Baillière's Clinical Rheumatology
Vol. 13, No. 3, pp. 391–401, 1999

BAILLIÈRE'S BEST PRACTICE & RESEARCH

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# The differential diagnosis of generalized pain

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Patients whose symptoms include widespread, diffuse musculoskeletal pain are commonly referred for rheumatological evaluation, even when the underlying cause may lie outwith the remit of rheumatology. A diagnosis of fibromyalgia may seem highly probable even from the referral letter, or after a few leading questions during the consultation. However, the lack of specificity of the many symptoms associated with widespread pain means that other diagnoses have to be considered. The history and examination must bear in mind alternative and concomitant musculoskeletal disorders, such as mild systemic lupus erythematosus, polyarticular osteoarthritis, rheumatoid arthritis, polymyalgia rheumatica, hypermobility syndromes and even osteomalacia. Non-rheumatological diseases may also have symptomatic similarities to fibromyalgia, including neoplastic and neurological diseases, hypothyroidism and other endocrine disorders, chronic infections, as well as a variety of psychiatric conditions. A rational approach to investigation will usually allow other diagnostic possibilities to be excluded without reinforcing the abnormal illness behaviour so common in chronic pain states.

**Key words:** fibromyalgia; chronic pain.

Whatever one's opinion of fibromyalgia as a diagnostic term there can be little doubt that anxious patients with generalized, chronic musculoskeletal pain commonly present to Rheumatology Clinics as well as to specialist Pain Clinics. Such has been the success of attempts to raise awareness of the syndrome in the medical literature that the primary care physician may have already made a confident diagnosis of fibromyalgia. Confirmation is sought, together with a request for advice on management. The lay press and Internet have alerted patients to fibromyalgia as a possible explanation for their chronic pain, disability and general ill health. Although the diagnosis may appear compelling from initial evaluation, it is incumbent upon the rheumatologist to be also a good general physician, and to be aware that fibromyalgia can be mimicked by diseases in other body systems. 'Red flags', indicating important alternatives to a diagnosis of fibromyalgia, must be sought first. These include recurrent headaches, altered bowel and bladder function, paraesthesia and weakness, weight gain or loss, fatigue and changes in personality or mood. Fibromyalgia can accompany other underlying diseases, some benign and others more sinister, whose symptoms are dominated by concomitant diffuse musculoskeletal aching. This chapter highlights potential diagnostic traps, and suggests a logical approach to the assessment of patients who have generalized musculoskeletal pain.

1521–6942/99/030391+11 $12.00/00 

## DIFFERENTIAL DIAGNOSES

### Rheumatological

In general, there are two stages to the rheumatological differential diagnosis of generalized pain. The first stage asks 'is there an alternative explanation to the diagnosis of fibromyalgia?'. The second asks 'if an alternative diagnosis is made, how much of the symptomatology might be attributable to a concomitant fibromyalgia-like problem?'.

### Alternative diagnoses

1. Systemic lupus erythematosus (SLE). This can easily be confused with fibromyalgia.[1] These two diseases share a similar long list of non-specific symptoms, including widespread, non-specific arthralgia and myalgia, stiffness and debilitating fatigue. Both predominate in young and middle-aged females. A Raynaud's-like peripheral acrocyanosis has been noted in fibromyalgia[2,3], as have livedoid skin markings.[4] Patients may have sicca symptoms, low levels of anti-nuclear antibodies, and skin biopsies which show increased deposits of IgG at the dermo-epidermal junction.[3,4] Both disorders can be associated with menstrual irregularities. The problem of diagnosis is perhaps worse if one considers so-called latent or non-criteria lupus.[5] Additionally, fibromyalgia and SLE may co-exist in the same patient.[1] This may cause difficulty in determining appropriate treatment because the ill health due to fibromyalgia will not respond to steroids and immunosuppressant drugs.
2. Sjögren's syndrome. Clinically there can be confusion between fibromyalgia and Sjögren's syndrome.[6] Bonafede et al studied 72 patients with fibromyalgia and found abnormal Schirmer tests in 38%. Only half had symptomatic dry eyes. A small number were anti-nuclear antibody (ANA) positive, and smaller numbers had anti-Ro or anti-La antibodies. Five of the 28 patients with abnormal Schirmer tests had abnormal salivary gland biopsies. The authors concluded that fibromyalgia and probable Sjögren's syndrome were associated in 7% of cases, and possible Sjögren's syndrome in 11%.
3. Rheumatoid arthritis (RA). Patients with fibromyalgia may present with arthralgia in the hands.[7] When this occurs in a young female who also complains of prolonged morning stiffness, functional deficits, paraesthesiae in the fingers (suggestive of possible carpal tunnel syndrome), and subjective or objective puffiness of the hand and fingers, it is necessary to exclude early RA. Fibromyalgia is not associated with elevation of acute phase reactants or seropositivity for IgM rheumatoid factor. Just as with SLE, fibromyalgia may co-exist with RA and cause increased pain, depression and anxiety.[8] Failure to recognize this combination may lead to overtreatment with increasingly toxic antirheumatic regimes, or to the inappropriate substitution of one disease-modifying antirheumatic drug by another.
4. Polyarticular osteoarthritis. Painful fingers in a middle-aged female suggests possible interphalangeal osteoarthritis (IPOA), but may also be the presenting feature of fibromyalgia.[7] Generalized musculoskeletal pain may occur when osteoarthritis affects additionally the cervical and lumbar spines, knees and hips, and acromio-clavicular joints. Generally speaking, such cases of polyarticular OA will occur in an older age group than does fibromyalgia, although the latter certainly occurs in the elderly.[9] Misdiagnosis is common. In the study by Yunus et al[9], 40% of elderly patients with fibromyalgia had been given a therapeutic trial of corticosteroids on

the mistaken assumption that they had polymyalgia rheumatica or an inflammatory joint disease.

5. Polymyalgia rheumatica (PMR). This, too, tends to occur in an older age group than does fibromyalgia, but lacks the marked predominance of females seen in the latter. Yunus reported that 6% of fibromyalgia patients aged over 60 years had previously been misdiagnosed as having PMR.[9] An elevated sedimentation rate and C-reactive protein discounts fibromyalgia as the sole diagnosis. In any event, the rapid improvement in the symptoms of PMR after the introduction of corticosteroids is not seen in fibromyalgia, in which patients may actually feel worse.[10]
6. Polymyositis. This may have a very indolent onset with non-specific fatigue, lethargy and weakness. An acute-phase response may be absent, and muscle enzyme levels may be normal or only mildly increased. Fibromyalgia may be considered, but electrophysiological tests and muscle biopsy will usually allow the diagnosis of polymyositis to be confirmed.
7. Osteomalacia. This is an uncommon condition in the industrialized nations, but may be seen in the elderly and among immigrants from the Indian subcontinent. General debility is accompanied by diffuse musculoskeletal pain, which may be severe. The diagnosis can be confirmed by appropriate biochemical and radiological investigations, with or without bone biopsy.
8. Regional pain syndromes. Patients who experience generalized musculoskeletal pain may present with dominant pain in one particular body part or region. Thus, the presenting feature may be pain in the hands suggestive of possible rheumatoid arthritis or interphalangeal osteoarthritis.[7] There may be particular pain in the elbows suggestive of lateral epicondylitis, in the lateral thigh suggesting trochanteric bursitis, or at the pelvic brim to suggest so-called iliolumbar syndrome.[11] Enquiry should be made for the presence of more widespread pain, stiffness, poor sleep, tiredness and disability. It is well recognized that generalized pain may develop in those who have been involved in road traffic accidents and who initially have predominant neck pain attributed to a 'whiplash' injury.[12] The local pain seems gradually to 'metastasize' to other body parts. This may be due to emotional factors or perhaps to sleep disturbance and reduction of physical activity and fitness. A study in Israel found that 21.6% of 102 patients with neck injuries developed fibromyalgia, at a mean of roughly 3 months after trauma.[13] In 74 of the 102 patients, trauma had involved a motor vehicle accident. In comparison, only 1.7% of 59 patients with leg fractures subsequently developed fibromyalgia.

   Mention must also be made of myofascial pain syndromes. The exact mechanism of such syndromes is unclear, but patients present with musculoskeletal pain arising in soft tissues, often adjacent to the spine and in anti-gravity muscles, but also perhaps responsible for the pain of temperomandibular joint dysfunction.[14] There is a localized tender area which, when palpated, feels firm and which causes referral of pain in a characteristic fashion, and which corresponds to the distribution of pain of which the patient complains.[15] The aetiology may relate to poor posture or to previous trauma, but often there is no obvious precipitating event. The trigger point is somewhat analogous to a so-called 'fibrositis nodule', and patients may respond to firm massage, acupuncture, injection with steroid and local anaesthetic, or stretch and spray techniques. The problem lies in deciding whether a patient has widespread pain due to fibromyalgia or has several simultaneous myofascial pain syndromes. Even experts in this area of rheumatology may have difficulty differentiating the two[16], although, in practice, the approach to management is usually very similar.

## CONCOMITANT DISORDERS

Generalized pain due to fibromyalgia may occur in association with a more obvious underlying locomotor pathology, such as osteoarthritis, rheumatoid disease, SLE and Sjögren's syndrome, as previously discussed. There is also a common co-occurrence of fibromyalgia in hypermobility syndromes[17,18], most of which are presumed to be variants of the Ehlers–Danlos syndrome. In one study 27.3% of 66 women with fibromyalgia satisfied criteria for joint hypermobility using an abbreviated Beighton scale. In contrast, only 11.4% of patients with a variety of other rheumatic diseases were hypermobile.[18] This association is especially true of children and adolescents. Gedalia et al[17] assessed 338 schoolchildren of mean age 11.5 years. Using standard criteria, 13% were hypermobile and 6% had fibromyalgia. Of 21 children with fibromyalgia, 81% had hypermobile joints, while 40% of 43 hypermobile children also had fibromyalgia.

**Table 1.** Differential rheumatological diagnoses of generalized pain.

| |
|---|
| Systemic lupus erythematosus |
| Rheumatoid arthritis |
| Sjögren's syndrome |
| Polyarticular osteoarthritis |
| Cervical and lumbar spondylosis |
| Polymyalgia rheumatica |
| Polymyositis |
| Regional pain syndromes |
| epicondylitis |
| trochanteric bursitis |
| iliolumbar syndrome |
| myofascial pain syndromes |
| Hypermobility syndromes |

### Neurological

In practice, serious underlying neurological disease is uncommonly confused with fibromyalgia. While carpal tunnel syndrome and cervical nerve root irritation may affect women of a similar age group, a careful clinical history and comprehensive general physical examination will usually allow for a correct diagnosis without recourse to specialized neurophysiological or radiological investigation.

Simms and Goldenberg reported that 135 of 161 consecutive patients with fibromyalgia complained of numbness or tingling at the time of diagnosis.[19] Of these, 33% had neurological symptoms in all four limbs, 28% bilaterally in the upper limbs only, and 7% bilaterally in the lower limbs. A further 15% had unilateral upper or lower limb paraesthesiae. Prior neurological assessment in 35 patients had suggested possible carpal tunnel syndrome, sensory neuropathies, cervical rib, and multiple sclerosis, although no diagnosis had been made in 14 cases. Of 36 patients investigated neurophysiologically, 94% had normal results. Only one patient of 11 with suspected median nerve compression had nerve conduction results compatible with the diagnosis. At review some 2 years later, the majority (97%) of 57 patients had persistent symptoms. None of the study patients was felt to have developed an underlying neurological disorder.

In his review, Bennett discusses possible explanations for pronounced muscle fatiguability.[20] Although metabolic myopathies may be considered, these are rare, and controlled studies using both light and electron microscopy have revealed no specific abnormalities in the muscles of those with fibromyalgia.[21] Appearances are those of muscles deconditioned through lack of exercise and physical fitness.

Tension headaches, and even migraine, are common in fibromyalgia.[22] When accompanied by poor concentration, weakness, or visual disturbances it is important to examine the fundi for pallor of the optic discs and papilloedema (evidence of multiple sclerosis and raised intracranial pressure), as well as tapping the reflexes to look for an upper motor neurone lesion. Demyelination may cause disturbances of bladder function, while fibromyalgia may be associated with 'female urethral syndrome', in which there is suprapubic and urethral discomfort associated with micturition.[23] There can be few rheumatologists who do not occasionally make the initial diagnosis of multiple sclerosis in a patient presenting with non-specific complaints such as fatigue, numbness, aching and weakness. Anecdotally, the author has seen patients with suspected fibromyalgia who have been subsequently diagnosed as having conditions such as motor neurone disease, hereditary spastic paraplegia and syringomyelia. A recent edition of *The Fibromyalgia Times*, published by the Fibromyalgia Alliance of America, reported on a possible link between some cases of fibromyalgia and cervical cord compression, including that due to an Arnold-Chiari malformation.[24]

## Chronic infection

The similarities between fibromyalgia and chronic fatigue syndromes (CFS) have been noted[25,26], and it was logical to consider whether the syndromes were essentially identical expressions of the same pathological process (post-viral complications, for example), but presenting to different clinical departments. In one survey reported by Goldenberg, 118 patients with fibromyalgia were asked if a specific event appeared to precipitate their illness.[25] Twelve patients (10%) thought that they had become ill after a preceding viral illness. In a second survey, 50 fibromyalgia patients were asked if their illness had begun with a viral or upper respiratory infection. Such a connection was made by 55% of patients. However, serology for antibodies directed against Epstein–Barr virus antigens shows no difference to a control population.[27] Similar negative results were obtained when patients with fibromyalgia were assessed for evidence of infection with human parvovirus B19.[28]

Bennett, in his review of the differential diagnosis of fibromyalgia, mentions possible chronic brucellosis[20], and the author has seen one elderly female with possible fibromyalgia who proved to have a low-grade infective endocarditis. As with CFS, some patients with fibromyalgia may be convinced that their illness is secondary to a viral infection, but there is little in the literature which would support such a contention.

## Hormonal/metabolic

There are two issues to be considered here. First, clinical syndromes which may cause diagnostic difficulty, and second, abnormalities which have been reported in patients with clinical fibromyalgia and which cause diagnostic confusion because of overlap with other conditions.

1. Hypothyroidism. Although thyroxine levels are normal in fibromyalgia, many similarities exist between fibromyalgia and hypothyroidism. Both are more

common in females, are associated with fatigue, non-specific aches and pains, intolerance of exercise and cold environments, and often loss of concentration, memory and other higher intellectual functions. Both may be associated with menstrual upsets and constipation. Even if the fibromyalgia seems clinically obvious it is wise to test thyroid function at least once.
2. Diabetes mellitus. One should at least consider non-insulin-dependent diabetes when a patient presents with weight gain, lethargy, non-specific myalgia, dry mouth, and sleep disturbance in association with nocturia. Dipstick analysis of the urine for glucose, blood and protein should anyway be a part of the initial assessment of all clinic patients.
3. Hyperparathyroidism. When occurring as a primary disorder, this may have a very insidious onset and be associated with non-specific ill health. The classical triad of 'stones, bones and abdominal groans' may well occur, and it is easy enough to attribute constipation to a sluggish bowel and analgesic use in fibromyalgia, and the bony pain to arthralgia and myalgia in the same condition. Where indicated, serum calcium, alkaline phosphatase and parathyroid hormone levels should be requested.
4. Hormonal and biochemical abnormalities in fibromyalgia 'overlap'.

It has become evident that chronic musculoskeletal pain syndromes can be associated with a number of reproducible abnormalities in the hypothalamic-pituitary-adrenal (HPA) axis[29,30], and that subtle anomalies in neuropeptide levels in serum and cerebrospinal fluid may occur in fibromyalgia.[31] As ever, it is difficult to know whether such anomalies are aetiologically significant or merely epiphenomena, but once again it might introduce diagnostic difficulties.

The pattern of severity of symptoms in fibromyalgia shows a diurnal variation, with stiffness more severe in the morning than in the evening, whereas fatigue is usually worse as the day progresses. Many patients feel at their best late morning and early afternoon, when stiffness has eased and before fatigue becomes marked.[32] Moldofsky in Toronto has also highlighted a seasonal variation in symptoms with pain, mood, sleep and energy all tending to be worse between November and March, and better from May to August.[33] This suggests an overlap with so-called seasonal affective disorder, and such seasonal fluctuations were more obvious in fibromyalgia than in a comparison group of patients with RA. Moldofsky postulated that light therapy might be beneficial in fibromyalgia.

Hormones, too, have a natural circadian variation. Endogenous steroid levels are higher in the morning than in the evening, while in adults growth hormone is mainly secreted at night during deep sleep. Such observations led to examination of the HPA axis in patients with fibromyalgia. Griep et al found statistically significant enhancement of adrenocorticotrophic hormone (ACTH) release in response to corticotropin-releasing hormone (CRH) and insulin hypoglycaemia tests in 10 patients with fibromyalgia who were compared to healthy controls, although there was no difference in cortisol production.[30] They postulated that fibromyalgia was associated with hyperreactive pituitary ACTH release and concomitant adrenal hyporesponsiveness, and that this might go some way to explain the poor exercise tolerance and muscle function so typical of fibromyalgia.

Ferraccioli et al[29] studied a variety of dynamic tests of hormone release in patients with fibromyalgia, RA and low back pain. A subset of fibromyalgia patients showed a blunted response of cortisol to stimulation with dexamethasone and an exaggerated release of prolactin in a thyrotropin-releasing hormone test. Of interest, those fibromyalgia patients without abnormal hormone responses were helped by treatment using EMG-biofeedback techniques, but not those with the abnormal responses.

Neeck and Riedel[34] found that basal thyroid hormone levels were no different in patients with fibromyalgia and a control group, but that the fibromyalgia group had a significantly lower thyroid response to TRH and significantly higher production of prolactin. The same group had significantly lower calcium and calcitonin levels, and yet normal levels of parathyroid hormone.

Because of some similarities between fibromyalgia and sympathetically maintained pain (reflex sympathetic dystrophy or complex regional pain syndrome type 1), Vaeroy et al[35] performed dynamic tests of sympathetic function in a group of 27 patients with fibromyalgia and in 29 healthy controls. Vasoconstrictory responses were reduced in the patients with fibromyalgia, and the authors postulated that the Raynaud's-like acrocyanosis seen so often in fibromyalgia might be linked to autonomic dysfunction. An unstable cutaneous circulation has also been linked to an exaggerated neurogenic inflammatory response mediated via the antidromic release of Substance P.[36] This same neuropeptide mediates the transmission of nociceptive stimuli at the level of the dorsal horn of the spinal cord. Serotonin (5-hydroxytryptamine) has also been studied in fibromyalgia because it is vitally important in the regulation of sleep, pain and mood, which are all disturbed in fibromyalgia. Bennett's group have found low levels of insulin-like growth factor (also called somatomedin-C) in some patients with fibromyalgia.[37] This factor mediates the activity of growth hormone, which helps to promote an ongoing repair process for all the damage our bodies sustain in the course of everyday life. Perhaps the widespread musculoskeletal pain of fibromyalgia is a reflection of this faulty repair process.

As yet the numerous observations relating to abnormal neuroendocrinology and neurochemistry in chronic pain syndromes have not been pulled together into a cohesive picture, but we can look forward to exciting new evidence-based hypotheses in the coming years.[38]

## NEOPLASTIC CONDITIONS

Generalized musculoskeletal pain is a feature of many malignant diseases, including multiple myeloma, metastatic breast, lung and prostatic cancers, and can be associated with non-metastatic manifestations of malignancy when tumours produce hormones such as PTH. There may be widespread tenderness to palpation, sleep disturbance, fatigue and poor exercise tolerance. Pain worse at night with unexplained weight loss should prompt careful clinical examination for evidence of malignancy. Routine haematological and biochemical tests, together with appropriate plain films and isotope bone scans, should be arranged.

## PSYCHIATRIC DISORDERS

There can be little doubt from the literature that chronic pain in general is often, if not usually, associated with perturbations of mood, thought and behaviour. Indeed, the International Association for the Study of Pain (IASP) defines pain in terms of affective/motivational inputs as well as those which are purely a function of sensation. The more chronic the pain and the less obvious the pathology, the more likely it is that psychogenic factors will have to be considered and tackled. Major affective disorders have a considerable overlap of symptoms with fibromyalgia, and it has been proposed that the latter is part of the 'affective spectrum disorders'.[39] Numerous studies using a

wide range of psychometric instruments have shown reproducible abnormalities in fibromyalgia. Many patients are currently depressed or have a history of depression, and there is often a strong family history of the same.[40] Fibromyalgia may represent a somatoform disorder, with many subjective complaints affecting numerous organs and body systems.[41] Frequently there are underlying anxieties and phobias of which the patient may be unaware. In those whose fibromyalgia develops subsequent to a distressing road traffic accident, there are often features of post-traumatic stress disorder.[42]

To diagnose a chronic musculoskeletal pain syndrome is not difficult. The difficulty lies in trying to explain how and why it has developed in that particular individual and why they are presenting at that particular time. The help of an experienced clinical psychologist or psychiatrist should be sought because analgesic regimes and exercise programmes are unlikely to cure clinical depression or allow a distressed patient to confront deep-seated anxieties.

## ASSESSING THE PATIENT WITH GENERALIZED PAIN

A comprehensive but flexible approach is more appropriate than following a simple predetermined protocol when evaluating a patient with generalized pain. It is rare for two patients to have identical clinical features for the same duration and with the same relevant aetiological factors. The same applies to most chronic diseases, because an individual's capacity to cope with distress and tolerate pain is as unique as their personality. The most important part of the consultation is to record the history in a careful and non-judgemental fashion. Not infrequently the rheumatology clinic is only one more referral among many. The patient may have seen a neurologist about their headaches, a gastroenterologist about their irritable bowel syndrome, a gynaecologist about their dysmennorrhoea or dyspareunia, a urologist about their urinary frequency, an orthopaedic surgeon about their chronic low back pain, and sometimes a psychiatrist about their depression. Often they will have had several courses of physiotherapy, and paid to see osteopaths, chiropracters, reflexologists, homeopaths, aromatherapists, and other practitioners of the healing arts. There is no evidence, however, that alternative medicine is any more successful in treating fibromyalgia than mainstream medicine.[43] Although a few anxious individuals may be reassured that they do not have inflammatory joint disease, cancer or multiple sclerosis, many more will only be happy with a positive, not a negative, diagnosis.

The history should enquire about the duration of symptoms, the pattern of development, aggravating and relieving factors, associated phenomena, periodicity, and all the other features of pain about which one learns as an undergraduate. Ask about stressful life events: patients with fibromyalgia often give a long list of distressing events such as sexual and physical abuse, bereavements, redundancy and divorce.[44] Perhaps the patient has a pet theory about why they have developed chronic pain, and this knowledge may allow management strategies to be more accurately targeted. Gently and tactfully enquire about past and present depression or other psychiatric problems. If done too early in a consultation the patient may assume, perhaps correctly, that they have already been dismissed as neurotic, that 'it's all in the mind'. The examination should be of the patient in a state of undress apart from the underwear. Look for evidence of hypothyroidism, such as bradycardia and sluggish tendon reflexes. Examine the skin for erythema ab igne, perhaps evidence of deep-seated malignancy. Check the hands for evidence of osteoarthritis and inflammatory

joint disease, and assess range of movement in cervical and lumbar spines. Test muscle strength and tendon reflexes for evidence of neurological disease, and palpate those areas typically hyperalgesic to light pressure in fibromyalgia. Are the signs reproducible and consistent, or is there inappropriate illness behaviour, such as apparent exaggeration, grimacing and verbalisation? Can the patient move more freely when dressing and undressing than during formal examination? Diagnostic tests should not consist of a battery of serological and radiological investigations in every patient. The general practitioner may have already performed full blood count, ESR, C-reactive protein, and a biochemical profile, including thyroid function tests, and there is little point in repeating these. An isotope bone scan is of help in cases of suspected disseminated malignancy or osteomalacia, but often shows only evidence of mild osteoarthritis. In the majority of cases of generalized pain such as fibromyalgia, there is no place for routine magnetic resonance and computed tomographic imaging. Judicious investigation may reassure both doctor and patient, but over-investigation may merely serve to re-inforce the patient's faulty beliefs about the nature and significance of chronic pain. Once a diagnosis of fibromyalgia has been made it is rare for long-term follow-up to reveal subsequent development of more serious organic pathology.[45]

## SUMMARY

Chronic musculoskeletal pain is not a disease, nor, in most cases, is it symptomatic of a single diagnosable disease. It represents a state of distress with a complex interaction of physical and emotional factors, some understood and many ill-defined. It may be a somatic presentation of failure to cope, or it may rarely be the most obvious manifestation of neurological, gynaecological, endocrine or oncological pathology. To dismiss the patient with a diagnosis of fibromyalgia represents an exercise in labelling, and using a rather unconvincing and unscientific label at that. Chronic generalized pain and fibromyalgia are not synonymous. Even those who satisfy current criteria for fibromyalgia may have another underlying problem outwith the usual remit of rheumatology. To be a good rheumatologist one must first be a good physician and also a caring individual. The large numbers of patients with diffuse pain being referred to rheumatology clinics may lead to a defeatist attitude, to the rapid dismissal of those

**Practice points**

- generalized musculoskeletal pain is a feature of many medical disorders. Assess the patient as a generalist, rather than considering only rheumatological conditions
- do not over-investigate. This can exacerbate abnormal illness behaviour in anxious patients
- try not to be pre-judgemental. The patient is unlikely to be trying to waste your time. There is a problem; help the patient to solve it
- drugs are often relatively unhelpful in chronic musculoskeletal pain. Explanation, reassurance, and changes in lifestyle are more appropriate than polypharmacy

people whose problems make us feel uncomfortable. Under such circumstances there is a risk of overlooking serious and potentially treatable diseases.

**Research agenda**

Unlike acute pain, chronic pain serves no useful purpose. Although psychogenic inputs must always be considered, future research should try to increase our understanding of the likely abnormal dynamic interactions of neuropeptides, endorphins, neurohormones and cytokines of the immune system in chronic pain disorders. Only by understanding pain at a biochemical level will novel drug therapies be described. Pain behaviour represents a huge therapeutic challenge. If possible, treatment regimes should be easily accessible to the community, place no major financial burden on the health care budget and produce good long-term results with few relapses. Future research should also consider how chronic pain can be best prevented, although the highly subjective nature of an individual's pain may mean that no single approach is feasible.

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