

# FMS Fact Sheet

## Syndrome Description

FMS is a chronic, body-wide pain disorder coupled with other symptoms, such as severe daytime fatigue, unrefreshed sleep (likely due to a number of sleep anomalies), irritable bowel, chronic headaches, morning stiffness, cognitive or memory impairments, reduced coordination and decreased physical endurance. The American College of Rheumatology published the diagnostic criteria for FMS in 1990.<sup>1</sup> This selection criteria was shown to be 88% accurate in identifying patients with this syndrome. Researchers have noted a significant overlap between FMS and chronic fatigue syndrome (CFS). A majority of these patients meet both the diagnostic criteria for FMS *and* the CDC criteria for CFS.<sup>2,3</sup> In fact, the American Association for CFS has elected to combine the two syndromes as part of their research education mission.

## Demographics

Research studies indicate that at least 2% of the general population are afflicted with FMS. This amounts to roughly five million Americans.<sup>4</sup> The majority of FMS patients are female, and symptoms may begin in young, school-aged children.<sup>5</sup> FMS is persistent and chronic. A longitudinal, multicenter study found that remissions of the symptoms of FMS are rare and the average health care cost per patient per year is close to \$2,300.<sup>6</sup> This same study indicated that the average FMS patient takes three different drugs daily in an attempt to control their symptoms, yet no single therapeutic agent was found to be effective in relieving the symptoms during the seven-year duration of the study (1989 to 1996).

## Disability Studies

Four reports have shown that FMS can be as disabling as rheumatoid arthritis(RA).<sup>7</sup> RA is listed in the Social Security Disability law book, and while FMS pain is acknowledged, the condition is not specifically listed. Due to the difficulties in gaining recognition for FMS as a disabling illness, the percentage of patients drawing SSD payments based on FMS is only 16.2%.<sup>8</sup> Yet, nearly 30% of FMS patients claim that they cannot hold down a steady job due to this condition. The total yearly drain on the U.S. economy is estimated to be over \$20 billion. Preliminary findings indicate that the cancer risk is also doubled in people with FMS.<sup>9</sup>

## Research Findings

Pain is the predominant feature of FMS, but its cause is unknown. Significant abnormalities in the central and peripheral nervous systems have been uncovered in recent years and most researchers in the field consider FMS to be a central pain state (e.g., central sensitization). Substance P (SP) in the spinal fluid is three times that of normal healthy people.<sup>10</sup> Nerve growth factor (NGF) in the spinal fluid is four times that of healthy people.<sup>11</sup> Increased production of nitric oxide in the spinal fluid and the peripheral blood of FMS patients has also been found.<sup>12,13</sup> Pro-inflammatory cytokines are excessively produced in patients with FMS, pointing to an immune system Th1/Th2 axis disruption.<sup>14,15,16,17</sup> The 2003 study by Ali Gur *et al.* demonstrated that the cytokine elevations correlated with abnormalities in brain blood flow based on SPECT scan analysis. Gur's 2002 study showed that elevated IL-8 levels corresponded with pain intensity. It is proposed that pro-inflammatory cytokines produced by activated glial cells within the central nervous system may play an aetiopathogenetic role in FMS. Indeed IL-8 has been implicated in a genetic profiling study using micro-arrays in patients meeting the CFS criteria.<sup>18</sup>

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Although the findings of elevated SP and NGF are substantial, recent research by the author of the NGF finding (Alice Larson, Ph.D.) clearly indicates that elevated SP and NGF are not at the heart of the etiology of FMS.<sup>19</sup> In fact, NK<sub>1</sub> receptor antagonists are only likely to help FMS patients when they are co-administered with an opioid and noradrenaline (whose metabolite is abnormally low in the spinal fluid of FMS patients – and the same holds true for serotonin and dopamine).<sup>20,21</sup> Other significant abnormalities in FMS patients include: (1) sleep disorder<sup>22</sup>, (2) autonomic nervous system dysfunction<sup>23</sup>, (3) elevated activity of CRH neurons which is believed to cause disruption of many hormonal axes including the HPA-axis<sup>24,25</sup>, (4) impaired brain blood flow to the thalamus and other pain-processing centers<sup>26,27,28</sup>, (5) substantially reduced production of growth hormone overall, and additional blunting of growth hormone during exercise<sup>29,30</sup>, (6) abnormal windup (or temporal summation) at rest and significantly exacerbated windup during exercise, which may explain the exercise intolerance that FMS patients exhibit<sup>31,32</sup>, and (7) failure of the diffuse noxious inhibitory control (DNIC or spatial summation) to respond to a painful stimulus.<sup>33,34</sup>

### Current Status of FMS-related Research Spending by NIH

Most FMS research at NIH is sponsored by NIAMS (National Institute of Arthritis, Musculoskeletal and Skin diseases). The 1997 FMS research funding level at NIAMS measured out to only 0.6% of their annual budget of \$257 million ... not much for the second most common rheumatic disease.<sup>35</sup> That same year, however, NIH created a Special Emphasis Panel (SEP) specifically for the review of FMS research grant applications, and this continues to lead to increased funding for the condition. In 1999, the National Institute of Neurological Diseases and Stroke (NINDS) and the Department of Defense (because of overlapping conditions such as Gulf War Illness) became involved in funding research on FMS as well. While the increase in research funding on FMS is encouraging, the NIH-funded research projects are, for the most part, still not focused on the patient-relevant issue of providing improved therapy options. A review of the NIH online CRISP system abstracts confirms that less than 10% of government sponsored research on FMS pertains to therapeutic interventions.<sup>36</sup> However, the combined NIH and DoD expenditures on FMS-related research are estimated to be roughly \$7 million annually.

### Recent Therapeutic Success

At the October 2002 American College of Rheumatology (ACR) meeting, several researchers presented successful treatment trials in FMS patients. In particular, a multicenter pregabalin study demonstrated that FMS is a condition that can be evaluated and that clinical improvement is possible.<sup>37</sup> Single bolus doses of fentanyl and dextromethorphan (tested individually) were documented to show clinical improvement and were also capable of substantially reducing windup in people with FMS.<sup>34,38</sup> However, highly effective therapies that specifically target the central pain state in FMS patients are in high demand. Human growth hormone, a therapy that targets problems in the peripheral tissues, was shown in a 9-month trial to be helpful in reducing muscular pain and relieving problems of exercise intolerance.<sup>39</sup> A novel immune modulation Staphylococcal vaccine-type therapy to target the cytokines in the periphery has also shown effectiveness.<sup>40</sup> Sodium Oxybate (a compounded version of the natural brain chemical gamma-hydroxybutyrate) has been tested in a placebo controlled crossover trial involving 17 overnight sleep tests for each of the 20 FMS participants and showed amazing results.<sup>41</sup> It produced significant increases in slow-wave sleep, decreased alpha-wave intrusion, decreased pain, and is suspected to also increase growth hormone secretion during sleep. The high prevalence, disability rate and health care costs associated with FMS should be motive enough to encourage the pharmaceutical industry to become involved in developing effective therapies for this condition.

## AFSA

The American Fibromyalgia Syndrome Association (**AFSA**) is in its ninth year, and has funded 23 research projects. **AFSA** has raised over one million dollars in patient-related contributions and over 90% goes to our research-funding mission. In addition to independent projects, **AFSA** also funds tag-on, or collaborative studies, with NIH as well as pharmaceutical companies, in its primary focus to look at patient relevant pharmacologic interventions. For a description of projects funded thus far, as well as an outline of **AFSA**'s research priorities, visit [www.afsafund.org](http://www.afsafund.org).

## Fibromyalgia Network

*The Fibromyalgia Network*, a patient self-help organization, has been in existence since 1988. *The Network* publishes a quarterly Journal, and provides educational materials to physicians and patients throughout the United States, as well as other countries. With a substantial base of patient members, support group leaders, and health care providers, *The Network* is in a unique position to aid researchers with patient recruitment for studies and has performed such services free-of-charge over the past several years. Its Web site is: [www.fmnetnews.com](http://www.fmnetnews.com).

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