there is regional spread of pain beyond the injured tissue. Additionally, other disease processes, particularly inflammation (through mediators such as prostaglandins and cytokines), cannot only activate the peripheral nociceptor itself but also increase its sensitivity to minor stimuli; this is known as peripheral sensitisation.
The combination of the particular process involved, be it injury, inflammation, or degeneration, and the specific muscle–tendon unit structure affected, results in predictable clinical features for different named disorders (see Table 3). These range from enthesitis or tenosynovitis through to muscle strain. The healing and resolution of symptoms from most common everyday painful musculoskeletal disorders will usually take place over days to weeks. Most important though is the intensity and duration of the nociceptor stimulation as this may significantly modulate this healing time. Other factors influencing central sensitisation may also be important, as will now be discussed.

**PAIN AS A COMPONENT OF MUSCULOSKELETAL DYSFUNCTION**

While ongoing tissue damage may lead to constant nociceptor stimulation, this is not the cause for the majority of chronic musculoskeletal pain cases in our community. Rather, the chronic pain relates to activation of further elements of the pain system which augment and amplify the basic pain mechanisms and interfere with host functions far more significantly. The key process behind this powerful response is again sensitisation, but in this case the main drive to change the sensitivity of deeply placed dorsal horn pain-transmitting neurones is not coming from peripheral nociceptive input, as described above, but is coming from central mechanisms. In this situation, the otherwise innocuous sensory inputs from the mechanoreceptor Aβ fibres play a much greater role in causing key symptoms. In particular, sensory information coming from deeply placed regions such as the spine is translated, through central sensitisation, into patterns of referred pain and soft tissue tenderness. This causes the characteristic and essential clinical features of these pain syndromes, i.e. regional or widespread pain and tenderness.

This central sensitisation process relates to change in descending modulatory influences on the relevant dorsal horn areas. Pathways from the mid-brain and other higher regions, using noradrenaline and serotonin as neurotransmitters, no longer downregulate pain-transmitting neurone function. Through uncertain mechanisms, central influences activate this process. Cognitions, personality, emotions, stress-centre activation, sleep dysfunction, and other influences may all contribute to different degrees in different people to this central sensitisation. Background musculoskeletal sensory inputs, which are affected by fitness, posture, injury, or disease, are further contributions to this equation.

The pain involved in these common chronic musculoskeletal pain syndromes thus represents, not a symptom of tissue damage but, an essential feature of a disorder of function of the pain system as a whole – from mind to body and back.

**MUSCULOSKELETAL PAIN IN THE COMMUNITY**

Around 10% of people will report widespread pain lasting for over three months, and 20% will report long-lasting regionalised pain. Frequency of complaints generally increases over the decades of age, with degenerative processes contributing more. Within these groups there is a subset, of perhaps 5%, who have widespread pain and tenderness without obvious peripheral cause. There have been difficulties in adopting a uniform nomenclature to best describe these cases. Community studies show increased rates of psychosocial distress in this group and psychological determinants appear to be important drivers of such widespread pain and tenderness.

**FIBROMYALGIA SYNDROME**

**General features of fibromyalgia syndrome**

Another approach has been to adopt a bland descriptive term and FMS is the current most used designation. The American College of Rheumatology classification criteria for FMS, published in 1990, combine widespread pain with abnormal tenderness at a large number of predetermined body sites. These criteria have resulted in over 2000 publications defining various biological, psychological, and social abnormalities seen in this population.

Fibromyalgia syndrome can vary from a mild and short-lived problem to a severe and persistent disorder, associated with significant disability. Fibromyalgia syndrome patients often also have a number of other disorders, most of which are associated with distress and bodily dysfunction. These comprise non-restorative sleep, fatigue (often aggravated by effort), stiffness, headache, irritable bowel and bladder, poor memory and concentration, nausea, restless legs, and hypotension,
among others. There is an increased tendency for patients to feel depressed and anxious.

Emotional distress seems the likely link to the clinical features of FMS. For instance, distress scores correlate with abnormal tenderness. Distress will activate brain stress centres. Dysfunction of the hypothalamic–pituitary–adrenal axis is found in FMS. For instance, the response of ACTH to corticotrophin-releasing factor is exaggerated in FMS compared with controls, and the subsequent cortisol response from the adrenal gland is blunted. The sympathetic nervous system is also overly active. Chemicals related to pain transmission, such as substance P, are elevated in the cerebrospinal fluid and blood serotonin is abnormally lowered in many. Cerebral blood flow is greatly augmented in pain response centres in the brain following peripheral nociceptive stimuli. In the periphery, Aδ and C-fibre activity is increased. Dorsal horn pain functioning is abnormal with evidence of sensitisation in various studies.

Thus the neurobiology of the FMS process primarily relates to central psychological events that impinge on the stress system. An associated change in dorsal horn pain-modulation function triggers the downstream musculoskeletal signs and symptoms.

The FMS process is a functional amplification of pain pathways which is in itself reversible, at least in the majority of people.

**Diagnosis of fibromyalgia syndrome**

The diagnosis of FMS requires a history of widespread pain to be present along with widespread bodily tenderness. Some body surface sites are normally more tender than others. These are good sites to determine the pain threshold. In FMS the pain threshold is particularly low at these sites, such that gentle pressure with the thumb or first finger, to the degree of causing the nail to blanch, will induce pain. This is deemed to be a tender point. Multiple tender points simply reflect low pain threshold (see Figure 3). Other tissues are also abnormally tender. This simple yet accurate sign is perhaps the most ignored in clinical medicine.

Patients presenting with widespread pain and tenderness may have other medical conditions which are acting as the stressors to induce the pain syndrome. Hence a comprehensive history and physical examination is always required and appropriate tests of organ-based systems might be needed. It is usual to check full blood examination, erythrocyte sedimentation rate or C-reactive protein levels, rheumatoid factor, anti-nuclear antibody, creatine kinase, thyroid function, calcium, and liver and renal function. Occasionally other investigations might be required to follow up specific physical findings. Some of the above investigations will rule out subtle conditions that might cause widespread muscular discomfort such as hypothyroidism, disorders of calcium balance, or more sinister causes. In the majority of cases, people with FMS have normal investigations and no more high-powered tests are usually required.

Some people with fibromyalgia will have positive ANA. This reflects the natural incidence of ANA positivity within the relevant age group. It is extremely important not to over-interpret the association between FMS and ANA without the presence of other features of lupus. On the other hand, patients with true lupus often have FMS as a co-morbid condition.
Musculoskeletal pain

Finally, FMS is neither a diagnosis of exclusion nor an exclusive diagnosis. It is a very common pain syndrome and can occur in any clinical setting.

Management of fibromyalgia syndrome

The key feature of FMS management is accurate diagnosis. Some clinicians choose not to use the term FMS but most nowadays are comfortable with the nature of the problem and can explain the diagnosis to the patient carefully. Explanation and education is essential. Labelling the condition as FMS in itself has not been shown to lead to abnormal illness behaviour.

The majority of patients have a mild self-limiting and reversible problem usually helped by encouragement of aerobic-based exercises, albeit at a slower pace than someone who doesn’t have this problem. It takes three times as long to become aerobically fit for a person with FMS compared with someone without fibromyalgia.

Identification of stressors in the person’s life and practical strategies to deal with them, or at least learn how to avert activation of their own stress systems, is important. Simple measures such as yoga, Tai Chi, or similar approaches are very useful. Some require more advanced counselling or psychological advice. Medication should be kept simple. Simple analgesics are useful in many cases. Low dose tricyclic antidepressant-type medication, e.g. 10–25 mg amitriptyline in the mid-evening, can be helpful in up to 40% of patients, particularly where sleep disturbance is prominent. Many find they cannot tolerate the side-effects of dry mouth and morning drowsiness but one has to weigh up the severity of the pain symptoms against what are often nuisance side-effects. Selective serotonin reuptake inhibitors tend not to be helpful for FMS symptoms. They may be useful if depression is also present. Agents that have a more balanced effect on serotonin and noradrenaline reuptake are giving better results in clinical trials and these include the drugs duloxetine and milnacipran. These agents are not yet widely available. Other drugs such as pregabalin, which interfere with other pain-related mechanisms, have been shown to have better benefit in clinical trials than currently available drugs.

RED AND YELLOW FLAGS FOR MUSCULOSKELETAL PAIN

Red flags may indicate important disorders such as infection, malignancy, or fracture. Yellow flags relate to psychosocial stressors. (See Table 2.)

OTHER MUSCULOSKELETAL PAIN SYNDROMES

Regional pain syndrome is characterised by regional pain and tenderness and has similar origins to FMS. Differential diagnosis must include consideration of a single lesion that could cause the clinical features, such as spinal pathology. Many with an injury to an upper limb muscle–tendon unit structure will develop superadded regional pain and tenderness, say to the whole upper quadrant. Thus an injury can quite commonly co-exist with a regional pain syndrome, making management complex. This often occurs in the context of an injury at work or in the car, when there are considerable psychosocial stressors present. Workers compensation, litigation, and disability issues force extreme and unique pressures on to the pain axis. Approaches to chronic pain in this environment are subject to vested interest and confusion, with different outcomes according to multiple subtle factors.

Complex regional pain syndrome, previously known as reflex dystrophy syndrome, is a variation on the above, where there are more features of swelling, colour change, or sweating and where soft-tissue tenderness may be severe. Debate currently exists as to the best way to classify and diagnose these disorders both for research purposes and for clinical use.

Myofascial pain syndrome is a very common disorder of muscle, where there is tightening and bunching of fibres associated with exquisite pain on palpation, so-called trigger points. The problem is usually present in the mid-belly of the muscle and usually occurs after injury or with overuse or postural strain. Ergonomic considerations and physical therapies are the mainstay of therapy.
Musculoskeletal pain is usually a symptom of an underlying disease process, such as injury, inflammation, or degeneration of one of the components of the muscle–tendon unit. Musculoskeletal pain may also be part of an illness, namely a chronic pain syndrome.

Fibromyalgia syndrome:
- is a common pain syndrome, characterised by chronic widespread pain accompanied by widespread tenderness, often linking to psychosocial distress;
- improves in the majority with a multimodal program incorporating explanation, exercise, stress management, and simple medication.

Regional pain syndromes share similarities to fibromyalgia syndrome.

Medicolegal, litigation, and disability issues distort and polarise the otherwise good outcome of everyday chronic musculoskeletal pain syndromes.

### KEYPOINTS

- Musculoskeletal pain is usually a symptom of an underlying disease process, such as injury, inflammation, or degeneration of one of the components of the muscle–tendon unit.
- Musculoskeletal pain may also be part of an illness, namely a chronic pain syndrome.
- Fibromyalgia syndrome:
  - is a common pain syndrome, characterised by chronic widespread pain accompanied by widespread tenderness, often linking to psychosocial distress;
  - improves in the majority with a multimodal program incorporating explanation, exercise, stress management, and simple medication.
- Regional pain syndromes share similarities to fibromyalgia syndrome.
- Medicolegal, litigation, and disability issues distort and polarise the otherwise good outcome of everyday chronic musculoskeletal pain syndromes.

### TABLE 2 Red and yellow flags for musculoskeletal pain.

<table>
<thead>
<tr>
<th>Red flags</th>
<th>Yellow flags*</th>
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<tbody>
<tr>
<td>Presence of older age in new symptom onset</td>
<td>History regarding family, work or personal stresses</td>
</tr>
<tr>
<td>Night pain</td>
<td>Personality or mood disorders</td>
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<tr>
<td>Fever</td>
<td>Substance abuse</td>
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<tr>
<td>Sweats</td>
<td>Just being ‘out of sorts’</td>
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<tr>
<td>Neurological features</td>
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<td>Previous history of malignancy</td>
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*Yellow flags may all be important in any one individual. These yellow flag items often drive emotional distress which can activate the pain pathways described above.

### FURTHER READING