

Ministry of Defence

Synopsis of Causation

Fibromyalgia

Author: Dr Tony Fisher, Medical Author, Medical Text, Edinburgh
Validator: Dr Selwyn Richards, Poole Hospital, NHS Trust, Poole, Dorset

September 2008

Disclaimer

This synopsis has been completed by medical practitioners. It is based on a literature search at the standard of a textbook of medicine and generalist review articles. It is not intended to be a meta-analysis of the literature on the condition specified.

Every effort has been taken to ensure that the information contained in the synopsis is accurate and consistent with current knowledge and practice and to do this the synopsis has been subject to an external validation process by consultants in a relevant specialty nominated by the Royal Society of Medicine.

The Ministry of Defence accepts full responsibility for the contents of this synopsis, and for any claims for loss, damage or injury arising from the use of this synopsis by the Ministry of Defence.

1. Definition

- 1.1. Fibromyalgia syndrome (FMS) is a chronic, non-progressive condition, characterised by widespread pain, fatigue, global debility, and poor aerobic fitness, along with an associated loss of concentration and diminished attention span.
- 1.2. A standardised case definition for this disorder was developed and published by the American College of Rheumatology (ACR) in 1990.¹ Their criteria include widespread pain that persists for at least 3 months and tenderness in at least 11 of 18 specific anatomical sites. However, many physicians feel that these criteria are unduly restrictive and it is widely acknowledged that many individuals with the clinical diagnosis of FMS do not fulfil the ACR definition. In addition, although using the number of painful tender points as a measure of severity is clinically expedient it is theoretically vulnerable to bias and may be influenced by subjective distress.²
- 1.3. The presence of accompanying diseases such as rheumatoid arthritis, [Sjögren's syndrome](#), osteoarthritis or [systemic lupus erythematosus](#) does not exclude the diagnosis of fibromyalgia syndrome as it may coexist with a wide variety of conditions. Successful management of a treatable concomitant disease does not substantially improve the symptoms of fibromyalgia syndrome.
- 1.4. There is significant overlap between FMS and chronic fatigue syndrome, with many individuals fulfilling the diagnostic criteria for both disorders. The Synopsis: *Chronic Fatigue Syndrome* contains further details of that disorder.
- 1.5. FMS most frequently affects people between the ages of 18 and 55 and prevalence, which is fairly consistent among westernised countries, ranges from 3 to 5 percent in the general population.³ There is a strong female preponderance with a female:male ratio of about 7:1, and prevalence increases with age.

2. Clinical features

- 2.1. The affected individual usually describes diffuse, chronic musculoskeletal pain, stiffness, and fatigue. The pain tends to be constant, aching, and concentrated in axial regions (neck, shoulders, back, and pelvis), although many patients complain of “pain all over”. Pain is often worse in the morning and is exacerbated by changes in the weather, by cold, and stress.
- 2.2. In a proportion of patients there are multiple, reproducible points of tenderness on palpation as described in the ACR case definition, but this feature is more clearly defined in some cases than in others. The tender points tend to be symmetrical and situated in specific loci in the [occiput](#), neck, shoulder, ribs, elbows, buttocks, and knees. However it is now recognised that most patients with the condition display increased sensitivity to pain throughout the body.
- 2.3. Many other symptoms are reported, including non-restorative, unrefreshing sleep, migraine and tension headaches, irritable bowel syndrome, dysmenorrhoea and urinary frequency. A variety of other musculoskeletal symptoms are not uncommon, including morning stiffness and a subjective, but not demonstrable, sensation of swelling of peripheral joints.
- 2.4. Characteristically, clinical examination is normal and although certain isolated anomalies have been reported, a wide spectrum of laboratory investigations fails to reveal any characteristic, defining abnormality.

3. Aetiology

- 3.1. No single specific cause of FMS has yet been identified. The absence of any peripheral pathology and the presence of widespread tissue [hyperalgesia](#) suggest a central mechanism for the syndrome rather than some pathological process in the muscles themselves. Patients with the condition experience allodynia, i.e. pain on normally painless (non-nociceptive) stimulus, such as touch or light pressure; another pointer to a central mechanism.
- 3.2. **Abnormalities in sensory processing** A number of investigators have found that while patients with FMS are not able to detect nociceptive stimuli at lower levels than normal subjects, (e.g. heat, electrical current, pressure), the threshold at which these stimuli induce a sensation of pain is lower. This observation is interpreted by some as being attributable to an abnormality in the normal pain-suppressing neural pathways between brain and spinal cord.⁴
- 3.3. **Neuroendocrine aberrations** Several studies have identified subtle abnormalities of the [hypothalamic-pituitary-adrenal axis](#) along with a loss of the normal rhythmic diurnal fluctuation in blood [cortisol](#) levels. Other evidence emerging from this line of enquiry includes low blood levels of [serotonin](#) relative to healthy controls, and unusually high levels of substance P (a peptide involved in the transmission of pain impulses) in the cerebrospinal fluid. Changes have also been noted in the growth hormone axis that suggest abnormal [hypothalamic](#) function. However these and other related anomalies have not led to greater understanding of the cause of the condition and their significance is not yet clear.⁵
- 3.4. **Psychological factors** Although some symptoms of FMS suggest a psychological component, careful studies have revealed no consistent relationship between the condition and psychological status. However in a number of studies an increased frequency of life stress has been found, accompanied in a significant proportion of patients by anxiety, low mood and poor coping skills. Most patients are not depressed and any onset of depression does not correlate with an alteration in the level of pain.^{6,7,8}
- 3.5. **Genetic factors** A number of studies have suggested familial aggregation and so possibly an as yet unidentified genetic link.⁹
- 3.6. **Sleep abnormalities** One of the original proposals with regard to causation was that patients suffering from the syndrome exhibited abnormal alpha-wave activity on [electro-encephalography](#) during certain phases of sleep. However the specificity of this observation has been queried and its reproducibility and causal significance challenged.^{10,11}
- 3.7. Other investigators have proposed that there may be impairment of the normal 24-hour

variability of heart rate, and postulate that excessive nocturnal [sympathetic activity](#) may result in non-restorative sleep and ensuing fatigue.¹²

- 3.8. However, although sleep abnormalities and morning fatigue are common in FMS, it is well-recognised that disrupted sleep, of whatever variety, and of whatever origin may result in muscle pain, fatigue and poor concentration.
- 3.9. **Peripheral mechanisms** A large number of investigators have attempted to identify abnormalities in the muscle tissue in FMS. However despite isolated abnormal findings no consistent relationships have been found.
- 3.10. **Reactive or secondary fibromyalgia** Fibromyalgia may arise insidiously and unheralded in an otherwise healthy individual, but in a proportion of cases there appears to be an initiating factor; for example a stressful event, or physical trauma, such as a whiplash injury or surgical operation. In some, there is a history of an influenza-like illness but immunological investigation in such patients has produced inconclusive or inconsistent results and there is at present no clear evidence that FMS is attributable to an infective process.
 - 3.10.1. **Trauma** Between 14 and 23 per cent of patients with FMS associate the onset of their symptoms with physical trauma. However no convincing evidence has been produced that there is any consistent causative link between traumatic events and fibromyalgia.^{13,14,15}
 - 3.10.2. A number of studies suggest that patients with so-called reactive fibromyalgia have more perceived disability, self-reported pain and affective distress than those in whom no initiating event was identified.
 - 3.10.3. There is however no single environmental exposure that is likely to trigger this illness. Instead, data from a wide variety of sources has led many investigators to conclude that when certain people who are genetically predisposed are exposed to any of a wide variety of stressors, including infections or other types of immune stimulation, drugs, physical trauma, infections or emotional stress – acute or chronic – they will develop a multisystem illness of this type.

4. Prognosis

- 4.1. FMS is frequently complicated by functional disability, distress, illness behaviour and long-term disability- and compensation claims, all of which appear to occur more frequently as time progresses. Many authorities are of the opinion that early diagnosis and energetic multidisciplinary intervention help prevent these complications but that once they develop the condition is much less amenable to therapy.¹⁶
- 4.2. No treatment has been found to be consistently helpful in this condition. Analgesics, non-steroidal anti-inflammatory drugs and local physical treatments are only partly effective and the best evidence to date supports the use of low-dose tricyclic antidepressant drugs, such as amitriptyline. However it appears that if tolerated, an individualised regime consisting of [cognitive behavioural therapy](#) allied to a careful, structured exercise programme that emphasises aerobic fitness training is the strategy most likely to produce improvement.
- 4.3. In one large study, 538 patients with fibromyalgia were followed up at 6-monthly intervals for 7 years. At the final assessment 94-98% of the patients had pain, with pain scores remaining constant throughout the study. Persistent and significant abnormalities also persisted in relation to fatigue, sleep disturbance and psychological status.¹⁷

5. Summary

- 5.1. Fibromyalgia syndrome is a common condition, affecting mainly women in the second to sixth decades. Salient symptoms include widespread musculoskeletal pain, fatigue and sleep disturbance, poor aerobic fitness and reduced concentration.

- 5.2. The current consensus of opinion suggests that the disorder results from a complex interaction of elements, including physical, psychological and psychosocial factors, and although no genetic links have been identified, there appears to be a familial predisposition to the disorder.

6. Related Synopses

Chronic Fatigue Syndrome

7. Glossary

cognitive behavioural therapy	A group of therapies that aim to reduce dysfunctional emotions and behaviour by altering thinking patterns and modifying behaviour.
cortisol	The major adrenal hormone; stimulates conversion of proteins to carbohydrates, raises blood sugar levels and promotes glycogen storage in the liver.
electro-encephalography	A diagnostic test which measures the electrical activity of the brain using highly sensitive recording equipment attached to the scalp by fine electrodes.
hyperalgesia	Excessive sensitiveness or sensibility to pain.
hypothalamic	Relating to the hypothalamus, a region of the brain which produces a number of important hormones.
hypothalamic-pituitary-adrenal axis	A major part of the neuroendocrine system that controls reactions to stress. It involves the interactions of the hypothalamus, the pituitary gland and the adrenal glands.
illness behaviour	Abnormal attitudes, ideas, and attributions in relation to illness.
occiput	The back of the head.
serotonin	One of a group of substances (neurotransmitters) that are released from certain cells of the nervous system. It is believed to play an important part in the biochemistry of depression, bipolar disorder and anxiety.
Sjögren's syndrome	A chronic disorder characterised by progressive destruction of the exocrine glands (sweat glands, lachrymal glands, salivary glands).
sympathetic activity	Activity of the sympathetic nervous system which promotes "flight or fight" response; i.e. raises rate of heart and breathing, dilates pupils, etc.
systemic lupus erythematosus	An inflammatory connective tissue disease affecting the blood vessels, kidneys, connective tissue, and skin.

8. References

- ¹ Wolfe F, Smythe HA, Yunus MB et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. *Arthritis Rheum* 1990;33:160-72.
- ² Gracely RH, Grant MA, Giesecke T. Evoked pain measures in fibromyalgia. *Best Practice & Research Clinical Rheumatology* 2003;17(4):593-609.
- ³ Gran JT. The epidemiology of chronic generalized musculoskeletal pain. *Best Practice & Research in Clinical Rheumatology* 2003;17(4):547-61.
- ⁴ Petzkea F, Clauw DJ, Ambrose K, et al. Increased pain sensitivity in fibromyalgia: effects of stimulus type and mode of presentation. *Pain* 2003;105(3):403-413.
- ⁵ Parker AJ, Wessely S, Cleare AJ. The neuroendocrinology of chronic fatigue syndrome and fibromyalgia. *Psychol Med* 2001;31(8):1331-45.
- ⁶ White KP, Nielson WR, Harth M, Ostbye T, Speechley M. Chronic widespread musculoskeletal pain with or without fibromyalgia: psychological distress in a representative community adult sample. *Journal of Rheumatology* 2002;29(3):588-94.
- ⁷ McBeth J, Silman AJ. The role of psychiatric disorders in fibromyalgia. *Curr Rheumatol Rep* 2001;3(2):157-64.
- ⁸ Herrmann M, Scholmerich J, Straub RH. Stress and rheumatic diseases. *Rheum Dis Clin North Am* 2000;26(4):737-63.
- ⁹ Yunus MB, Khan MA, Rawlings KK, Green JR, Olson JM, Shah S. Genetic linkage analysis of multicase families with fibromyalgia syndrome. *J Rheumatol* 1999;26(2):408-12.
- ¹⁰ Moldofsky H. Fibromyalgia, sleep disorder and chronic fatigue syndrome. *Ciba Foundation Symposium* 1993;173:262-71.
- ¹¹ Rains JC, Penzien DB. Sleep and chronic pain: challenges to the alpha-EEG sleep pattern as a pain specific sleep anomaly. *J Psychosom Res* 2003;54(1):77-83.
- ¹² Bengtsson A, Bengtsson M. Regional sympathetic blockade in primary fibromyalgia. [Clinical Trial. *Journal Article. Randomized Controlled Trial*] *Pain* 1988;33(2):161-7.
- ¹³ Al-Allaf AW, Dunbar KL, Hallum NS, Nosratzadeh B, Templeton KD, Pullar T. A case-control study examining the role of physical trauma in the onset of fibromyalgia syndrome. *Rheumatology* 2002;41(4):450-3.
- ¹⁴ Buskila D, Neumann L. Musculoskeletal injury as a trigger for fibromyalgia/posttraumatic fibromyalgia. *Curr Rheumatol Rep* 2000;2(2):104-8.
- ¹⁵ White KP, Carette S, Harth M, Teasell RW. Trauma and fibromyalgia: is there an association and what does it mean?. *Semin Arthritis Rheum* 2000;29(4):200-16.
- ¹⁶ Clauw D. Fibromyalgia. In: Ruddy S, Harris ED, Sledge CB, editors. *Kelley's textbook of rheumatology*. 6th Ed. Philadelphia: WB Saunders Company; 2001. p.417-427.
- ¹⁷ Wolfe F, Anderson J, Harkness D et al. Health status and disease severity in fibromyalgia: result of a six-center longitudinal study. *Arthritis Rheum* 1997;40:1571-1579.