FIBROMYALGIA: THE ANSWER IS BLOWIN' IN THE WIND

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How many times can a man turn his head and pretend that he just doesn't see?
--Bob Dylan, 'Blowin' in the Wind'

These immortalized words have rung true repeatedly throughout the sordid history of humankind. Yet it should seem startling that Dylan's words might apply to physicians, who recite the Hippocratic Oath, and promise to ease pain and suffering and "do no harm." Nonetheless, these words too often do apply to physicians, perhaps no more frequently than when many such physicians are asked to deal with fibromyalgia (FM). For those unfortunate patients who suffer from FM, "Hippocratic" often rings more like "hypocritical." In desperation, patients turn to those learned in Medicine and professing to help them, only to hear their malady called — nothing at all: "an illusionary entity"(1), "a common non-entity"(2), "mass hysteria"(3),"the syndrome of feeling out of sorts"(4). Many in the medical profession have chastised FM, calling for "a return to common sense"(5) by discarding the label, and the concept, altogether. But why? And why are these comments so often laced with venom? Why are those who oppose the FM concept so verbal and destructive, many going out of their way to write position papers about an area in which they have done no research, and seem so oblivious and impervious to the research of others?

The answer lies far beyond a lack of acceptance of a poorly understood and poorly treated entity. We have little understanding of disease mechanisms for many well accepted disorders, such as polymyalgia rheumatica, migraine headache, and trigeminal neuralgia. And we have very few effective treatments for disorders such as scleroderma and ankylosing spondylitis. Yet none of these disorders comes under the same intensely zealous scrutiny as FM.

What is it about FM that provokes such ire? It should not be that FM symptoms all are subjective — all symptoms are, by definition, subjective(6,7), irrespective of their setting. Whether caused by FM or cancer, tendonitis or ischemic heart disease, symptoms such as pain, fatigue, nausea, and dizziness cannot be measured objectively. We must rely on patient reports, then choose to believe them, or not.

Some have used objective evidence of tissue pathology, such as gross swelling or radiographic changes, as an objective proxy for pain; the corollary to this is that they believe that the absence of objectively measurable tissue pathology is an argument against the presence of "true pain." However, both halves of this reasoning are flawed. Medical practice abounds with disorders in which the degree of pain and degree of objective tissue pathology do not correlate: headache, migraine headache, trigeminal neuralgia, phantom limb pain, kidney stones, and the Charcot joint. We cannot and should not fool ourselves into believing that we can estimate another individual's pain. One day, technology capable of measuring the pain of others will exist, but it does not exist — at least for use in clinical practice — at the time of this writing. We all will have to wait.

No one can reasonably justify the zealous anti-FM movement by arguing that there are no objective physical findings among FM patients. First of all, there are many well accepted disorders that lack objective physical findings. The same physicians who have such difficulty understanding and accepting FM have no problems at all injecting or operating on patients with de Quervain's tenosynovitis, medial and lateral epicondylitis, rotator cuff tendonitis, and greater trochanteric bursitis, despite the utter absence of any ‘objective’ physical findings in any of these conditions. Tenderness, certainly, cannot be considered ‘objective’. And yet, it is one of the mainstays of physical examination, be it of the teeth, the abdomen, the muscles, the joints, or elsewhere. Moreover, should we be any less believing when we identify tenderness on examination, than we should be when we identify alterations in sensation, cognition, or strength? Again, we badger our medical students on the importance of examining for all of these. Why? Why, indeed, if these ‘non-objective’ findings are not fit to be believed anyway?

Many FM patients do have measurable alterations in skin tissue compliance and reactive hyperemia, findings that are measurable and objective(8). FM naysayers pay no attention to this, perhaps claiming that these are non-specific findings that, further, many patients with FM do not have. And yet I have observed the same physicians enthusiastically gather around them a horde of medical students to demonstrate livedo reticularis as a sign of systemic lupus erythematosus (SLE).

The acidic reaction towards FM cannot be justified by arguing that there are no pathophysiologic changes in FM patients. To begin with, for years there has been a large and rapidly expanding body of scientific evidence demonstrating numerous pathophysiologic differences between FM patients and healthy controls. As early as the late 1970s, Moldofsky was reporting alterations in brain wave activity in Stage IV sleep, alterations found in other chronic pain states but not in dysthymia(9). These findings have been replicated many times over, and most recent research has found that alpha wave intrusion into Stage IV sleep is predictive of symptom severity(10). How possibly could FM research subjects manipulate these results? The answer is that they could not.

For more than 10 years, we have known of various hormonal and other biochemical changes such as abnormal diurnal variations in corticosteroid secretion(11), low serum concentrations of somatomedin-C(12) and tryptophan(13), low cerebrospinal fluid (CSF) levels of 5-hydroxytryptophan(14), and high CSF levels of substance P(15). More recent research has provided a potential explanation for some of these findings, including reduced serum activity of prolylendopeptidase (a cytosolic endopeptidase responsible for the inactivation of a variety of algesic peptides, including substance P)(16).

Thermographically measured skin temperature appears to be lower in the back(17) and higher in the hands(18) in FM patients compared to healthy controls, implying some alteration in normal dermal sympathetic activity in FM. More recent research has shown

further evidence of altered autonomic nerve function in response to orthostatic stress(19).

Two small recent studies suggest an alteration in the pattern of cerebral blood flow(20,21), which may help to explain the debilitating fatigue and cognitive difficulties described by these patients. The list of scientifically demonstrated physiologic abnormalities in FM patients goes on and on. Detailing them all is far beyond the scope of this editorial. Nonetheless, this research exists and no critic should verbalize his or her opinions without performing an educated and unbiased review of it. Through all this research, FM has become the prototype chronic, systemic pain disorder, much the way that SLE is the prototype chronic, systemic autoimmune disorder. Scientists who accept that we have much to learn about pain have learned much, much of this knowledge coming from studying FM. Such knowledge has been attained by reaching beyond the over-simplistic, grossly anatomic view of the world to which so many of us seem confined.

Some argue that these pathophysiologic irregularities are not specific for FM. But this, also, is not a valid argument against the acceptance of FM. If it were, we would be forced to question the validity of an almost endless number of otherwise well-accepted disorders for which all pathophysiologic changes are non-specific. Foremost among these would be SLE. The positive predictive value of the detection of antinuclear antibodies (ANA) is no greater than one percent, which makes the testing for ANA 50 times less predictive than the flip of a coin. In addition, not one of the many other pathophysiologic abnormalities of SLE is specific to SLE. Does SLE not exist? How about rheumatoid arthritis (RA)? Polymyalgia rheumatica (PMR)? The list goes on.

Claiming that FM is psychological is no defence either. When are we going to finally discard the outdated concept that psychological and physical illnesses are opposites? A huge body of research tells us that psychological and physical ill health move in tandem. What chronic illness does not affect us psychologically? Are newly diagnosed cancer patients not psychologically distraught? What about recent stroke victims? Does

this make cancer and stroke psychological diseases? Of course not. The reality is that chronic physical illness begets chronic psychological distress, and vice versa. Numerous research studies have demonstrated alterations in physiologic function including immune response in those who are depressed(22-25). The dramatic increase in mortality in the year following the death of a spouse(26-28) is poignant evidence that psychological distress affects us physically. This is all part of the biopsychosocial understanding of illness, a concept that is far better supported by current research than the biomedical model so many of us were taught in medical school. Moreover, so-called *psychological disorders* are not without physiologic changes. Physiologic changes have been identified in and pharmacologic treatments justified for numerous psychiatric diagnoses including schizophrenia, major depression, bipolar disorder, obsessive-compulsive disorder, and attention deficit hyperactivity disorder, to name a few. As such, the distinction between physical and psychological illness becomes increasingly meaningless. The distinction between a physical symptom and a psychological one becomes more blurred. What is important is that all such patients are in distress, and that physicians can help (or hinder) if they so choose.

The callous disregard exhibited by some health care professionals (and others) for FM also is not defendable by arguing that the FM label is a distinctly poor one, although it is true that the FM label may be flawed. The tautologic (round-about) method by which FM was defined in 1990(29) (collecting a group of individuals believed to have FM and then looking for characteristics that distinguish them from those believed not to have FM) is the same scientific method that has been used to develop classification criteria for every other disorder (including SLE and RA) for which they exist. What other method might be employed in the absence of a gold standard confirmatory test? And what possible justification could there be to develop classification criteria for a disorder in which a gold standard confirmatory test already exists? The answer to both of these questions: there is none. The FM label, like those of SLE, RA, and many other disorders, may be tenuous. But that may just be the nature of the diagnostic labelling process itself.

The claim in medicine that we have 999 diseases is a myth. The truth is that we have 999 labels. Some of these labels, such as pneumococcal pneumonia or gout, work very well. FM, SLE, RA, PMR, and many other disorders that fall under the rheumatic disease umbrella are not well labelled. Nonetheless, these labels do serve many purposes. Certainly, there is very little discussion about discarding the SLE label, or the RA label, or the PMR label. Why must we discard the FM label? Despite arguments to the contrary, there is no evidence that the FM label is any more or less useful than those of SLE and RA.

The most oft-used argument has been that the FM label is harmful by creating illness behavior and disability, causing individuals to take on a ‘sick role’ and behave as if they are ill(19,28,30,31). But this argument is flawed at both ends. First, as has been shown repeatedly in controlled studies of FM patients versus controls, these people are ill. As stated earlier, the FM cohort differs physiologically from the normal population, in many instances in a physiologically predictable way. One would expect individuals reporting high levels of pain to have higher levels of neurotransmitter pain agonists in CSF, and FM patients do(15). One would expect individuals reporting non-restorative sleep to have electrophysiologic alterations in deep sleep, and FM patients do(9). In fact, as stated earlier, the number of alpha wave intrusions in Stage IV sleep is highly correlated with daytime symptoms(10). Hence, this cohort of patients with symptoms of illness and pathophysiologic changes consistent with illness, irrespective of their specificity, must be considered ill. Can you truly tell an individual complaining of feeling hot and having a core temperature of 40°C (104^{o}F) that they are not ill because fever is not a specific finding?

And second, recently published research in a prospectively followed, representative community cohort of adults newly diagnosed with FM found that the FM label itself does not cause worsened future outcome(32). These individuals did not act more ill. They actually reported fewer symptoms over time. They did not use more health services. And the majority continued working. Hence, the FM label is flawed, admittedly. But it

does not stand out in this regard. Numerous other diagnostic labels, such as SLE and RA, are equally flawed. Should they be discarded as well?

Perhaps the most volatile concept inducing venomous responses against FM is that of disability. This issue has not only medical, but also strong medicolegal implications. Some have argued that the only reason that FM exists is that an overly generous compensation system is in place that is ripe for the picking by individuals who claim to be too ill to work. (It takes no imagination at all to see how this anti-FM agenda might be pushed aggressively by those health care providers among us whose incomes come largely from performing independent medical evaluations for insurance companies.) However, evidence now exists to rebut even this contention.

The recently published study in which FM was found to be even more prevalent among Amish than non-Amish populations should serve as an antidote against such venom. Moreover, the finding of FM in the Amish should not be considered surprising. Previously published general representative (randomized) population studies have demonstrated FM to be more common in countries in which compensation availability might be expected to be less (for example, Pakistan(33), Poland(34), and South Africa(35)) than in countries in which compensation availability might be expected to be greater (Sweden(36), Denmark(37), and Finland(38)). Nonetheless, the venomous attacks continue(39,40). One author even insinuates that the motives of the Amish study investigators were purely political, and hence the results might somehow have been manipulated(41). And yet, the same author seems to take no exception to the endless armchair philosophizing of so many who have claimed, while making no attempt to gather any evidence to support their contentions, that FM is a compensation-driven illness.

Why? Why is FM unrelentingly held up to a level of scrutiny to which no other musculoskeletal disorder is held? Some authors, such as Ehrlich, Hadler, and A.S. Russell (42) (n*ot to be confused with I.J. Russell, who has contributed greatly to our current understanding of FM through thoughtful, innovative research*.) seem to have

made a career out of writing opinion papers chastising FM, while publishing virtually no research at all to support any of their claims. Why? Why do those who belittle the concept of FM offer virtually nothing more of an argument than their own feeble versions of ‘common sense’, while repeatedly ignoring a huge and ever-growing body of evidence supporting its legitimacy?

I cannot answer for those who choose to utilize their positions of influence in this way. Nor can I answer for those who are much less verbal, but who choose to believe the armchair critics while exercising no effort to explore the research literature for themselves. But I believe that soon, the evidence supporting FM will become so insurmountable, so undeniable, that even the most violent FM-beaters will have to relent.

The answer is blowing in the wind and soon it will be felt. Technology ultimately will catch up with reality and will prove FM doubters wrong. We will be able to see and measure FM, in the clinical setting, just as relatively recent technological advances now allow us to measure hypothyroidism without goiter, and relapsing-remitting multiple sclerosis, two conditions whose pasts are not entirely unlike fibromyalgia's present. Hypothyroidism without goiter: how possibly could this have been diagnosed or conceptualized before we could test levels of thyroid function? These patients were just middle-aged, overweight, and lazy — or so it was thought. Relapsing-remitting multiple sclerosis: until the advent of magnetic resonance imaging and other technologies, these women were dismissed as being psychologically disturbed or malingerers, complaining of odd neurological symptoms like blindness and dizziness and drunken gait, yet appeared virtually neurologically intact on examination.

Let FM not be another tragic example of letting ill-informed, malicious logic derail conscientious, methodical attempts to gradually discover the truth. To quote Bob Dylan again:

"How many ears can one man have
before he can hear people cry?"

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