Editorial

Fibromyalgia Among Friends

I have been urged by my friends to take up my pen, to write of this subject — so difficult in detail yet so simple in all its fundamental aspects — and I do so on one condition. That I may be allowed to say as strongly as possible that although my name has been associated with this queer word "fibromyalgia," yet talk of priority in this kind of context is almost meaningless[1]. When doctors don't know, they speak Latin. When they really don't know, they use Greek. Thus the unsuitable "fibrositis" became "fibromyalgia"; hardly an advance in clarity.

White and Thompson documented a normal or high prevalence of fibromyalgia (FM) among an Amish population, as compared with 2 large and appropriate control groups, in a well-conceived and concise report[2], just one of a series of carefully designed and implemented studies by the London, Canada, group. Known risk factors were reviewed, but "there are some who consider fibromyalgia to be factitiously driven by misinformed media reports and an overly liberal compensation system." The Amish were of interest because many of them use no electricity, do not subscribe to newspapers or magazines, do not use cars, nor utilize governmental or commercial compensation systems. Litigation is also not a motivating factor. Still, they may have chronic pain, limiting fatigue, and tender points.

In the same issue *The Journal* featured 3 editorialists, all articulate gentlemen, with surprisingly unkind results[3-5]. None really addressed either the science of the paper or the inferences. The most surprising response was that of Dr. Wolfe (see below). The responses of Drs. Ehrlich and Hadler were predictable. Despite the Amish study, Dr. Ehrlich still talks of non-disease, and even the "dollar poultice." It is difficult to pin down Dr. Hadler. He is sympathetic to "people with persistent widespread pain...bedeviled by challenges that may render Sisyphean any quest for some sense of being well..." He prefers the more recent if less specific label of "medically unexplained symptoms" (MUS). This group of conditions includes regional problems such as headache ("migraine") and upper limb and low back pain. Dr. Hadler too easily attributes them to "functional somatic symptoms," "a somatization if you will." But the term MUS surely suggests that the confusion may lie with the medical professional. Much has been learned about the neurological and neurochemical mechanisms involved in pain transmission and amplification since the publication of the American College of Rheumatology (ACR) 1990 Criteria for the Classification of Fibromyalgia[6], but none of this literature is cited.

Far too many papers introduce the topic of FM by stating, "we don't know the cause, and there is no cure." This misstatement allows freedom for free speculation, though few can match the rhetorical skills of Ehrlich and Hadler. We would prefer more data and fewer words. At least they can learn to assess tenderness, and teach these clinical skills. There are languages by which patients convey information that do not involve words or even emotions.

Do we really need a label? Here are two descriptions of such a patient, studying at Oxford, at 20 years of age.

> "While he was at Lichfield, in the college vacation of the year 1729, he felt himself overwhelmed with a horrible hypochondria, with perpetual irritation, fretfulness, and impatience: and with a dejection, gloom, and despair, which made existence misery. From this dismal malady he never afterward was perfectly relieved; and all his labours, and all his enjoyments were but temporary interruptions of its baleful influence... Johnson, who was blessed with all the powers of genius and understanding, in a degree far above the ordinary state of human nature, was at the same time visited with a disorder so afflicted, that they who know it by dire experience will not envy his exalted endowments... Johnson, upon the first violent attack of this disorder, strove to overcome it by forcible exertions. He frequently walked to Birmingham and back again, and tried many other expedients; but in vain...[7]

> "But not little men triumph upon knowing that Johnson was a HYPOCHONDRIAC, was subject to what the learned, philosophical, and pious Dr. (George) Cheyne has so well treated under the title of 'The English malady.'[8]

See other editorials and letters on FM in this issue.

[Figure 1]. Though he suffered severely from it, he was not therefore degraded. The powers of his great mind might be troubled, and the full exercise suspended at times; but the mind itself was ever entire.[7,11]

Did Dr. Johnson have what may now be labeled FM? We learn also that he slept poorly, and lay late in bed in the morning, feeling guilty. Another characteristic feature: he presented his physician with a long account of his many symptoms, *in Latin*. Unfortunately, this account was lost, and the above words, and the poetic, comma-driven rhythms, were chosen by Boswell. They include irritation, misery...but do not specify whether pain was present or absent. And the pious Dr. Cheyne did not assess tender points. But there needed to be a label, and several were given.

What is FM? It seems that the authors, the editorialists, or the many correspondents, do not know! Yet it is "so simple in all its fundamental aspects." Referred pain and amplifying factors. The pain is of deep, somatic origin. The areas to which pain is referred are innocent, and the source of the pain is unknown to the patient, and to too many health professionals. There are many referred pain syndromes, and the subgroup labeled FM is at a more severe end of the pain spectrum, and complicated further by fatigue, physical deconditioning, and other symptoms.

Suppose you were a Neanderthal. You had a tool-making culture lasting at least a quarter of a million years, survived extreme cold as well as heat, buried your dead, and invented a 4-note flute. Your brain was as large as ours. But that brain could not conceive of agriculture, architecture, or the abstract symbols that enable these ideas to develop and spread. You certainly were not stupid, but you could not conceive of the square on the hypotenuse.

It is fascinating that among the earliest evidences of high-level use of symbols by modern humans are artistic; the cave paintings in southern France and Spain, which show color, shading, perspective, and motion — not just things. Our brain has evolved so that we can do all this and much more. But we can't feel the deep structures of our body, and specifically the bones deep in the low neck and low back. They were not included in the famous map of the sensory cortex constructed by Penfield[9]. They are not included in Kellgren's "body image"[10]. My consultation letters must begin: "It may be helpful to preview the findings at today's examination. There are major mechanical problems in the lowest part of the lower cervical and lumbar spine, problems which have not been specifically identified and dealt with in the treatment program to date." The details are then reviewed, and the treatment program follows. I often do not need the label "fibromyalgia," but do need tender points.

Kellgren suggested that "this false localization over muscles has been responsible for old concepts such as "fibrositis"[11]; but he left us with no clinical strategy to test this hypothesis. He did, however, describe "The deep tender spot, (which) frequently lies outside the distribution of the pain, ...the patient is not aware of its existence until it is discovered by the physician." This is clearly distinguished from the more diffuse tenderness to be found in regions to which pain is referred.

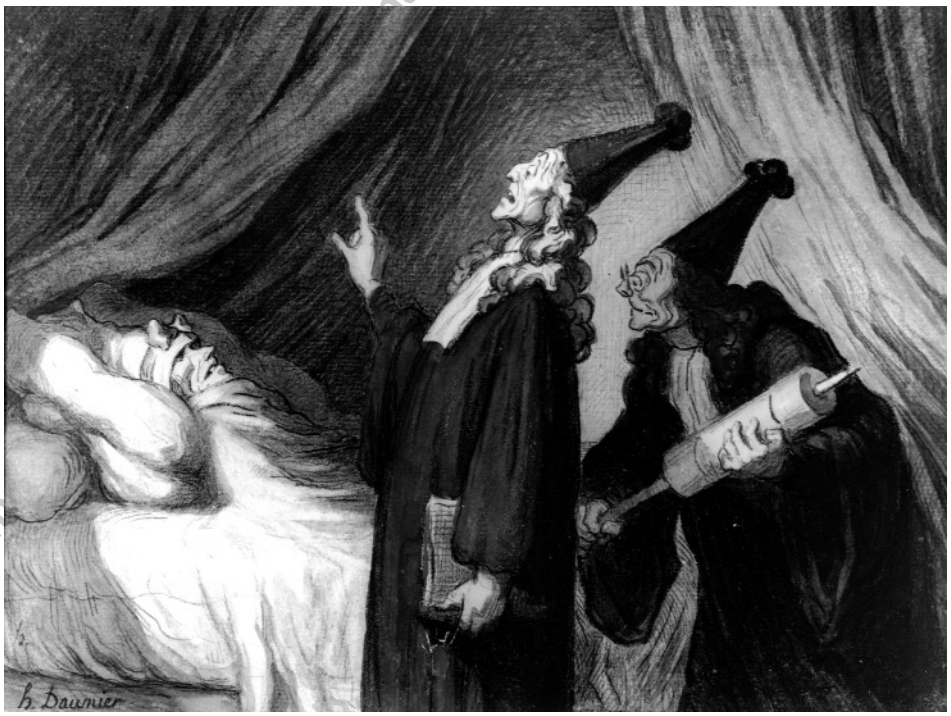

Figure 1. "The Hypochondriac" by Honoré Daumier, courtesy of the Courtauld Institute of Art, London.

Let me now jump to the very specific set of tender sites incorporated in the 1990 ACR Criteria[6], and to the additional list described in the C6–7 syndrome[12,13]. Many of these sites, such as midtrapezius, suboccipital, scapular, and buttock sites, lie in regions to which pain is commonly referred, and are of use only when they are not tender. By contrast, low anterior cervical and medial knee tenderness sites well proximal or distal to the joint line (and other sites) are located in regions where there is no local pain, so that "the patient is not aware of its existence until it is discovered by the physician." This finding and interactions among sleep disturbance, pain, and tenderness described by Moldofsky, *et al*[14] were all objective findings available in the 1970s and reproduced by all who cared to look.

Let us now (briefly) examine the determinants of the equally characteristic symptom patterns. In the upper body, referred symptoms (pain or pain equivalents such as numbness, tingling, tightness, stiffness, swelling) may affect the forehead, eyes and jaw (the distribution of the first division of the trigeminal nerve), the back of neck (eased rather than aggravated by massage), the muscles that control the shoulders, including those in the anterior chest and interscapular area, as well as the arm, forearm, hand and fingers. (Not the tongue, not the nipples, both sensitive, and well represented in the cortex.) The distribution clearly cannot be explained by the anatomy of a single nerve or segment. The organizing principle is the neurology of eye–hand coordination, which has evolved spectacularly over 4 million years. Some of us can throw or hit a baseball, or play a musical instrument; but we cannot sleep in the fetal position without at some time developing symptoms from the above menu. We have long clavicles and broad shoulders. When we lie on our side, the lower shoulder tends to rise toward our cheek, so that delivery of reliable support to the low neck is blocked.

In the lower body, the pattern of characteristic symptoms also includes regions not obviously linked to the low back and lower limbs. The pelvic floor is represented in the form of the irritable bowel[15] and irritable bladder[16], and low abdominal pain is also common. The neuroanatomy of this pattern is not simple, but functionally they are all linked to the special demands of the upright posture.

Why did we begin to walk upright 4 million years ago, with (often locked) lumbar hyperextension? We couldn't run faster or walk further. But it gave us freedom to use our hands, and major changes in our thumbs, shoulders, and rib cage rapidly appeared[17]. There were huge gains in function, at the cost of vulnerable low backs and low necks.

Symptoms can develop at any age, and are common in children, as "growing pains" in the lower body, head, neck and "shoulder" pains, and numb hands in the upper[18]. At this age the discs are normal, and the nucleus pulposus, like articular cartilage, has no nerve supply. The pain must arise from other structures, such as bone or attached ligaments. I go into this detail because it is clear that rheumatologists (and others) are not good at necks or backs, or the ambiguous meanings of regional pain, problems that can be resolved by a disciplined search for hidden sites of referred tenderness. Is "hip" or "knee" pain due to osteoarthritis, or referred from the back? This discussion relates to much more than FM.

The most surprising of the critical editorials was that by Dr. Wolfe[5]. The methods used in the Amish studies were very similar to those Wolfe had previously used, and the importance of the tender point criteria was strongly reinforced by the data reported in the 1990 Criteria study[6]. This study was at that time unique, in that it was driven by data, appropriately gathered and appropriately analyzed for sensitivity and specificity, using control groups with pain rather than "normal" controls. Why did Dr. Wolfe disown his offspring? Because now he must do without tender point counts.

The arrival of a large number of biological and other new treatment agents has given rise to the need for an increasing number of double-blind studies, necessarily multicentric, as sample sizes must be very large to address issues of safety as well as efficacy. Hence the need for The National Data Bank for Rheumatic Diseases. Given his clinical and statistical expertise, plus his diligence and proven ability to work diplomatically with others, the choice of Dr. Wolfe as director was welcomed by all.

Research, like politics, is the art of the possible. Reliable tender point counts can be expensive in dollars and time, if one includes the costs of training new (preferably independent) assessors, of collecting and analyzing the data, and of responding clinically to the findings. In any case, many rheumatologists do not and will not include these assessments into their physical examination. Indeed, some of the editorialists in *The Journal* proudly make this refusal a matter of principle.

Dr. Wolfe has published a series of articles in which he developed a definition of FM that used data derived from questionnaires, not requiring physical assessments. So he cannot use the 1990 ACR Criteria. Instead, "operational criteria" to identify "fibromyalgia-like" patients among groups referred for clinical trials with an unqualified diagnosis by rheumatologists, of unresponsive rheumatoid arthritis (RA). From his own work, and that of many other investigators, he accepts that FM is common in patients with RA (and many other diseases), especially in those who are referred for research studies, because their pain and fatigue are not relieved by aggressive therapies for RA.

FM-like features concomitant with RA (RA/FM) were identified by a Regional Pain Score $\geq$ 8 and a visual analog scale fatigue score $\geq$ 6[19]. These cutoff points were developed from records on 11,866 patients with RA in The National Data Bank for Rheumatic Diseases, and identified 1731 patients with RA/FM who were very different from the other patients with RA.

How likely is it that the new criteria will be accepted for research use? This will depend on sensitivity and specificity

(among other things). We have relevant data from the 1990 Criteria study. Widespread pain (as defined then) was 97.6% sensitive, but only 30.9% specific. The controls had pain associated with neck, back, and regional pain problems, and a few had RA. Fatigue was 81.4% sensitive, 60.8% specific. Application of other criteria identified clinically similar groups, trading sensitivity for specificity.

How many of the FM-like subjects in the current study would have met 1990 Criteria for FM? More importantly, did they have "evidence of major mechanical problems in the lowest part of the lower cervical and lumbar spine, problems that have not been specifically identified and dealt with in the treatment program to date?" Should such patients be immunosuppressed? Can we do meaningful cost-benefit analyses of new treatments without prior recognition of those subjects at risk of being given a hazardous therapy because of incomplete or inaccurate diagnosis?

It might even work. The cytokines that participate in inflammatory or immune responses are often widely distributed in the nervous system (among others), where they act as intercellular messengers performing a great variety of functions. Tumor necrosis factor is one of these. It has been extensively studied in a model of chronic back pain, where it arises in glial cells[20,21]. The effects of etanercept have now been studied on many patients with RA, by rheumatologists, *who did not do tender point counts!* This concern has been expressed by others[22].

Many of my colleagues will not accept referrals of patients with FM. There are a number of reasons, relating to time, economics, and the need to concentrate their energies on patients liable to improve under their care, or who have conditions matching their research interests. This is understandable, but the blunt fact is that they are seeing such patients, and failing to recognize evidence of major mechanical problems in the lowest part of the lower cervical and lumbar spine, "problems which have not been specifically identified and dealt with in the treatment program to date."

In clinical research studies, patients should be pleased to participate, because the standards of assessment and care must be higher than in routine practice. But in very large scale studies, they may become objects, not subjects. Assessments may take place solely on the basis of uniform, brief questionnaires, suitable for computer input and analysis. The patient's uniqueness is unrecognized, or is a nuisance variable.

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