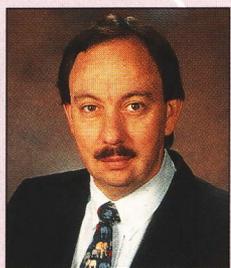


# FIBROMYALGIA SYNDROME

## Part II: The pathophysiology and management of FMS



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**A**lthough there is now widespread acceptance of fibromyalgia syndrome (FMS) as a distinctive syndrome, there is less certainty regarding its pathophysiology. As a result of the lack of obvious physical findings and absence of investigational abnormalities, many patients were formerly diagnosed as having "psychogenic rheumatism".

The relationship between the mind and the body is important in the etiology of FMS and it is essential to understand this interplay at the level of its effect on altered physiology. It is generally accepted that FMS is not a psychiatric disorder, and that an abnormal psychiatric status is not necessary for developing FMS features. FMS is most likely to be a multi-factorial syndrome with neuro-endocrine aberrations<sup>32</sup> and possibly a genetic predisposition<sup>33</sup> which, along with other stresses (e.g. mental, infection, trauma), may cause a neuro-endocrine dysfunction.

Poor sleep, also related to neuro-endocrine factors, is likely to be another important interacting factor.

### Central mechanisms

Increased activity of the excitatory neurotransmitter substance P, or a deficiency of the inhibitory neurotransmitters, may be part of the pathophysiology of FMS and a significantly increased level of substance P in the cerebrospinal fluid of FMS patients, has been demonstrated<sup>34</sup>.

Moldofsky and colleagues showed that patients with FMS have non-REM Stage 3 and 4 sleep electroencephalograph patterns that were disrupted by a pattern of "alpha-intrusion". Often, more than 60% of FMS patients' non-REM sleep was disrupted - this phenomenon, however, is not specific to FMS<sup>17</sup>. This sleep abnormality may be related to deficient levels of serotonin which influences both deep restorative sleep and pain perception<sup>17</sup>.

Serotonin is known to modulate the function of substance P, particularly with reference to the interpretation of sensory stimuli<sup>35</sup>. A decreased level of 5-hydroxyindoleacetic acid (a metabolite of serotonin)

in the cerebrospinal fluid of FMS patients, has been confirmed in a controlled study<sup>36</sup>. Serotonin deficiency has also been demonstrated in the serum of FMS patients and it has been shown to correlate with pain symptoms<sup>37</sup>.

Other abnormalities of neuro-endocrine functions are supported by findings of an abnormal hypothalamic-pituitary-adrenal axis in these patients<sup>38</sup>. These proposed neuro-hormonal dysfunctions may be triggered in a genetically predisposed individual by non-specific stresses, such as physical and psychological trauma, as well as by infection.

The cognitive dysfunction observed in some FMS patients, as well as the poor sleep, may also be due to an abnormality in the neuro-endocrine (serotonin is a modulator of NREM sleep as well as pain).

### Peripheral mechanisms

Peripheral factors probably play a role in the pathogenesis of FMS in a subgroup of patients. From currently available data, muscle biopsy findings in patients with FMS do not differ from those of normal controls. However, some patients who develop acute localised musculoskeletal pain (e.g. in the neck region) following trauma, may develop more widespread pain with tender points at a later time<sup>39,19</sup>.

There is evidence that persistent release of neurotransmitters (e.g. substance P) from the dorsal root ganglia and subsequent "spillover" leads to an "unmasking" of adjacent dorsal horn-connections and this may eventually become the total body pain syndrome of FMS<sup>19</sup>.

Pain is not only a sensory experience but also an emotional experience and therefore, events during childhood (such as sexual abuse, family sick role environment and other factors) can modify an individual's interpretation of pain<sup>19</sup>.

Spinal stress and poor posture are probably forms of indirect trauma that may contribute to pain in FMS.

It seems that the most important pathophysiological mechanisms in FMS involve

*This series of articles concentrates on areas of family medicine that prove problematical in practice. The authors offer new insights and approaches in order to help practitioners address these areas.*

central mechanisms with abnormal neuro-endocrine function, explaining the patients' widespread pain and tenderness, fatigue, poor sleep and cognitive impairment. The hypothesis that low levels of serotonin may be responsible for fibromyalgia is interesting because of the associated conditions, e.g. affective disorders, migraine and irritable-bowel syndrome, which are probably due to the same mechanism.

### Management

FMS is a complex spectrum of problems with considerable variations from patient to patient. This implies that no single strategy is effective in all patients, making the management of these patients time-consuming but challenging.

FMS is usually readily recognisable by its pattern of symptoms, but the process of taking a personal history allows assessment of the patients' individual manifestations and psychosocial circumstances. Communication skills, empathy and a supportive attitude, help to promote a positive patient-centred doctor-patient relationship which forms an integral part of the management.

### Explanation and education

This is an integral part of the initial management<sup>10, 19</sup>. A handout explaining FMS and its interacting factors is helpful. Possible mechanisms should be explained and the education reinforced during follow-up visits. It is helpful to involve the spouse, a family member or a supportive companion.

Patients should be informed on particular contributory factors, e.g. poor sleep hygiene, lack of physical exercise, work stress, emotional trauma, etc. Patients should be encouraged to take an active role in the management - a passive approach by the patient is rarely successful<sup>10,16,19</sup>.

### Myofascial pain

Pain is the presenting complaint of FMS patients and total elimination of pain is mostly impossible - the aim therefore, is to improve function and restore the patient to a more functional lifestyle.

The usual pain medications such as non-steroidal anti-inflammatory drugs and even narcotics are often ineffective in FMS<sup>19,40</sup>.

The use of myofascial trigger point injections is a well established technique and should be used as an adjunct to the overall treatment programme, to increase the range of motion and relieve pain. In general, trigger points are located where muscle joins tendon or bone: e.g. the insertion of the extensor muscles of the hand at the lateral epicondyle of the elbow<sup>41</sup>.

Needle diameters of 25 or 27 gauge are satisfactory for most patients. Insertion of the needle in the appropriate location usually generates a "muscle-twitch" response. Efficacy has been demonstrated with lido-

caine (1% and 2%) without epinephrine, bupivacaine, diclofenac and prednisolone. The critical factor is the mechanical disruption of the trigger point rather than the solution used, and therefore, precision in needling (using the "peppering" technique) of the exact trigger point is most important<sup>19,41</sup>.

Only one functional anatomic area should be treated at a time and, following an injection, it is essential that the muscle be stretched to the fullest range of motion. The goal of the treatment is to deactivate the trigger points and to restore the shortened muscles to their full range of motion<sup>19,41</sup>. As pain subsides, an active programme of stretching should be initiated.

Other physical modalities to assist stretching include manipulation techniques, ultrasound, dry needling, infra-red, massage, ischaemic pressure and transcutaneous electrical nerve stimulation (TENS)<sup>41</sup>.

### Exercise

All FMS patients need to have a programme of muscle stretching, gentle strengthening and low impact aerobic exercises<sup>10,19,42</sup>. The patient starts at the level that results in a mild pain on the following day. Patients often complain after exercising of painful muscles, but no physical harm will result from such effort - patients should be encouraged to work through the initial worsening of the pain.

It is best to start with exercise which does not unduly load the joints of the extremities and the use of bicycle ergometry or walking is often better tolerated than jogging. Patients who are very deconditioned should start with water exercise, using their arms and legs against the resistance of the water.

Physical exercise will lead to enhanced cardiovascular fitness and muscle flexibility and the resting heart-rate will decrease over time. Regular exercise needs to become part of the usual lifestyle and should be done 4-5 times a week. It is rare for patients to have lasting improvement unless they become involved in an aggressive programme of low-impact aerobic and stretching exercises<sup>10</sup>.

### Pharmacological treatment

Clinical trials have been completed, showing that both amitriptyline and cyclobenzaprine (not available in the RSA) are effective in the treatment of FMS<sup>43,44</sup>.

The recommended dose of these drugs (e.g. 10-50mg of amitriptyline) is much smaller than the dose used in the treatment of depression - even these low doses are often poorly tolerated in FMS patients as a result of what seems to be an extreme sensitivity of their central nervous system to anticholinergic side effects. Low doses of other tricyclic agents (e.g. imipramine, clomipramine, trimipramine and dothiepin) have had anecdotal

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success. Zopiclone, a nonbenzodiazepine hypnotic, has been reported to improve subjective sleep complaints but not the pain symptoms<sup>45</sup>.

Benzodiazepines have no place in the long-term treatment of FMS and narcotics should also be avoided<sup>10,16</sup> - not only because of their addictive potential, but also because of their detrimental effect on deep sleep.

The SSRI fluoxetine has been studied in two cohorts of FMS patients<sup>46,47</sup> and no improvement in visual analogue pain or fatigue was demonstrated.

The dose of bedtime anti-depressants should be kept low to avoid unwanted side-effects, however, when depression is prominent, an increase of anti-depressant doses may be necessary. Addition at this stage of a SSRI (e.g. paroxetine) in the morning and continuing with amitriptyline 10-25mg at night is, however, often better tolerated<sup>19,46</sup>. (Also the author's own experience.)

Anti-inflammatory medications have shown disappointing results in clinical trials. In controlled randomised trials, prednisone and naproxen were not more effective than placebo<sup>40,48</sup>.

### Sleep

Most patients with FMS are light sleepers with frequent awakenings and wake up feeling tired - also called "non-restorative" sleep<sup>19</sup>. Some FMS patients have a primary sleep disorder which should receive treatment (e.g. periodic limb movement disorder, restless legs syndrome and sleep apnoea syndrome). However, in most patients, no obvious cause will be found for the sleep disruption.

The importance of "good quality" sleep should be emphasised and the natural steps recommended include not "taking worries to bed", allowing enough hours of sleep, no daytime naps, having a quiet room and other sleep hygiene measures including going to bed earlier and at the same time each night, avoiding caffeine, alcohol and nicotine, etc. A significant problem for some patients is simply inadequate time allowed for sleeping, due to a hectic lifestyle or because of rotating shifts at work.

Low-dose tricyclic anti-depressant medication to improve sleep is often used - these probably increase serotonin levels in the brain which are important neurotransmitters in both sleep and in descending pain inhibitory pathways<sup>19</sup>. Benzodiazepines as hypnotics have no place in the long-term treatment of sleep disturbance in FMS patients<sup>16</sup>.

### Cognitive behavioural therapy

Patients often require some degree of emotional support, but usually not formal psychotherapy. The family practitioner plays a very important role in this aspect and the majority of patients could be managed opti-

mally at this level by a knowledgeable and skillful family practitioner. The following "coping strategies" are often helpful in the management of these patients:

- Develop optimistic attitudes and try not "to fear the worst"
- Strive to maintain calmness and control of anxiety by addressing problems "one at a time"
- Strengthen interactions with family and friends
- Engage in pain-distracting activities and develop behavioural habits that combat depression
- Accept some degree of pain but know that chronic pain modulation to a large degree lies within the patient's own control
- "Workaholics" and over-achievers should learn to gain satisfaction from relaxation
- A family conference may help to identify areas of stress and also identify allies in the management of the patient.

FMS, as a chronic pain syndrome, provides an opportunity for the patients to reflect on their lives rather than just using drugs and physical therapy.

A minority of FMS patients require formal consultation for significant psychological disturbance and will have a co-morbid psychiatric diagnosis (anxiety disorders, dysthymia, depression, etc.)<sup>19</sup>. Referral to a psychiatrist or psychologist with experience in treating patients with FMS is sometimes indicated, although many family practitioners have adequate skills and experience to manage these aspects.

A stress-reduction programme, employing many of the techniques of cognitive behavioural therapy (CBT), has been found to be successful in some FMS patients. The primary goal of CBT is to decrease "learned-helplessness" behaviour<sup>10</sup> and to assist patients in developing an active self-management approach to coping with FMS. These techniques are used in conjunction with aerobic exercise, physiotherapy, relaxation therapy, etc.

There is a subset of FMS patients who become inactive and deconditioned, and they become convinced that they can do nothing - not even participate in their own rehabilitation or employment ("maladaptive pain behaviour"). This small group of FMS patients is difficult to treat and there is often an unrecognised psychiatric component, including a personality disorder<sup>19</sup>.

There are no objective parameters to measure functional disability in FMS and this continues to be a question of contention and controversy. Disability pensions, which may be necessary in some patients, should be the ultimate measure - every effort should be made to counteract the patients' disability and working incapacity<sup>3</sup>.

### Summary

FMS is a common chronic muscle-pain syn-

drome and is associated with many other conditions. This syndrome and its associated conditions, including affective disorders, probably have common centrally mediated causes. Current understanding is that FMS is not considered a reflection of a psychiatric disorder<sup>23</sup>. Both central and peripheral mechanisms of pain in association with genetic and other factors, have been proposed in its pathogenesis.

A major advance has been the development of reliable classification criteria consisting of widespread musculoskeletal pain and multiple tender point areas. It is no longer considered as a diagnosis of exclusion and

can be confidently diagnosed using the positive features of the clinical presentation<sup>31,50</sup>. Failure to recognise FMS patients often results in patient frustration and unnecessary cost-generating investigations.

A number of interventions have been studied and a broad range of treatments is available to the practising physician. Although the disorder has no cure, prompt recognition and proper management often lead to substantial symptomatic improvement<sup>51</sup>. FMS represents a major challenge to the medical profession and providing optimal treatment is a true test of a physician's skill<sup>50,51</sup>. ●

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