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FIBROMYALGIA

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Upon learning they will be seeing a person diagnosed with fibromyalgia, many health care professionals feel like running out of their offices screaming. It's no wonder. There are many possible symptoms and patients are very complex and time-consuming. Some people respond to some therapies but not others that get responses from other people. Fibromyalgia is not a specific disease but a collection of symptoms, many that vary from person to person—thus it is referred to as fibromyalgia syndrome (**FMS**). Thankfully, research has, over the years, created a somewhat clearer picture of the underlying determinants and potential therapies that can help.

FMS is more common than rheumatoid arthritis. It affects 3% to 5% of North Americans, women far more than men (although men and children can have the disorder). Incidence increases with age; in women aged 55 to 64, it may be as high as 8%. [1] Fibromyalgia literally means "pain in the fiber of the muscles." After 1990, when fibromyalgia was medically recognized, a diagnosis was made by exam and history with a required 11 out of 18 tender points found positive. In 2010 the American College of Rheumatology developed new criteria. Instead of specific tender points, diagnosis is made by the Widespread Pain Index (score >7), a Symptom Severity Scale (score ≥5), the presence of symptoms for at least 3 months, and ruling out other disorders that would otherwise explain the pain. The new criteria recognize that FMS is more than just body pain. [2] There is no lab test for FMS. The idea that it is hereditary has been considered but remains largely unsupported. [3,4] Prominent symptoms include widespread chronic musculoskeletal pain and aching, local tenderness, disturbed sleep patterns, morning stiffness and fatigue. Other symptoms differ among individuals and are often similar to other conditions such as chronic fatigue syndrome (CFS), thyroid insufficiency, rheumatoid arthritis, adrenal fatigue, systemic lupus erythematosus, ankylosing spondylitis and more—all without clear-cut (laboratory, clinical) diagnostic evidence. There is frequently depression and/or anxiety, palpitations, poor concentration and memory. Sleep disturbances involve trouble falling asleep and staying asleep, but circadian rhythm is normal. Research shows that the basic causes of FMS include dysfunctions in the central **nervous** system, **endocrine** system and **immune** system. Russell Jaffe, MD, describes these disturbances including loss of immune tolerance induced by irritants specific for the individual rather than the condition (reactions that reflect high sensitivity to specific substances). There is also evidence of **mitochondrial** dysfunction. The mitochondria produce ATP (adenosine triphosphate), the body's main storage form of energy, as well as FADH (flavin adenine dinucleotide) and NADH (nicotinamide adenine dinucleotide), other energy producers. Inadequate energy stores due to mitochondrial dysfunction cause muscle shortening and pain that is worsened by loss of deep sleep. [3,4,5] Many substances, toxins and individual intolerances can affect mitochondria. For example, high-fructose corn syrup can deplete hepatic ATP and could reduce muscular levels as well. [7]

People with FMS can suffer from headaches, depression, paresthesias, bowel and bladder disturbances (such as irritable bowel syndrome and irritable bladder syndrome), Raynaud's phenomenon, variable soft tissue swelling, and less often, rhinitis, bruxism, bursitis, sciatica, temporal mandibular joint (TMJ) dysfunction, and respiratory allergies. Most report that stress, anxiety, poor sleep, extremes of humidity, cold, warmth, and weather changes significantly worsen their symptoms. [8] Some years ago, scientists believed there was a large inflammatory component to fibromyalgia. But research showed that levels of well-recognized inflammatory markers are not elevated. It is now recognized that the pain is **neuropathic**—a problem with the pain-sensing nerves. The source is in the central nervous system rather than in the periphery. There are actual physical changes in the structure of such areas as the frontal, motor, and cingulate cortices of the brain. [8,9] About half of people with FMS report that there was an event in their lives after which their symptoms came on or worsened. A traumatic event, injury, illness, surgery, assault, difficult childbirth or a repeated musculoskeletal injury are among the triggers. However, there is no precipitating event for the other half of those with FMS. Indications are that chronic stress is the cause in these people. [5,6]

Endocrine/ hormonal imbalances include the pituitary (growth hormone which, in adults, regulates repair and maintenance of muscle), adrenal (stress hormones, cortisol, DHEA), thyroid (T_3, T_4), leptin (hormone released

by fat cells to signal satiety) and ghrelin (peptide secreted by the stomach that stimulates appetite). [3] DHEA (dihydroepiandrosterone) is a precursor of the gonadal hormones testosterone and estrogen which can be lowered in FMS patients. [11,12] Generally there is no clear, obvious evidence of one particular disorder; rather there are subclinical, subtle indications of disturbance. Salivary but not serum cortisol may be low, for instance. Dr John Lowe contends that there is a difference between hypothyroidism and thyroid hormone resistance. In the latter (which he says occurs in FMS), thyroid hormone levels within normal cannot adequately maintain proper metabolism. [13] A number of studies showed an impaired ability to properly activate the hypothalamic-pituitary-adrenal (**HPA**) axis. [14-19] Many common FMS symptoms, including widespread muscle pain, achiness, fatigue, poor sleep, depression and gastrointestinal problems, regularly occur in people with neuroendocrine disorders including those manifested by HPA dysfunction. [20] Some researchers believe that suppression of the HPA axis (likely from chronic stress) which results in lowering hormones (such as cortisol, DHEA, human growth hormone, thyroid hormones and others) is aggravated by the chronic pain and poor sleep of FMS—a vicious cycle. [7,21-23] Yet standard laboratory testing aimed at identifying a single hormone deficiency caused by gland failure is not reliable in FMS; there are only subclinical imbalances. Some people have moderate adrenal fatigue and/or borderline subclinical hypothyroidism, usually with normal blood cortisol and TSH. [24,25] The **hypothalamus** appears to be most involved. It produces hormones that signal the pituitary which, in turn, releases hormones that signal the adrenals, thyroid, and ovaries or testes. "Dysfunction of hormonal, sleep, and autonomic control (all centered in the hypothalamus) and energy production centers can explain the large number of symptoms and why most patients have a similar set of complaints." [5] The hypothalamus regulates body temperature, emotions, water balance and appetite. It is a chief region for integration of parasympathetic and sympathetic nervous system activities; it receives and transmits messages from the nervous system and hormones. The hypothalamus helps to regulate:

- Blood pressure—often low in those with FMS
- Digestion—bloating, gas, indigestion, and reflux are common in FMS
- Circadian rhythms (sleep/wake cycle)—consistently disrupted in FMS
- Sex drive—low of libido is a common complaint for people with FMS
- Body temperature—often low in FMS
- Balance and coordination—people with FMS have balance and coordination problems
- Heart rate—mitral valve prolapse (MVP) and heart arrhythmias are a common finding in FMS
- Sweating—it is not unusual for people with FMS to experience excessive sweating
- Adrenal hormones—tendency to be on the low side in FMS patients
- Thyroid hormones and metabolism—often subclinically under-functioning in people with FMS. [4,5]

With a disturbance in HPA axis function, numerous symptoms from neurological and hormonal disruption can occur. One effect is depletion of stress-coping biochemicals including **serotonin**. A reduction in serotonin causes an increase in substance P, a peptide that can enhance pain receptors, creating more pain. Poor sleep and chronic stress can lead to fatigue, weakness, mood disorders, irritable bowel, adrenal fatigue, decreased DHEA, lowered immune function, thyroid dysfunction, and lowered resistance to stress. [26] Chronic stress is an "underlying catalyst for the onset of HPA dysfunction and fibromyalgia," as demonstrated in several studies. [22,23,26,27] Immune system dysfunction can increase susceptibility to insult or injury (such as sinusitis), parasites, Candida overgrowth, and the like. It is important to support a healthy microorganism system in the gut. [5] People with "classic" FMS have lower levels of serotonin, **norepinephrine** and **dopamine**. Drugs that increase both norepinephrine and serotonin (SNRIs, serotonin-norepinephrine reuptake inhibitors) seem to have greater pain-relieving benefit than selective serotonin reuptake inhibitors (SSRIs) alone. Use of drugs such as Lyrica™ and Neurontin™ decrease pain by stimulating production of GABA-like substances that function as inhibitory neurotransmitters. There are often lower levels of serum tryptophan, somatomedin-C and other serum amino acids related to neurotransmitters that inhibit neuronal excitation.

People with FMS have lower pain thresholds than normal. Stimuli that should **not** be painful—even tickling or light touch—are felt as extremely painful due to hypersensitivity of the nervous system. [7] Brain cells become more excitable, exaggerating and prolonging the pain sensation. This over-amplification of pain is referred to as 'central sensitization.' [22, 23] At first FMS was thought to be a psychological problem but that notion was ruled out by several studies. Any anxiety or depression experienced is secondary to the illness. [22,28] A 2010 study showed that brain activity in people with FMS differs from that in healthy controls. Cognitive dysfunction

relating to attention and working memory is common. There is increased connectivity between brain regions "known to process evoked pain..." There are elevated concentrations of the excitatory neurotransmitter glutamate that correlate to self-reported pain levels. [29,30] There is altered blood flow in specific areas of the brain. [10] So far, no real defects in muscle have been found. Yet the physical fitness levels of people with FMS, including aerobic capacity and muscle strength, are extremely low. The immunologic load and immune system integrity are involved but need more study. [4] But FMS is **not** "autoimmune" or an inflammatory disorder.

WHAT CAN HELP? No single treatment is right for every person. Successful treatment involves a combination of lifestyle measures and other therapies. Assistance to restore adequate energy production, nerve health and endocrine function through nutrition, sleep support, and elimination of stressors (situational, chemical, toxic, food intolerances, etc.) allow muscles to release, pain to resolve, fatigue to abate, mood to improve, deep sleep to be restored, and a sense of wellbeing to return. Medical doctors tend to use **drug** therapy. Three drugs are FDA approved to treat FMS: **1**. Lyrica, an anticonvulsant that alters neurotransmitter levels to improve pain and sleep. Side effects include dizziness, drowsiness, weight gain, fever, swollen hands and lower legs, vision changes, confusion, concentration difficulties, muscle pain and weakness. **2**. Cymbalta, a SSNRI to treat depression, anxiety and chronic nerve pain. A few of the side effects are muscle stiffness, agitation, headaches, fatigue, memory problems. **3**. Savella, similar to Cymbalta but approved only for FMS. Studies on Savella alone found no statistically significant improvement in pain. There was some relief only after it was taken for three months. The European Medicines Agency determined that Savella is ineffective and unsafe and turned down approval for it as well as Lyrica to treat FMS. Doctors also prescribe pain relievers like acetaminophen, other antidepressants, sleep medications, muscle relaxants, anti-anxiety agents, and others—with limited benefits. Non-steroidal anti-inflammatory drugs, aspirin, corticosteroids and opioids are ineffective. [4,7,31-34] Drugs are **not** a solution; they may only mask symptoms for a while. Chronic use increases risk of serious side effects. Underlying causes should be approached. Alternative therapies include:

Stress reduction and relaxation techniques geared to individual circumstances and preferences. Stress and pain go hand in hand. Fear of pain itself is stressful and chronic pain amplifies stressors.

Reduction of reactant loads. Elimination trials help people with FMS who are often highly sensitive to toxins, medications, many supplements (particularly those containing isolated or synthetic ingredients), altered or processed nonfoods, additives and some foods. Since these people may be taking multiple medications—some for 'treating' side effects of others—they present a challenge. Drug reactions can block the benefits of elimination of other toxins and intolerances. If the individual decides to discontinue medications, it should be done (with a MDs' supervision) slowly, one at a time, to ease withdrawal effects. **Food intolerances** are determined by an individualized elimination diet. Foods rarely found to be a problem for most people may be problems for the person with FMS. A flare-up of symptoms may be experienced in the early days of elimination due to withdrawal, but usually fade by the seventh day. Toxic inhalant triggers—at home and the workplace—should also be discovered since they can interfere with the results of an elimination diet. [35] When **reactive** foods were removed from the diet of people with FMS and a program begun to support nerve, endocrine, immune and digestive systems, remission of symptoms was greater than 85%. This approach continues to show promise in 10-plus-year follow ups. Sustained remissions are observed in over 80% of cases of "intractable" FMS. [4] Food intolerances involve a disturbed condition of the digestive tract that affects nervous, hormonal and immune systems. (A number of neurotransmitters are produced or found in the digestive tract including 90-95% of serotonin.) Avoiding reactive foods for a period of time while supporting the digestive tract, nervous system, hormonal balance and immune function usually results in the capacity to reintroduce most or all foods that caused reactions. Exposure to herbicides, pesticides, petroleum products, heavy metals and other **toxins** can damage or disrupt mitochondrial DNA, nerve tissues, hormones, immune function and other areas. Heavy metal excretion has been found in patients with FMS. Elevated urinary levels of mercury, arsenic and cadmium are among findings linked to symptoms. [36] Since people with FMS tend to be sensitive to toxins, they should avoid fluoride, tap water (fluoride, chlorine, etc.), cigarettes and items such as high-fructose corn syrup, refined sugars, artificial chemical additives, commercial table salt and refined over-processed nonfoods. [25] A minority of people with FMS have Multiple Chemical Sensitivity which triggers attacks. A **detoxification** (purification) program is imperative as well as supplying more nutrients needed by the organs and tissues involved in detoxification. [35] The purification program can include freshly-made juices (vegetables—including

greens—plus apples). This supplies concentrated nutrients in an easily digestible form and aids detoxification. There are well-documented cases of people with FMS who significantly improved when they avoided aspartame (an artificial sweetener) and MSG (monosodium glutamate)—both of which stimulate pain receptors in the brain. In some cases, even minute doses of MSG and aspartame caused a full return of symptoms within 48 hours. Studies have found elevated levels of glutamate and aspartate (or their metabolites) in the cerebrospinal fluid of people with FMS. Aspartate is one of the two amino acids in aspartame. MSG and aspartate act as excitatory neurotransmitters and, when used in excess, can lead to neurotoxicity. [10, 37]

Dietary improvement. There is no one real 'fibromyalgia **diet**' although a number have been suggested. Since people with FMS differ and can have various food intolerances, a single diet cannot be recommended. [1] Two small studies suggest that a vegetarian or vegan diet may provide some relief. But this may be due to the avoidance of toxins that are higher in conventional animal-based foods. Or a vegan diet may eliminate many foods to which people with FMS are intolerant. There is also the possibility of a placebo effect in these two small studies. [38] The best course is avoidance of refined, over-processed, chemicalized nonfoods and consumption of real, whole natural, organically-raised foods (while avoiding individual reactant foods).

Support to the digestive tract. When healthy intestinal **bacteria** are balanced and the proper habitats are established, they expand and become "nutrient factories." They also produce compounds that can aid repair processes. [39] Some people with FMS have a 'sick' bacterial overgrowth in the small intestine. [10,40] Quality pre- and probiotics will usually help get rid of the unhealthy bacteria, although at the same time, support to the gut lining (real food, fresh juices, digestive aids, food supplements) is imperative.

Supplements. D-ribose is often used to increase energy levels. Mitochondrial energy molecules ATP, FADH and NADH are produced predominantly from D-ribose plus B vitamins. [5,41,42] Usually the body makes enough D-ribose. But people who have certain illnesses may have energy demands that exceed what their bodies can produce. [42-44] Should D-ribose be used as a supplement? It is not a nutrient. You can't get it from food. Rather, it is a type of sugar that the **body** makes for every cell **from** food. Supplemental D-ribose acts more as a drug which can cause imbalances and side effects such as stomach upset, nausea, diarrhea and headache; it makes some people sleepy and saps them of energy. It can lower blood sugar, so anyone with hypoglycemia or diabetes should avoid it. For those who can tolerate the supplement, energy levels, daytime sleepiness and brain fog improve within two or three days, occasionally within an hour. Such a rapid boost is a drug effect, **not** a nutritional effect. [45,46] Instead, it makes sense to consume foods and food supplements rich in nutrients required to make D-ribose—**B** vitamins, particularly riboflavin (vitamin $\mathbf{B_2}$), are essential for both mitochondrial energy production and nerve health. Food sources include eggs, milk products, vegetables, nuts, fish, meats.

People with FMS have reduced levels of Coenzyme Q10 (**CoQ10**, ubiquinone) in mononuclear blood cells and salivary cells but elevated levels in blood plasma—altered distribution. [47,48] Several studies reported that CoQ10 supplementation **reduced** FMS symptoms including pain, tender points, fatigue, morning tiredness and headache. [49] CoQ10 is made by the body and found in every cell to produce energy (ATP) for cell growth and maintenance. Highest concentrations are in the liver, heart, kidney, pancreas, muscle and brain. It is naturally present in small amounts in a wide variety of foods, but in larger amounts in organ meats such as heart, liver, and kidney as well as beef muscle, mackerel, sardines, sesame oil and peanuts. **Isolated** CoQ10 taken regularly as a supplement can cause loss of appetite, nausea, diarrhea, abdominal pain, heartburn, rashes, dizziness, irritability, insomnia, fatigue, headache and sensitivity to light. Elevated levels of liver enzymes have been found in people taking 300 mg per day for long periods of time. Thus, isolated CoQ10 behaves more like a drug, not like a food. Instead, it would be sensible to consume foods and food supplements high in CoQ10 and its associated nutrients. [50] **Carnitine** transports long-chain fatty acids **into** mitochrondria so they can be oxidized ('burned') to produce energy, and transports generated toxic compounds **out** of mitochorndria. It is concentrated in tissues like the liver, cardiac muscle and skeletal muscle that use fatty acids as a fuel. The liver and kidneys of healthy people produce sufficient amounts of carnitine from the amino acids lysine and methionine. But some people can't make enough. This can be due to a rare genetic disorder (manifest by age 5), but usually occurs due to certain disorders (such as chronic renal failure) or under particular conditions (such as the use of certain antibiotics) that reduce carnitine absorption or increase its excretion. Studies usually use the acetyl-L-carnitine form because it is better absorbed and more efficiently crosses the blood-

brain barrier. It can improve some symptoms such as fatigue. A study using 500 mg capsules and intramuscular injections showed some decline in musculoskeletal pain and tender points. This is another drug approach. Side effects include nausea, vomiting, abdominal cramps, diarrhea, and a fishy body odor. To obtain more nutritionally, the best food or food supplement sources are animal products like meat (generally, the redder the meat, the higher the carnitine), fish, poultry, and milk (primarily in the whey). [51, 52]

People with FMS have decreased **magnesium** (Mg) levels in white blood cells. It's thought that Mg deficiency in muscle cells may play a role in the development of FMS. Supplementing with high doses of Mg improves symptoms including the number and severity of tender points. Mg is a component of enzymes required for production of ATP and for release of energy from ATP. It is also a component of enzymes involved in muscle contraction and protein synthesis. Most people with FMS don't have low blood serum Mg levels; serum levels don't reflect tissue levels of Mg, so physical signs of deficiency should be noted. Using Mg as an isolated, non-food source in large amounts can cause imbalances including relative deficiencies of calcium, potassium and other nutrients, resulting in side effects—long-term use can cause headache, watery diarrhea, muscular pain and mild gastrointestinal symptoms. Some medications impair Mg absorption, decreasing its effects; they include allopurinol, phenothiazines, tetracycline, digoxin, penicillamine and iron salts. [53,54,55] Mg deficiency is associated with increased levels of substance P which is produced by the body in response to stress and increases susceptibility to pain. Mg can be obtained from foods such as vegetables (especially dark green, leafy types), nuts, seeds, legumes, fruit and some whole grains. **Malic acid** is important to ATP production and is found particularly in in fruits and especially in apples and pears. When malic acid levels are low, the body often shifts to an inefficient means of generating energy which can lead to muscle pain, achiness and fatigue. Minerals have long been used to overcome pain and fatigue. All **minerals** are important; supplementing with only one changes the balance of others. Food and food supplements are the best sources. [56,57]

An adequate intake of essential **fatty acids** from foods such as fish oil, flaxseed oil, evening primrose oil and vegetables is necessary for production of prostaglandins (unsaturated fatty acids) which support repair and improve mood. Omega-3 fatty acids improve brain and joint function and may help relieve pain. Low levels of vitamin **B_{12}** have been shown to worsen pain in people with FMS. Low B_{12} levels can also lead to fatigue and diminished cognitive function. People with FMS often have reduced levels of vitamins **A**, **C** and **E**. [56-58] Those with a vitamin **D** deficiency may experience some symptom improvement with supplementation. [59] **Iron** is essential for neurotransmitter synthesis; people with FMS have lower levels of several, including dopamine. Low-normal ferritin (iron-containing protein) levels are associated with restless leg syndrome, another disorder involving dopamine. Studies show decreased red blood cell volume in FMS. If the ratio of blood cell mass to blood volume is decreased, hematocrit will show up as normal despite anemia; B_{12} and folate may be needed. A small trial's positive results opens the possibility that iron supplementation may reduce FMS symptoms, though this preliminary. [5,60] **Niacinamide** may enhance mitochondrial function. [49] **Herbs** that may be helpful include licorice, rehmannia, Korean ginseng, ashwaganda, and eleuthero to improve the HPA axis response. Eleuthero and nettles are tonics for the nervous system and adrenal glands. St John's wort is thought to help repair an injured nervous system and may improve depression. Chamomile, skullcap, valerian, zizyphus and passionflower are muscle relaxants that soothe and calm the nervous system and may help improve sleep quality. Ginkgo biloba and ginger both help improve circulation, including that in the brain. Since ginkgo also has memory-boosting properties, it may assist brain fog. White willow bark contains natural salicylates that have pain-relieving effects for arthritis, so may also ease FMS pain. [61-63]

Exercise figures prominently in treating FMS. A number of studies show that low-intensity or graded aerobic exercise, resistance exercise, yoga, tai chi, qigong and similar activities help improve the pain, muscle tone, circulation, relaxation, sleep quality, psychological distress and physical performance. It is important not to overexert at the onset, but to slowly and gently increase exertion. Most people with FMS become physically inactive because they are terrified of pain; they become so deconditioned that tissue damage and the level of functioning deteriorate to the same degree. [64-68] **Obesity** increases a woman's risk of developing FMS by 64%. Irrespective of body weight, if a woman exercises at least four times a week, she is almost 30% less likely to develop FMS than a woman who does not exercise. A woman's risk of developing FMS due to being over-weight decreases by 27% if she exercises at least an hour a week. People with FMS often say that exercise is too painful, but it is critical to engage in some form of activity. Otherwise, the vicious cycle of pain, lack of

activity, weight gain, and more pain only picks up speed. [69] Researchers at the University of Utah found that 47% of FMS patients studied were obese and another 30% were overweight. The obese patients reported the greatest pain sensitivity, decreased physical strength and lower-body flexibility, and more sleep problems. Disturbed brain chemistry that affects feelings of hunger and fullness may also contribute. [70] It is imperative that a person with FMS stick to a healthy whole foods diet and engage in regular physical activity. Physical activity, especially if varied, improves strength, functionality, and pain. [71,72,73]

Other therapies. Therapies such as **chiropractic** treatment, **acupuncture** and **massage** can be useful for improving adherence to and maintaining participation in exercise programs. Further, they can help relieve pain, fatigue, anxiety and other symptoms. Acupuncture has been shown in many studies to improve symptoms. [74]

The following **supplements** are a suggested foundation. Any supplement containing an ingredient to which the person is intolerant should be eliminated. Support to other areas, depending on individual manifestations, can be added. For example: With adrenal symptoms add, with third meal: 2 Drenatrophin PMG and 3 Cataplex C; or with thyroid symptoms add, with third meal: 2 Thytrophin PMG, 2 Nutrimere; or with digestive problems, add, with two largest meals: 1 Zypan and/or 1 Multizyme; and so on. Supplementation begins after detoxification.

Just Before Two Meals:
1 Hypothalmex—hypothalamus support
3 Cataplex G—B complex with B_2
2 Cataplex B—B complex, iron
1 Neuroplex –CoQ10, B complex, HPA support

After Two Meals:
1 ProSynbiotic—pre- and probiotics
1 Cod Liver Oil—vitamins A & D, omega-3 fats
1 Chlorophyll Complex—A, E, Mg
1 SP Green Food—Mg, K, iron, other minerals

With One Meal: 2 Tablespoons Whey Pro Complete (mixed in liquid)—carnitine, other amino acids

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