Alternative Treatment of Fibromyalgia Using the Oxytocin -Hormonal-Nutrient Protocol to Increase Nitric Oxide

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Medical Perspective

FM and CFS are different diseases but closely related. Patients with these diseases have in common a decrease in corticotrophin releasing hormone (CRH) which controls cortisol output from the adrenals.[1-4] Both groups of patients have shown a decrease in levels of arginine vasopressin (AVP), a hormone that controls the ability of the body to release fluid.[1,2,5] With a lack of this hormone the patients would feel increasingly thirsty and have frequent urination — about every 20-30 minutes. Both of these hormones are produced in an area of the brain called the supraoptic nucleus. Another hormone of importance, called oxytocin (OT), is produced by the same nerve cells. The same neurons that make OT also have the capacity of making CRH and AVP.[6] As of September 2007, no one in the medical literature has described an OT deficiency. An attempt to define an OT deficiency will be done here. The vast majority of the medical literature has been written about the medical problems of FM. Hence the bulk of references referred to in this paper pertain to FM.

Oxytocin

OT is a hormone produced in many parts of the body. In the brain, it is produced and released on a daily rhythm with its peak in the human brain occurring at around noon.[7,8] OT is also produced in the posterior retina, in the pineal gland, thymus, pancreas, testicle, ovary, and adrenal glands. Oxytocin's known functions will be discussed later.

***Microcirculation*:** OT is known to be one of the controlling factors of the microcirculation of the human body and brain.[9-12] A decrease in OT can cause problems with decreased circulation in the extremities. Therefore, patients often complain of cold hands and feet, along with history of recurrent headaches. Oxytocins ability to vasodilate the blood vessels is due to its capacity to stimulate the body's cells to produce nitric oxide, a powerful vasodilator of the microcirculation.[9-11] If vasodilation, such as blushing, does not occur when OT is given intramuscularly to a patient, then a serious defect in nitric oxide production is present. This defect of poor circulation is often present among patients with FM patients.[13-15]

***Lactation and Libido*:** OT is released as a mother nurses her baby.[16] Stimulation of the hormone release causes the mother to have an instinct to want to cuddle. As she nurses the child, her desire to cuddle intensifies. This same feeling can be experienced during intimacy — OT has the ability to increase libido.[17,18] Therefore, patients lacking this hormone may often notice that they do not wish to cuddle, to be held, or to be intimate. It has been noticed that stress can restrain the production of OT.[19-25]

***Mental Function*:** OT seems to stimulate the ability of the brain to concentrate, contributes to mental alertness and improves memory. [26] Patients lacking this hormone may find difficulty in concentrating, and feel like they are thinking in a fog. This has been noted in FM.[27-29]

***Pain*:** OT can occupy multiple hormonal receptor sites in the body. My theory is that an empty receptor for OT can potentially cause pain. Administering OT causes the empty OT receptor sites to become full, thereby diminishing or completely obliterating pain. Animal studies reveal that because of this particular characteristic, OT has been an effective tool in weaning addicted animals from narcotics, suggesting that OT has the ability to occupy not only its own receptor sites, but opiate (narcotic) receptor sites as well.[30-36] Oxytocin has been given to humans to kill cancer pain, low back pain, and bowel pain from irritable bowel syndrome.[37-39]

***Vision*:** OT is produced in the posterior retina of the eye.[40] A decrease in OT level can cause problems with intermittent blurring of vision. When OT is given, it can sharpen the vision (clinical observation). In a patient with a reduced level of OT, one can expect complaints of pain in the posterior eye, sometimes so severe that only narcotics provide effective pain relief. Visual disturbances in FM have been observed.[41,42]

***Sleep*:** OT is made in the pineal gland of the brain, as is melatonin, a hormone which enhances sleep.[40,43] In animal studies, as the level of OT goes up in the brain, a deep sleep is induced.[43] (Insomnia is a sleep disorder frequently seen in patients with FM/CFIDS, and could indicate a deficiency in melatonin). It should be noted that recent research indicates that melatonin has the ability to activate the immune system, so the use of this product is usually contraindicated in the presence of autoimmune disease such as lupus, rheumatoid arthri-

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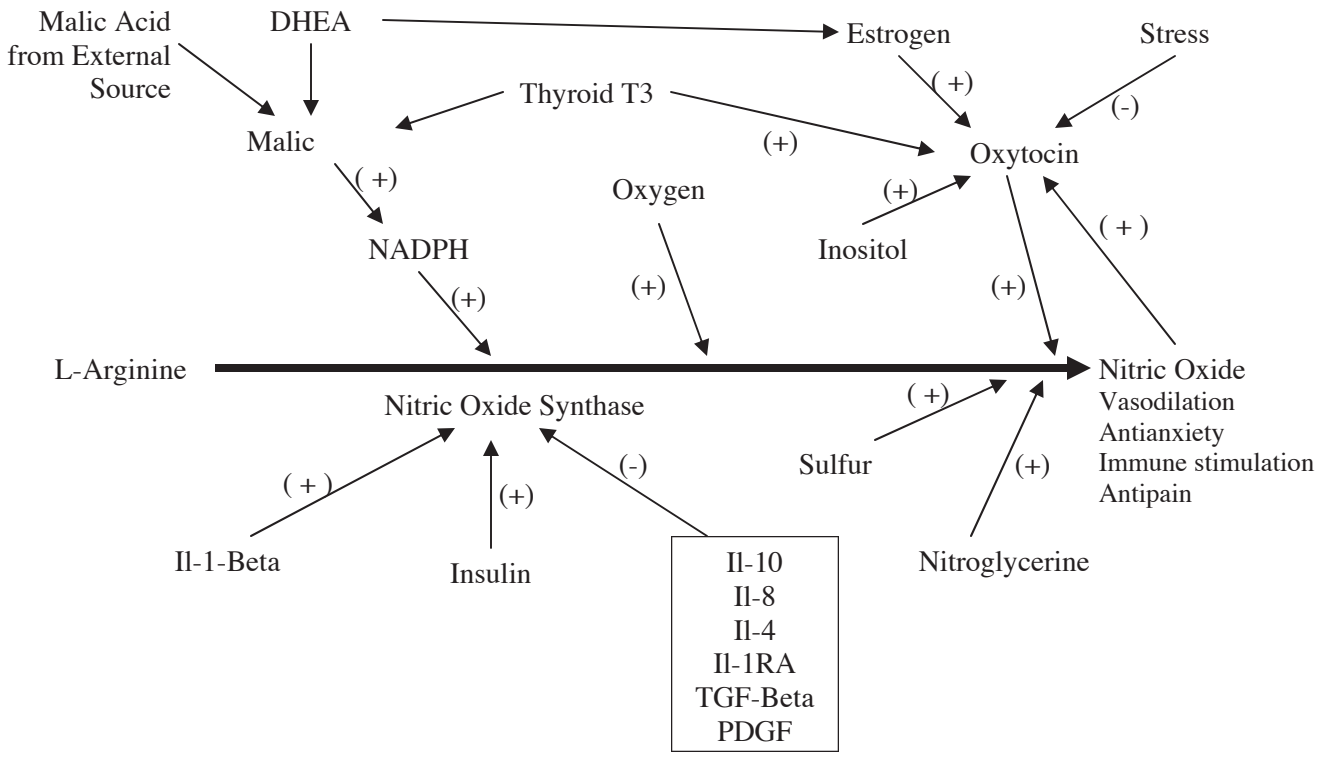
Figure 1

Factors Influencing Nitric Oxide Production



tis.[44]

***Ovary*:** The ovaries make OT[45,46] where it helps in the fine-tuning of progesterone release.[45] When patients lack OT, they may frequently complain of ovarian pain, even though pathology does not support the presence of either cysts or tumors. Ovulation function may be impaired with menstrual irregularity.[41]

***Adrenals*:** OT is synthesized in the adrenal glands where it can stimulate or inhibit steroid production.[21,47-50] Patients with a decreased OT level often complain of flank pain underneath the posterior ribs. Malfunction in the adrenal steroid production has been seen in FM.[51,52]

***Thymus*:** OT is created by the thymus gland[53,54] which utilizes OT to help process white blood cells that help control autoimmunity. Normal levels of OT also help stimulate these cells into greater action.[53-59] For example, it is a known fact that women who nurse their children have a greatly reduced incidence of breast cancer. This hormone may be protective in its ability to prevent breast cancer, through its influences on the immune system.[60]

***Pancreas and Bowel Function*:** OT is produced by the pancreas[61] where it is known to stimulate the production of glucagon, a hormone which helps the intestines to relax.[62,63] Therefore, in treating a patient with decreased levels of this hormone, one would expect to see problems with increased intestinal spasms, secondary to a lack of glucagon production from the pancreas.

***Anxiety and Depression*:** OT can function as an antianxiety agent in the brain. It can also stimulate social behavior.[64] A lack of this hormone may be expressed as antisocial behavior with some anxiety. OT can also function as an antidepressant.[65] In low levels of OT, one would expect to see depression, which has been noticed in FM/CFIDS.[28,66]

***Blood Pressure Control*:** OT can serve as a regulator of cardiovascular function and autonomic nervous system function.[67,68] This explains why patients lacking this hormone have trouble controlling their blood pressure when going from a sitting to upright position, or when standing for a long period of time. This is known as neurally mediated hypotension. They often complain of near syncope (light-headedness) and possible dizzi-

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ness.[41] OT is found in those sections of the brain where the baroreceptors of the body are controlled.[68] A drop in OT levels in the brain, leads to manifestation of baroreceptor malfunction. Restoration of OT through an oral tablet (Belmar Pharmacy) corrects the symptoms of neurally mediated hypotension (clinical observation).

***Body Fluid Control*:** OT has the capacity to induce the body to mildly retain fluid. This is in part due to its physical and biological similarity to arginine vasopressin.[11,69,70] AVP is a hormone that controls fluid metabolism, pain, and memory.[1,2,5,39,71-73] With a lack of OT, patients have increased thirst. They also have increased urinary output due to decreased ability to retain fluid.[41]

As can be seen, the actions and normal functions which have been associated with the use of OT are broad and varied. The following diagram (Chart 1) helps to illustrate and contrast the known functions of OT and other symptoms of FM, which are not commonly known in the regular medical literature.

Nitric Oxide

As research in FM continues, there is increasing evidence showing disruption of blood microcirculation in patients. This disruption of circulation has been seen in the brain and in the skin.[82-84] A major controller of circulation in the body is a gas called nitric oxide(NO).[85]

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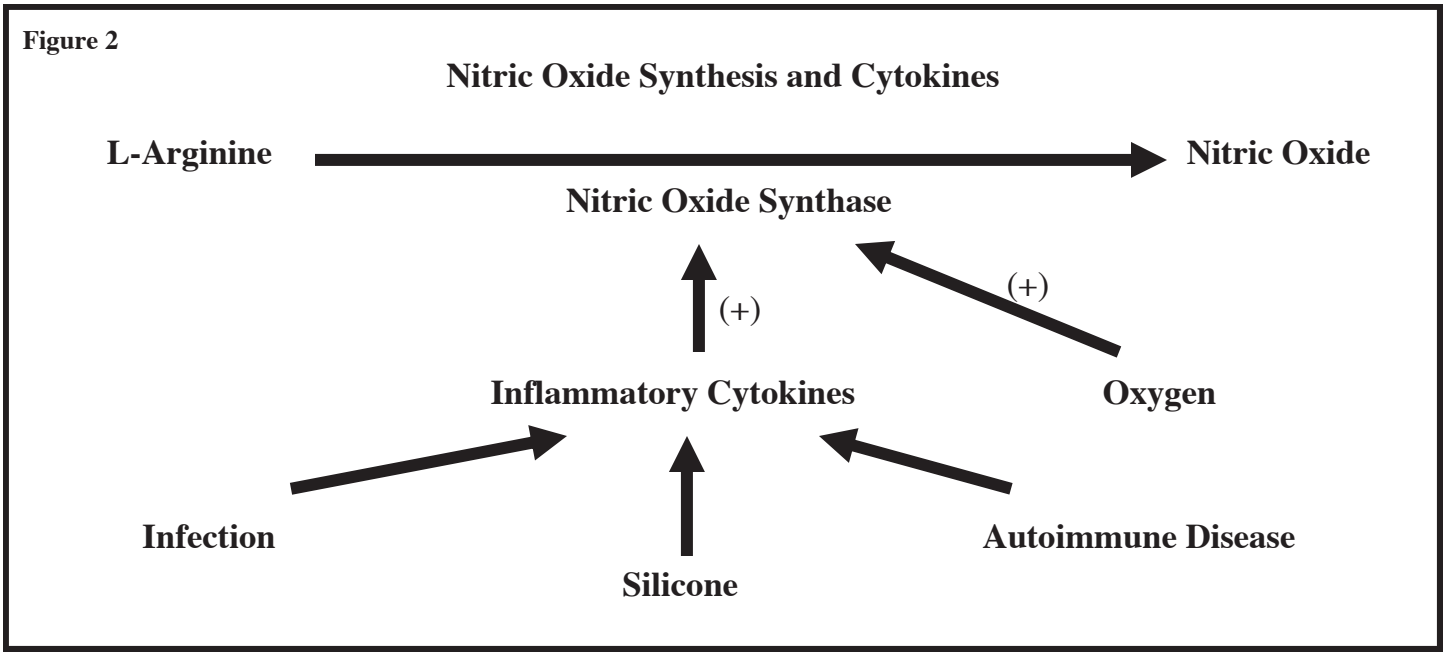
Chart 1

Contrasted List of Symptoms of Fibromyalgia and the Known Functions of Oxytocin[41,74-81]

Symptoms/Syndromes Associated with Fibromyalgia	Functions of Oxytocin
Cognitive difficulties: memory loss, decreased concentration, depression	Increases alertness, concentration, desire to cuddle
Headaches	Improves and restores memory
Numbness or tingling	Combats depression
Eye complaints	Promotes clear vision
Vestibular complaints: dizziness, vertigo	Stabilizes neurological control of blood pressure
Temporomandibular joint syndrome	Enahnces fluid retention
Esophageal dysmotility	Enhances sleep and relaxation
Mitral valve prolapse: heart palpitations, chest pain (non-cardiac)	Enhances microcirculation of hands, feet, and head
Lung symptoms	Helps to control pain in muscles and joints
Joint hypermobility	Stimulates or inhibits steroid production in the body
Irritable bowel syndrome	Helps bowels to relax
Painful menstruation	Increases thermogenesis (body warmth)
Interstitial cyctitis	Stimulates lactation
Vulvodynia: painful sexual intercourse	Stimulates labor in childbirth
Vestibulitis	Improves sperm function
Female urethral syndrome	Plays an important role in achieving orgasm
Multiple chemical hypersensitivity	Fine tune progesterone production from the ovary
Painful arches of feet	
Microcirculation disturbances: cold hands and feet	

Figure 2



When NO is deficient, there is a down regulation of the cardiovascular system.[85] Two research papers have been recently written documenting low levels of nitric oxide in patients with FM.[86,87] Nitric oxide is known to be produced in a 1:1 ratio with citrulline.[85] In FM, citrulline has been found low P=.028.[88] In FM, L-arginine is low normal P=.06.[89] Both L-arginine and citrulline point indirectly to the fact that nitric oxide may be a key factor in understanding FM.

NO helps to increase dopamine production, increase serotonin production, and decrease pain.[90-96] It also works as an anti-anxiety agent and improves sleep.[97,98] In FM there has been documented decreased serotonin, increased pain, increased anxiety, and decreased restful sleep.[99-106] Low levels of serotonin or dopamine have been associated with depression.

One of the main precursors for making NO is the amino acid L-arginine.[85] As mentioned before, this amino acid has been found at lower than normal levels in FM. L-arginine under the influence of an enzyme called nitric oxide synthase (NOS), can make NO.[85] NOS is also a dioxygensase. This implies that the enzyme is oxygen dependent for NO to be produced.[107] Oxytocin controls microcirculation via NO.[9-12] In the brain, oxytocin can be stimulated by NADPH-diaphorase, the identical enzyme as nitric oxide synthase, except found in certain neurons. This enzyme helps to convert arginine into nitric oxide. AVP is not stimulated by this enzyme. NADPH-diaphorase can be stimulated by nitroglycerin.[108]

Some factors are known to stimulate NOS. They are as follows:

- **Exercise —** Known to stimulate the enzyme,[107] exercise also helps FM patients to improve overall.[109]
- **Immune System Stimulation of NOS —** The inflammatory cytokines of the immune system are also known to stimulate production of NOS.[85] Theoretically, they can stimulate chronic activation of NOS by chronic infections, such as TB, gonorrhea, syphilis, etc. Inflammatory cytokines can also be activated by silicon such as seen in silicone breast implants or silicon implants in other locations in the body.[110-113] Inflammatory cytokines can also be elevated in the presence of autoimmune disease such as rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, etc. Theoretically, chronic activation of inflammatory cytokines can lead to substrate depletion and hence a breakdown of the system to produce NO.
- **Decreased Production of NOS —** Down regulating NOS can be accomplished by the use of glucocorticoids, such as cortisol.[114] This can also occur with interleukin 10 and TGF Beta, which are non-inflammatory cytokines of the immune system.[114]
- **Other Factors in NO Production —** The biochemical reaction from L-arginine to NO is calcium dependent.[115] It is also dependent upon an energy molecule named NADPH, which is made in mitochondria by an enzyme known as malate

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- dehydrogenase.[116] Malate dehydrogenase is stimulated by DHEA and thyroid free T3. These hormones stimulate the DNA of mitochondria to produce this enzyme in cells.[116] Studies have been done to show that supplemental use of malic acid can help to decrease the pain in FM.[117]
- **Other External Forces —** Other external forces which are known to stimulate NO production include exercise, hyperemia, shear stress, and pulsatile flow. Hypoxia has also been shown to stimulate NO production.[85,107,118] Moist heat, in the sense of a hot bath or hot moist fomentations, helps to decrease FM pain that patients experience. Massage of body tissues in turn behaves as a shearing stress to help decrease FM pain.[119]

L-arginine, as a substrate for making NO can become depleted by different mechanisms. Some of the conditions whereby this can happen are as follows:

- Some FM patients are known to have problems with recurrent herpes virus infections. The amino acid L-arginine is very crucial in the making of herpes viruses. This would make it difficult theoretically to place a patient on L-arginine supplementation therapy.
- One of the major hormones that helps to control fluid metabolism in the body is arginine vasopressin. This hormone is dependent on arginine for its existence. Studies have shown this hormone to be low in FM patients.[1,2,5] This particular hormone not only helps to maintain body fluid balance, but it also helps in the formation of memory. Hence one would expect to see problems with patients having frequent urination, increased thirst, and memory problems.[120]

***Nutrition and Nitric Oxide*:** Nuts are known to be high in L-arginine.[121,122] Recent work done in the field of nutrition has shown that high levels of fat in the blood inhibits NO release. This effect of fat is neutralized by vitamin E (800 units per day) and vitamin C (1,000 mg per day).[123] Acetylcholine is a major chemical in the bloodstream that stimulates nitric oxide production. There are chemicals in the food chain that destroy acetylcholine. These chemicals are foods in the nightshade family: white potatoes, green and red peppers, tobacco, eggplant, tomatoes, and paprika.[124] It would be advantageous for all FM patients to avoid these foods for one month. They should then introduce them back into the diet one by one every three days to see if pain worsens. If the pain does become worse, then avoidance of this family of food is mandated. Every researcher in FM knows that the tobacco user is among the most difficult patients to care for. The use of tobacco should always be discouraged in FM.

In some FM patients where their medical problems would make it difficult to give them L-arginine, a way to bypass the need for this amino acid supplementation would be to give them nitroglycerin tablets. Nitroglycerin via the cyclic GMP system can make NO.[85] The cyclic GMP system, however, is dependent upon the presence of sulphur for NO production.[125] Cyclic GMP can also be stimulated into production by growth hormone, insulin-like growth factor-1, and DHEA from the adrenals.[126,127] As mentioned earlier in this paper, NO can also be produced by stimulation with oxytocin.[9-11]

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Figure 3

Elements that Stimulate or Inhibit Nitric Oxide Production

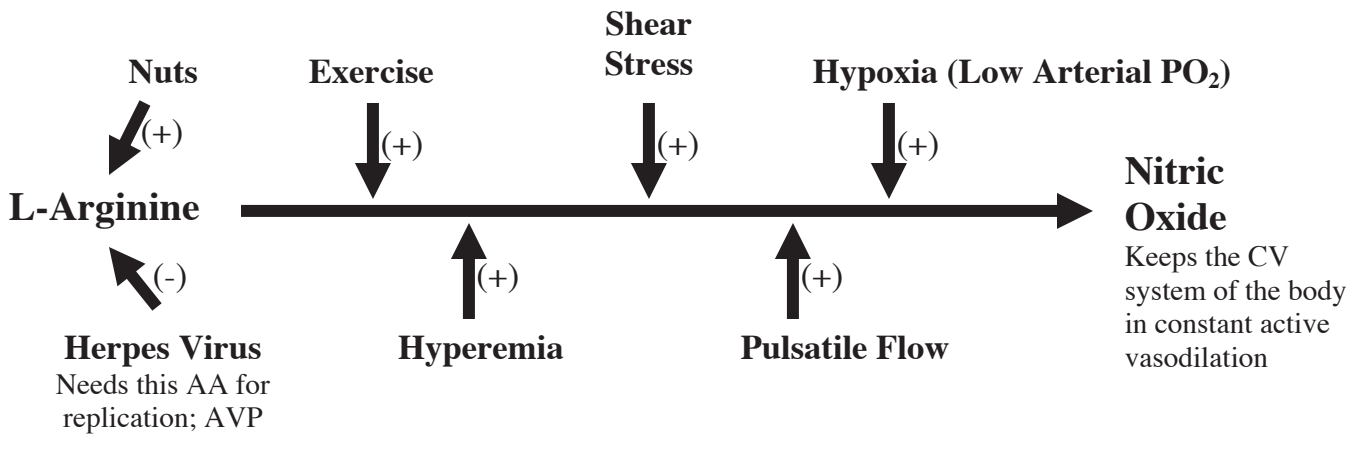
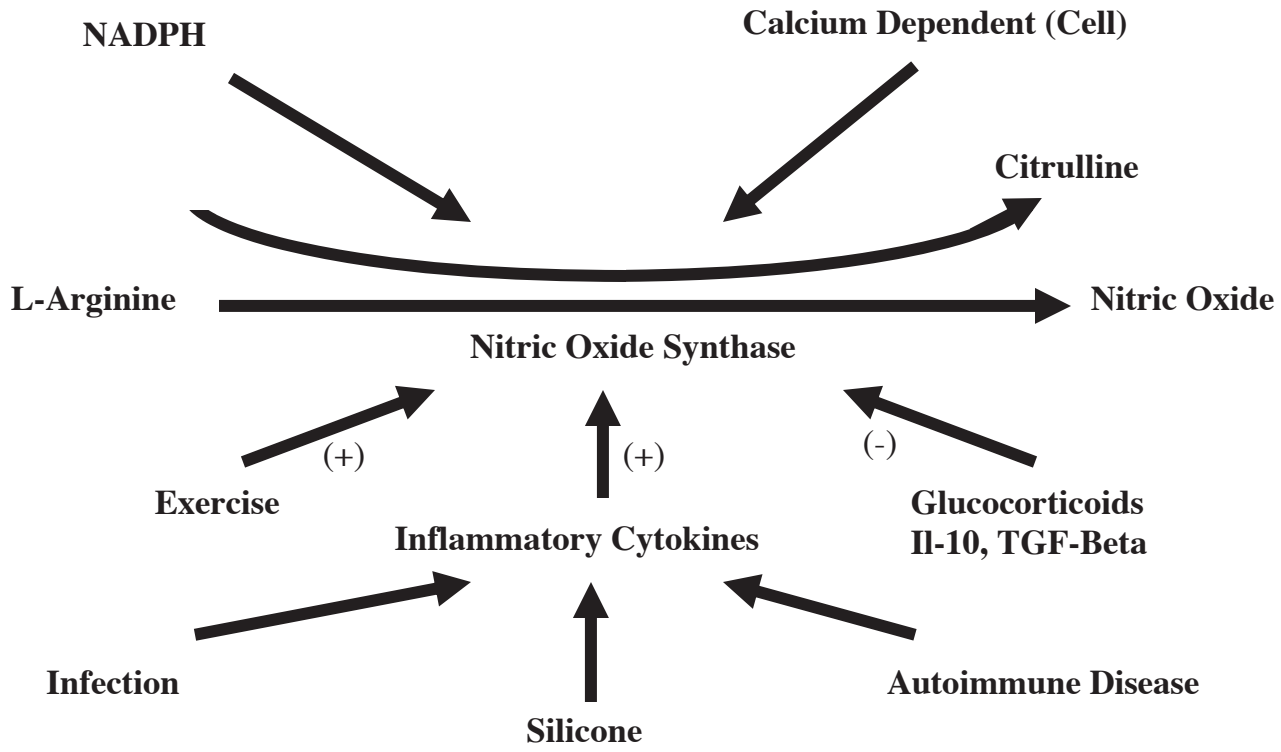


Figure 4

Key Factors in Fibromyalgia that can Influence Nitric Oxide Production



***Nitric Oxide Receptor*:** The control of NO release is receptor dependent. The receptor is stimulated to release NO in the presence of acetylcholine.[128] Acetylcholine, being a primary neuroendocrine chemical used by the central nervous system to communicate with muscles. Through choline supplementation, acetylcholine production can be improved. L-arginine has been shown to improve acetylcholine induced blood vessel relaxation.[123] ATP, which is a major energy component in the body, serves as a stimulant for the cellular receptors of the cardiovascular cells to release NO.[129,130] In FM, ATP production has been documented to be low.[131] Another chemical regulating the control of NO production is bradykinin, which is a chemical produced in the body in the presence of an allergic reaction.

Independent agonist, or independent stimulators of NO release, can be such things as calcium-ATPase inhibitors, polycations, and calcium ionophores/inositol.[85] The phosphatidylinositol pathway, when activated by OT, can independently stimulate release of NO.

Dehydroepiandrosterone

In treating FM/CFIDS patients, a hormone of importance is dehydroepiandrosterone (DHEA). The adrenal glands produce 30-50 mg of DHEA per day compared to 2-3 mg of cortisol. Hence, the major steroid released by the adrenals is DHEA. DHEA sulfate is the water soluble form of the hormone inside the body. DHEA, as produced by the adrenals, is a waxy substance and is very difficult for the body to transport from the adrenals to the tissues. Therefore, by sulfating the hormone, the body makes it water soluble and easier to transport to the respective tissues that need it.

***Physiologic Functions*:** The physiologic functions of DHEA need to be explored. DHEA is the primary steroid produced when a baby is in utero.[132,133] At that time, the level of DHEA in the fetus is around 200 mcg/dl. At birth, DHEA levels drop considerably within a period of two to three weeks and will not significantly rise again until the age of 7. The hormone will then continue to rise until the age of 25 in males and 32 in females. From these ages on, DHEA levels start dropping, and at 60-70 years old, it will be just 5-10% of the hormone level of a normal 30-year-old.[134]

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***Skin*:** DHEA assists in the production of oil in human skin, as do thyroid and betacarotene. When DHEA is lacking, the skin becomes dry and rough.[135] Patients with low DHEA levels find themselves constantly applying lotion. DHEA also helps to control all hair production in the female, from her head to her toes. A woman experiencing a low level of DHEA will notice a decrease in hair production on the legs, underarms and pubic area and some loss of hair on top of the head. Sometimes women will simply notice a need to shave less often. Some patients report that DHEA therapy has helped to increase oil production in their hair. Patients on DHEA hormonal replacement therapy have also noticed that skin and nails begin to get thicker, hair becomes less gray, grows faster and becomes more dense. Smoother, younger-looking skin has been an additional benefit many patients find attractive while taking DHEA.

***Bone*:** DHEA helps to maintain skeletal mass. Therefore, patients with a decrease in DHEA will have accelerated problems with loss of bone mass.[136,137]

Immune System: DHEA can stimulate the immune system.[138-143] Therefore, with low DHEA, problems with increased infections are noted. Additionally, a person with low levels of DHEA requires a longer period of time to recover from a cold, and other illnesses as compared to normal individuals. The steroid also declines with aging.[144]

***Adrenal*:** As mentioned earlier, DHEA is the primary steroid produced by the human adrenal glands.[134] When the body undergoes inflammation from infection or surgical stress, the production of DHEA drops, and adrenal cortisol output increases.[145,146] This process is known in the medical literature as adrenal adaptation syndrome.[145] Chronic inflammation, as seen in lupus, rheumatoid arthritis, tuberculosis, or any long-term infection, can potentially move the adrenals towards chronic adrenal adaption syndrome. This results in a chronically low level of DHEA, which in the long run is not in the best interest of the body. Overcoming infection when the adrenals are functioning properly is much easier and accomplished in much less time than it is when the immune system is compromised, with constant inflammation persisting.

DHEA can override cortisol's immunosuppressive effects on the immune system. One chemical pathway by which DHEA accomplishes this is by reversal of cortisol inhibition of the synthesis and secretion of gamma interferon.[147] Gamma interferon is a hormone produced by white blood cells to help stimulate the immune system into protecting the body against infection such as is seen in a viral infection.

***Herpes*:** DHEA is known to inhibit the cellular transformation of the Epstein-Barr herpes virus, the virus known to cause mononucleosis.[148-150] When the human body has plenty of DHEA, the immune system is able to control the mononucleosis virus more effectively. When DHEA is low, one would then expect to see reactivation of not only the mononucleosis virus, but possibly other herpetic viruses potentially leading toward a syndrome known as latent herpes virus reactivation phenomena. This would help to explain why patients with CFIDS and FM may have reoccurrences of herpetic infections such as genital herpes, cold sores, and shingles. Shingles is a reactivation of the chicken pox virus, a known herpes virus.

***AIDS*:** Patients with AIDS, who have lower levels of DHEA, have been noted in medical studies to die sooner than those with higher levels of DHEA.[151] It appears that an AIDS patient with a higher level of DHEA presents a challenge to the HIV virus.

In laboratory studies, animals given an intentionally lethal dose of a virus predictably died.[151] In these same studies, animals given DHEA a few hours before receiving the "lethal dose" of a virus injection have been shown to survive. This demonstrates DHEA's ability to help the body resist viral infection.

***Immune Centers*:** DHEA can increase the size of the spleen germinal centers suggesting stimulation of the B-lymphocyte dependant areas of the immune system. These cells are responsible for antibody production.[152] DHEA helps in the antibody conversion of IgM to IgG.[140] As the B-lymphocytes of the immune system produce antibodies, one of the major antibodies is the IgM antibody. This is a large molecule that needs to be separated apart to make the IgG antibody. It is felt by some that the separation of the IgM molecule into IgG is controlled by DHEA.

***Cancer*:** Studies indicate that DHEA acts as an anticancer steroid.[153-156] Low levels of DHEA are associated with an increase in breast, bladder, gastric, and prostate cancer.[157-161] A cancer diagnosis could imply that a low level of DHEA probably existed prior to the time of diagnosis.

***Liver Detoxification*:** The ability to detoxify chemicals is controlled by the liver. Drugs and other foreign substances in our bodies, such as silicone, antibiotics and

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other drugs, are referred to as xenobiotics. Metabolism, or detoxification of these xenobiotics in our bodies take place via two different major pathways — Phase I (oxidation) and Phase II (conjugation).

Phase I occurs inside the cell, while Phase II occurs in the liver. It is possible to measure both of these operations, to determine whether each is functioning properly. Common problems facing a chemically sensitive patient are that one, or both, of these processes is overworked or depleted. It is not only possible to determine if a patient is suffering from chemical overload, but also to identify which part of the detoxification pathway is damaged. This is important to determining appropriate nutrient therapy and beginning to repair the affected pathway.

Testing can also identify whether exposure to chemicals is causing cellular damage and other disease symptoms. Measurements can be taken after a few days at home, then repeated after a few days at work. Using this approach can help to establish which environment is more damaging to the detoxification pathways.

According to experts, most patients suffering from a major illness would exhibit a low level of DHEA if tested. Unfortunately, these untested, chronically ill patients are often the very ones who are investigating detoxification as a potential approach to improve overall health. Experts fear that those initiating a detoxification program with a low DHEA level could potentially place more stress on an already burdened liver. This would in turn prolong the detoxification process, and possibly even create additional complications which could threaten the well-being of the participant.

On the other hand, initiating such a program once the DHEA level is higher could afford the participant less discomfort throughout the detoxification period, as it is known that DHEA has demonstrated the ability to stimulate the Phase II (liver) detoxification process and also assist in Phase I detoxification.[162,163]

Patients receiving DHEA therapy experience less sensitivity to medications. Patients frequently find that they are able to tolerate both increasing the dosage of existing medications, and adding additional medications. Clinical observation has suggested that once DHEA therapy is in place, the patient is able to detoxify drugs and other chemicals coming into the body effectively, as the body approaches a normal detoxification process.

***Thyroid and Adrenal Feedback*:** DHEA has unique properties that are responsible for the way it interacts with itself. DHEA has no feedback on itself.[164] There is no documented evidence of DHEA production being inhibited with hormonal replacement therapy of DHEA.[165] It is known that the self-production of thyroid greatly decreases when patients are given oral thyroid hormone. This same principle holds true for the administration of cortisol; the adrenal gland slows its production of cortisol when a patient receives cortisol preparations.

DHEA also has unique functions when interacting with other hormones. The active hormone produced by the thyroid is a hormone called thyroid T3. Although DHEA has no direct effect on the T3 levels of the body, recently, it has been shown that DHEA works to potentiate the active free T3 function, making it more effective in its work at the cellular level.[166] In diabetes, it has been noted that DHEA helps to enhance insulin binding to its receptors on the cell membrane and also to its action on cells.[167,168]

***Libido*:** It is felt that DHEA is the main hormone which helps to control the female libido.[169] Most female sex steroid hormones are dependent on DHEA for their existence.[169] Therefore, DHEA controls the production of estrogens and androgens (male hormones). This can potentially influence fertility and libido as well as improve PMS (clinical observation).

***Thermogenesis*:** Inside each cell of the body are approximately eight hundred mitochondria which help produce energy for the cells. This energy can be used by cells for normal cellular function or be used to help heat the body. The process of heating the human body is called thermogenesis. It has been shown that when DHEA is given, thermogenesis increases.[170] Patients receiving oral DHEA therapy report feeling warmer.

Inside the mitochondria, DNA is present, and helps to produce some of the enzymes inside the mitochondria. DHEA is known to stimulate the DNA production of these enzymes[171,172] and has been shown to increase basal oxygen consumption.[166] When added to thyroid T3, it has proven to be helpful in activation of the malic enzyme gene transcription inside the mitochondria.[171] Overall, DHEA and thyroid T3 interact synergistically to stimulate the body to have more energy via the cellular mitochondria.

***Treatment with DHEA*:** In human studies DHEA has been used in the treatment of cirrhosis,[173-175] psoriasis (as a topical solution),[176-179] lupus,[22] hereditary angioneurotic edema,[180] arteriosclerotic heart disease,[181] AIDS,[149] and porphyria,[182] and has been shown to increase natural

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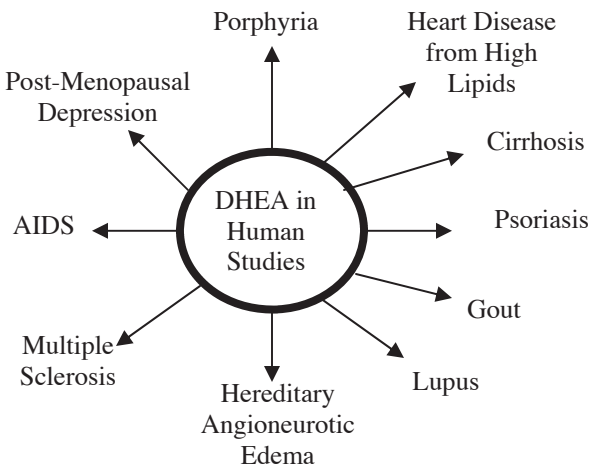
Figure 5

Diseases Where DHEA Has Been Used in a Treatment Protocol



killer cells cytotoxicity.[183] DHEA has now been used in the treatments of disease such as multiple sclerosis,[184,185] post-menopausal depression,[186] and gout.[186] Clinically, it has been successfully used to treat a patient with porphyria. The patient could not tolerate five minutes of sunshine. When exposed to the sun, her skin would develop blisters and cause her to have severe itching. Within one month of hormonal replacement therapy with oral DHEA, she was able to be in the Florida sunshine for greater than eight hours per day with no reaction to the sun.

***Immune Function*:** In the presence of DHEA, natural killer cells of the immune system are able to kill cancer cells and yeast cells more effectively. Clinically, it has been noted that yeast infections come under better control with less recurrences in the presence of taking DHEA. The overall number of natural killer cells can be seen to increase in the presence DHEA.[183]

***Anti-aging*:** DHEA has shown to be an anti-aging hormone. Clinical observation of patients who have high levels of this hormone shows them to suffer much less from the ravages of aging as compared to those who have lower amounts of this hormone.[163]

***Depression*:** DHEA has recently been shown to stimulate the production of serotonin which is a chemical used by the brain to inhibit depression.[187] Hence, low levels of DHEA can manifest as depression. In FM, plasma serotonin levels have been found to be low.[188-190]

***Fibromyalgia*:** In recent medical literature, Dr. I. Jon Russell, a prominent FM researcher, and others have shown that patients with FM have a much lower level of DHEA sulfate compared to normal patients.[51,52]

Relationship between Oxytocin and DHEA

***Inositol*:** OT travels to its receptor sites in certain cell membranes of the body, binds, and activates a chemical messenger called cyclic AMP (cAMP).[45] Cyclic AMP creates a signal which moves through the cell membrane directly into the cell, then activates the phosphatidylinositol system. Research supports that the phosphatidylinositol system is DHEA, cortisol dependent, and necessary for optimum OT function.[191] When this system is activated, the cells of the body are free to do the jobs they are designed to perform. OT acts much like a fine tuner, enhancing the functions which the body is already performing on its own.

Inositol is a substance found in the liver, kidneys, and skeletal and heart muscle and is part of the vitamin B complex. Its highest levels are found in the brain.[192,193] In nature it is found in brown rice, vegetables and fruit. The activity of cells throughout the body is governed by an intricate network of signaling systems which translate outside information into internal signals, or second messengers. Inositol acts as a signal enhancer to transduct many cellular processes, such as secretion, metabolism, cell growth, and neurotransmission of light.[194-198] Inositol is released into the cytoplasm (the inside body of a cell), where it acts as a second messenger for mobilizing calcium contained within the cell. Secondary messengers, or signal transductors, are important because it is thought that an imbalance of these messengers may be, at least partially, responsible for normal cells converting into cancerous ones. This system is also responsible for the ability of a cell to produce nitric oxide.[118] From my research, 80% of FM patients have a defective phosphatidylinositol pathway. This would imply difficulty with night vision, since the photoreceptors of the eye are dependent on this pathway to be effective. Thyroid stimulating hormone (TSH) and thyroid releasing hormone (TRH) are both dependent on this pathway for normal cellular stimulation.

At this point it is important to recognize that other natural chemicals have been found to enhance the human body's response to OT and DHEA. These are choline, malic acid, magnesium, creatine, and thyroid T3.

***Choline*:** This nutrient is involved in protein, fat, and normal carbohydrate metabolism. Its highest concentration in nature is found in the soybean. Although phosphatidyl choline (PC) is a natural component of every

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single membrane, it plays an especially notable role in supporting the membranes responsible for making energy, detoxifying chemicals, and preventing cancer. Dysfunction within the membranes of the body produces allergies, hormone dysregulation, and disease. A deficiency in this essential nutrient can slow the improvement or recovery phase of an illness, produce gradual memory loss, and encourage chemical over-sensitivity. Studies indicate that the use of this nutrient in combination with others has been successful in slowing down some early cases of Alzheimer's Disease.

Diets are usually lacking in sufficient quantities of choline as well as others nutrients needed for metabolism of PC. Successful PC treatment requires careful balancing with these other nutrients necessary for assimilation into body chemistry. Experts describe this nutrient's potential for healing as phenomenal, because the effects of a satisfactory level are so far-reaching.

As the body detoxifies chemicals, even more phosphatidyl choline is needed, especially since our modern world exposes us to so many chemicals. If one part of the body is lacking sufficient PC to perform its job, it will simply borrow from another area. For example, if the body's liver needs more and elects to borrow from the brain, the brain becomes deficient in this substance and can produce mood swings, poor memory, or perhaps even a disease such as Alzheimer's. The components necessary for building PC are also necessary for forming acetylcholine, which is the main neurotransmitter of the brain and a potent stimulator of nitric oxide production.[128,199] Correcting a PC deficiency often produces marked improvement in short-term memory as well as in overall health.

According to nutritional experts, a dosage which supplies approximately 3 g of phosphatidyl choline is preferred. This dosage is sufficient to increase the choline levels in the brain by 50%; nine grams can actually double the brain's choline level. However, manufacturers are constantly changing formulations and diluting the product to become more cost effective, so finding the appropriate dosage can be a challenge.

***Malic Acid*:** A valuable adjunct to this therapy, because it plays an essential role in sugar metabolism and in the formation of ATP — malic acid is the energy currency for physical activity and other important body functions. The energy we use to perform physical and mental tasks, as well as to maintain normal function of the organs in our body, comes from food product combustion after digestion. Energy comes from these combusted, digested food products combined with oxygen. This energy is stored as ATP for future use. ATP production requires magnesium, phosphates, and oxygen. Conditions, such as hypoxia (reduced oxygen supply), can lower ATP production. Further compromise, such as lower than optimal levels of magnesium, phosphate, and substrates, will let the body accumulate excessive levels of certain products which literally "shut down" the complete utilization of sugar for the manufacture of ATP.

As a result, the body will then switch to a very inefficient system of generating ATP. This involves the breaking down of proteins in muscles and other tissues. This is harmful to the body in the long run, resulting in damage to the affected parts. Physical symptoms usually associated with this breakdown are pain, decreased function, and fatigue. ATP levels have been found low in FM.[131,200]

When OT levels are low, the cells of the body can go into a state of hypoxia. This happens because OT via nitric oxide acts as a vasodilator to the capillaries. A lack of OT can potentially cause blood vessels to go into spasm, creating viscous cycles of spasms which worsens the condition. It also further decreases the oxygen supply and food substances needed for ATP production. Malic acid is unique in its ability to increase the utilization of substances needed for ATP synthesis, and also has oxygen-sparing effects because it is able to generate ATP effectively by using sugar as fuel, even under low oxygen conditions. This increase of ATP production under hypoxic conditions actually reverses blood vessel spasms and increases the amount of oxygen and food substances available to muscles and other tissues. Malic acid has also found uses in the treatment of liver disease because of its ability to eliminate ammonia, a substance very toxic to the brain. There are no known contraindications for the use of malic acid.[201]

***Magnesium*:** In addition to malic acid, the other major player is magnesium, the fourth most abundant mineral in the body, and the second most abundant in muscles and organs. Magnesium is required for normal activity by three hundred enzymes, including those involved in energy transfer from food to ATP and further for transfer of energy from ATP to physical and mental activity. ATP forms a complex with magnesium, in order to stabilize the ATP molecule. An inadequate supply of magnesium can inhibit this process of energy production and the stability of its major energy component, ATP.[201] Magnesium insufficiency has been documented in both FM/CFIDS.[201-203]

***Creatine*:** Both FM/CFIDS patients have low levels of

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creatine phosphate.[204-206] In the body creatine is used as a chemical to store energy. It can also serve as a major fuel for normal brain metabolism and as a stimulant for muscle building.[207-209]

***Thyroid T3*:** The thyroid produces two major hormones, T4 and T3. Thyroid T4 will be absorbed in certain cells of the body where it is converted into T3. Many cells such as those of the liver, heart, skeletal muscles, and kidney, have a much lesser ability to convert T4 into T3 and must absorb T3 directly from the plasma. Thyroid T3 does its work in the DNA of the nucleus and of the mitochondria. The conversion of T4 to T3 will decrease under certain conditions. Some factors are aging, infection, inflamation, selenium deficiency, massive weight loss, fasting, and drugs.[210-216] When the thyroid T4 blood level is normal, and the free T3 blood level is low, this is called euthyroid sick syndrome.[217] FM has been associated with hypothyroidism (low thyroid).[218-220] Recent medical research shows a possible defect in the thyroid T3 receptor inside a cell. A gene mutation may result with a low-affinity of thyroid hormone receptors. This would yield partial peripheral resistance to thyroid hormone. The normal thyroid hormone regulation of DNA and mitochondrial DNA gene transcription would be altered. The results would be tissues in the body which look and behave hypothyroid despite normal circulating thyroid hormone levels.[221]

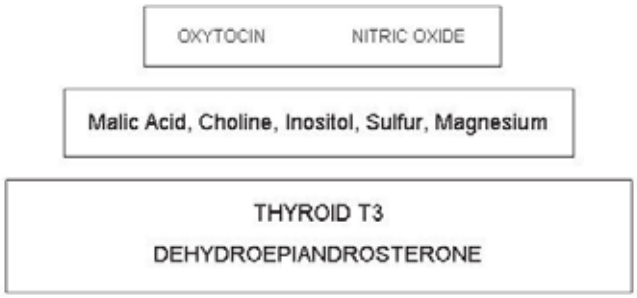
Treatment Plan

Understanding that the true success of any approach to treatment lies in the ability to reach patients outside the parameters of a single medical practice, a protocol has been developed for other treating physicians, using the aforementioned preparations. Double-blind, placebo-controlled testing of these hormones and nutrients has not been performed because of lack of funding. The clinician may wish to try them sequentially in individual patients. The results of an open trial study are presented below for patients seen at Flechas Family Practice between July 1996 and July 1997. Figure 7 is a decision making tree. Once a diagnosis is made, lab work needs to be done to find the metabolic abnormality that may be interfering in the making of nitric oxide. A biological probe is also done with oxytocin and nitroglycerin. This probe does a function analysis of the body. It helps to determine what therapy needs to be instituted during the first office visit. Once the lab work on the individual has come to the doctor's office, the appropriate hormonal replacement therapy or mineral is started. A prescription is mailed to the patient. By the time of the next office visit, the patient will have already begun therapy.

***First Office Visit*:** During this visit the diagnosis is made of a patient's medical problem. Lab work is done to get a baseline on the patient. This lab work includes thyroid T3, DHEA sulfate, thyroid T4, TSH, serum creatine, C-reactive protein, and RBC magnesium blood levels are measured on all FM/CFIDS patients.

Figure 6

Oxytocin and Nitric Oxide Function



This pyramid depicts the significance of the extremely important relationship between these substances. Both oxytocin and nitric oxide function best when these other hormones, natural nutrients, and minerals are present.

***Thyroid Testing*:** A thyroid free T3, T4, and TSH are drawn. Many patients will be found who are low in T3 with normal T4. This is known as euthyroid sick syndrome. For best energy production a T3 level of 3.5 pg/dl or above is desirable. T3 works synergistically with DHEA in the mitochondria to produce energy. The energy production is logarithmic. If either of these two hormones is low, the mitochondrial energy production function is linear.[222]

***DHEA Testing*:** The recommendations of DHEA researchers are that the blood levels of both male and female patients should be around 200 mcg per dl or greater. If the DHEA sulfate level is lower in a patient, then they are started on hormonal replacement therapy with DHEA. If the patient does not respond to the OT test dose with facial flushing and redness of the ears, then they are placed on DHEA in the morning for three months and on. If the DHEA-S04 value is below 200mcg/dl, a good starting point is to begin treatment with DHEA 25 mg p.o. (by mouth), every morning. DHEA converts to DHEA-S04 in the liver and is a stable hormone; a steady state exists between DHEA and DHEA-S04. Therefore, treatment with DHEA-S04 would not be of value. (Please see below for dosage based on blood levels.) Recent work on neurosteroids from the brain have shown that DHEA in some patients may be excitatory to the brain. Hence, if one experiences problems with insomnia with DHEA, then the hor-

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mone should be taken in the morning.

***Magnesium Testing*:** During the first office visit, an RBC magnesium level is drawn. If the RBC magnesium level is low, the patient should be started on Mag 200, two tablets twice daily. Mag 200 is a magnesium product that was developed to give the least amount of bowel irritation with excellent absorption.

***Creatine Testing*:** Also measured at the first visit is the creatine blood level. If found low, then replacement therapy is begun. Once the patient is responding to the therapy as listed in this paper, they can then be started on creatine monohydrate one tsp four times per day for one week, then two tsp every morning. Creatine can be mixed with juice, water, or applesauce. It is best given in the morning. If it is taken at night, it can keep an individual awake. Some patients with sensitive stomachs may have difficulty in taking creatine monohydrate and may need a lower starting dose.

***C-Reactive Protein Testing*:** The C-reactive protein is measured. This protein goes up when the inflammatory hormones (cytokines) of the immune system are activated. Recent research done with colloidal gold (trade name Aurasol sold by Belmar) has shown this gold suspension to decrease these inflammatory hormones. The gold used in regular medical practice is a gold salt. This product can cause rashes, mouth sores, and kidney failure. Pure gold as found in colloidal gold, is approved by the FDA. It is felt that colloidal gold is non-toxic and safe for human consumption. Aurasol has so far proven itself safe and very effective. As mentioned before, when the inflammatory hormones of the immune system are activated, such as when a person has an infection or a chronic inflammatory illness such as lupus, the symptoms of fibromyalgia get worse. When the C-reactive protein is positive, it is prudent for a physician to look for a chronic inflammatory illness.

***CMO Testing*:** Recently a new product has been intro-

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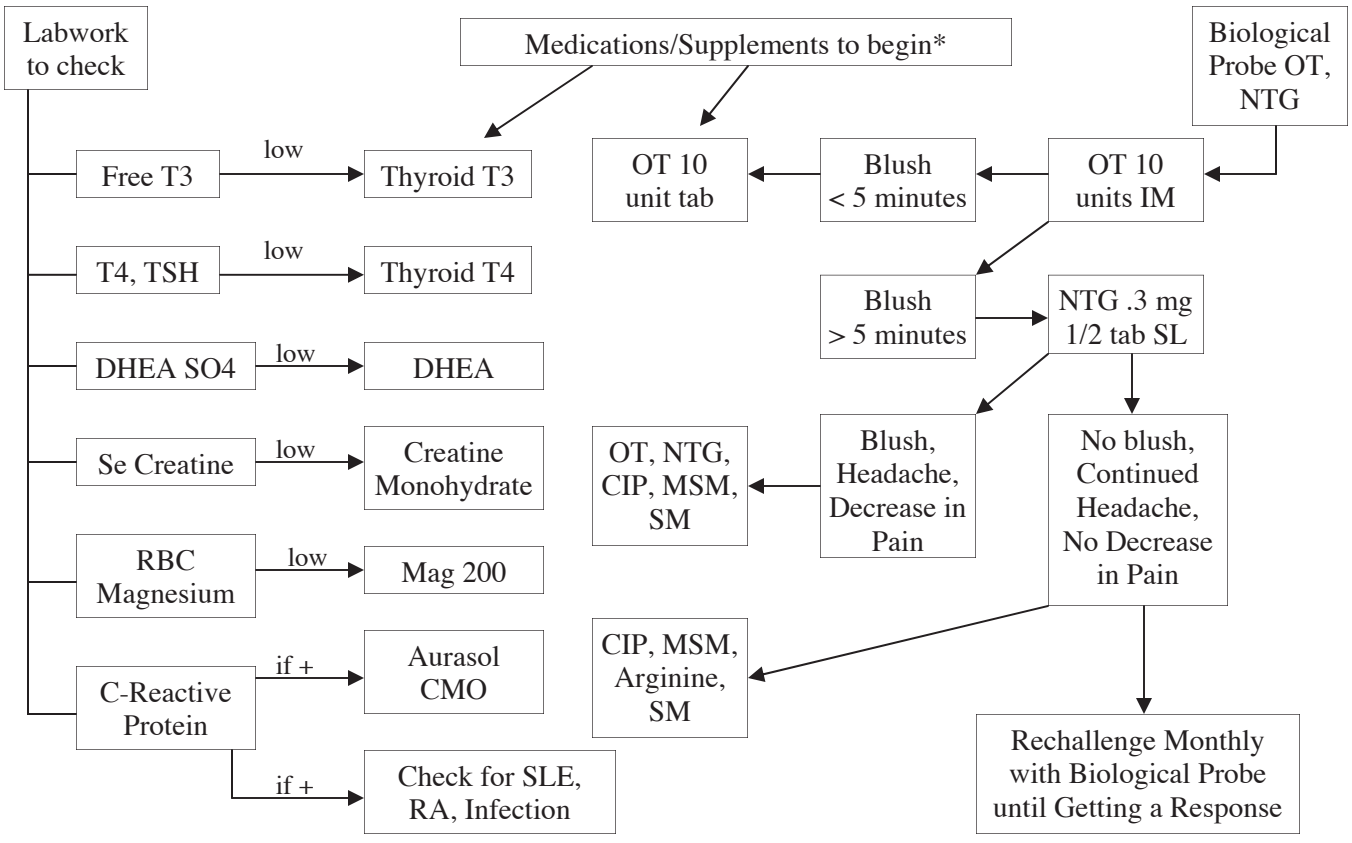
Figure 7

Decision Making Tree for Workup and Treatment



* CIP choline (1500 mg/day), inositol (1500 mg/day), paba (500 mg); NTG nitrostat 1-2 or 1-4 tabs sublingual; SM super malic 3 tabs twice a day; MSM 1000 mg twice a day; L-Arginine 10000 mg twice a day

duced into the market. This product is called CMO. This product was developed at the National Institutes of Health in 1971. It is an oil that was found to protect white mice from developing arthritis. In March 1994, a report on injectable CMO was published in the *Journal of Pharmaceutical Sciences* entitled "Cetyl myristoleate isolated from Swiss albino mice: An apparent protective agent against adjuvant arthritis in rats." Since its discovery, the oil has now been found in the fat of cows. The oil was at one time injectable and is now available as a capsule. It was first tested in an immunology and arthritis clinic in San Diego, California. The patients had rheumatoid arthritis, osteoarthritis, and psoriatic arthritis. The response rate to the oil was 95% of all patients. The pain went down 50-100% in the 1,800 patients tested. The oil has now been tested in our office. We can confirm that it stops the pain of osteoarthritis. We have also discovered that it will stop the pain of FM. We are currently in the process of discovery with CMO to see how long the pain of FM will stay away. Our recommendations at this point are to take three capsules, two times a day for 10 days. During the time period of taking the capsules, patients should avoid the use of oily foods and foods in the nightshade family as listed elsewhere in this primer. During the initial studies done in San Diego, it was found that patients taking methotrexate and cortisone did not do as well as those who were off these medications. It is felt that these medications alter liver function and hence the ability of CMO to function normally. The researchers also found that patients should avoid beans, lentils, wheat, rye, corn, and barley. Patients should also abstain from the use of alcohol, caffeine, and chocolate. This also includes non-alcoholic beer, coffee (even decaffeinated), black tea, and colas. During the 10 days that a person is taking CMO an individual may eat rice, sweet potatoes, fruit, vegetables, squash, pumpkin, turnips, fish, chicken, and turkey. Remember, no fried foods.

***Oxytocin-Nitroglycerin Biological Probe*:** DHEA stimulates the DNA of the cells to produce the enzymes of the inositol triphosphate system. This allows the cells to be more reactive to OT stimulation when it occurs. This increase in reactivity of cells to OT may take up to three months to become fully operational. An easy way to probe this reactivity is by giving a patient a test dose of OT 10 units IM in the office along with .25 cc of xylocaine without epinephrine. OT injectable is a liquid. It has a pH of around 2-4 and can cause significant burning pain when given, hence the use of the xylocaine. If within the first 2-3 minutes the patient feels his or her face becoming warmer and the ears warm, the patient would then seem to have adequate amounts of DHEA. In the office, 92 patients were challenged with the biological probe of oxytocin and 20% of first time patients responded. If a person responds to the OT injection, then they should also respond to the use of oral OT tablets. There have now been three patients who did not respond to the oral tablets and were placed on injectable OT for three months. After three months they were successfully transferred to oral OT with no problem. It is still recommended that a DHEA sulfate level be drawn to get a baseline level on the patient. This will give a starting point for a particular patient's treatment.

In the office, 80% of patients do not respond to injectable OT. If no blushing occurs, patients are then requested to start on choline, inositol, and paba (five tablets per morning). Choline and inositol help load the enzymes that are being made by DHEA in order to help the inositol triphosphate system to respond to OT. Choline (1500 mg) and inositol (1500 mg) may also be found in local health food stores.

Once a patient does not respond to OT, they are then challenged with nitroglycerin. As noted above, OT can stimulate the body to vasodilate its capillaries to give a person better circulation. Two recent medical papers have shown that OT vasodilates the body's small blood vessels via the mechanism of stimulating production of nitric oxide. Nitric oxide is a very potent gas produced at the capillary level of the tissues. One of its major jobs is to improve tissue oxygenation. A few patients have trouble making this gas, even in the presence of the hormones and nutrients thus far discussed. By giving a patient nitroglycerin, nitric oxide can be produced by a different mechanism. We give sublingual nitroglycerin half tablet of .3 mg every four hours (Nitrostat .3 mg slq 4 hrs). This therapy can increase the blood supply to the brain, heart, and tissues. A sign the therapy is working is when the patient develops a headache. This headache is due to increased blood supply to the brain. The headache will last 1-15 minutes and then disappear. When the headache is gone, the individual will also notice a greater relief from their fibromyalgia pain. The pain relief will last about 4-6 hours before another sublingual tablet is required. The nitroglycerin works best in the presence of OT. If nitroglycerin is given by itself, a poor response may occur. The first pill should always be given in a doctor's office in case hypotension should develop. Of all patients given nitroglycerin, 27% do not respond, by blushing or by even getting a headache. Some researchers feel this is due to a lack of enough sulfur in the cells to convert nitroglycerin into nitric oxide.[125]

In order to repair this defect, MSM (methylsulfonylmethane, a safe sulfur containing com-

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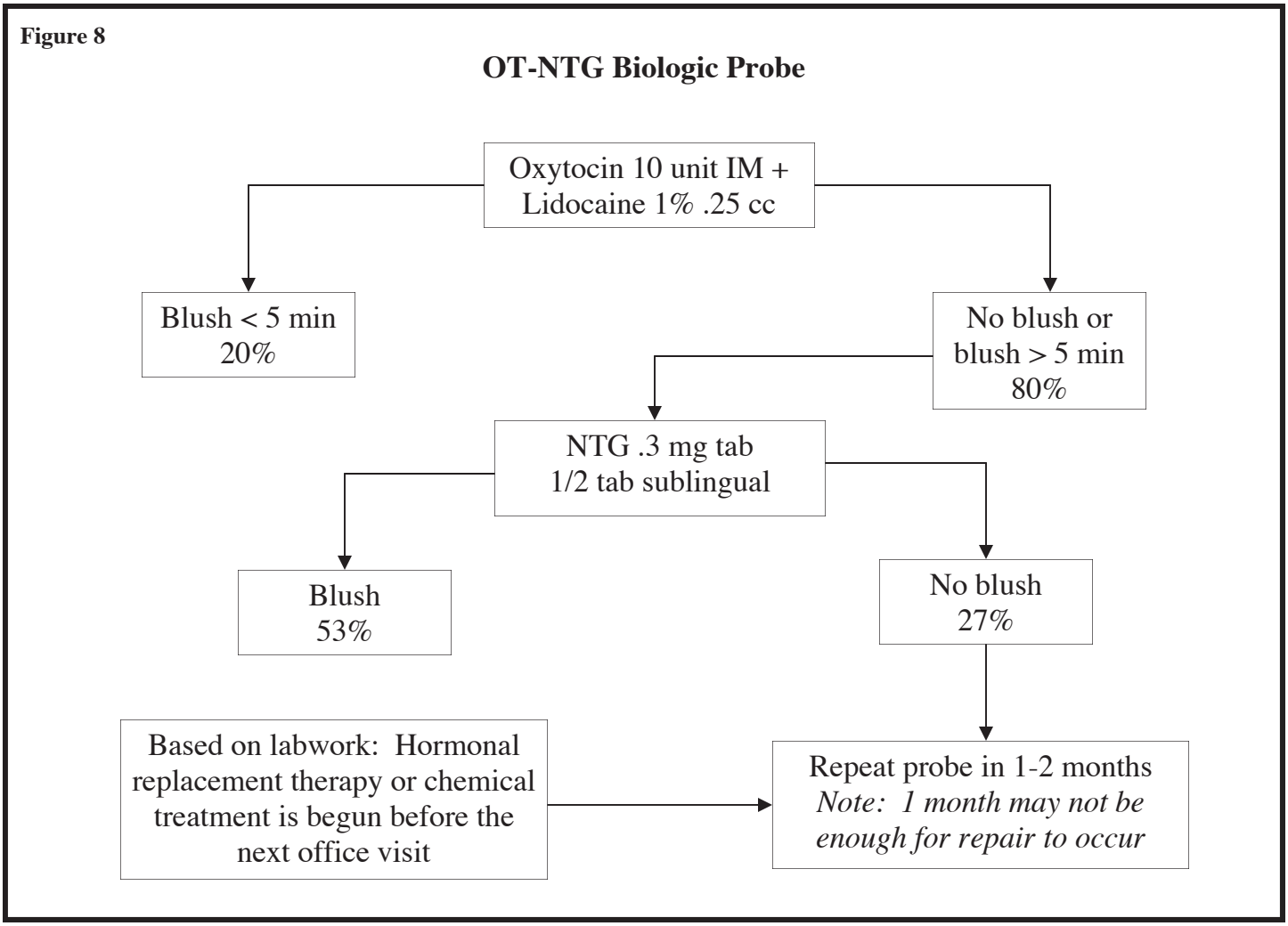
Figure 8



pound) is begun. The dose is 500 mg per capsule, two in the morning and two in the evening. Arginine (the mother amino acid for making nitric oxide is also begun) at the dose of 500 mg two in the morning and two in the evening.

Of the therapy described so far, 73% of all first time patients who walk into a medical practice, will one hour later walk out of the medical practice with much less pain. For those who do not respond, they are begun on arginine, MSM (methylsulfonylmethane), choline, inositol, and paba for the next month and rechallenged with OT and nitroglycerin.

Due to patients having so much pain, they are placed on Super Malic, a malic acid and magnesium preparation that has undergone the rigors of a double-blind, placebo-controlled trial and proven itself to be effective, 3-6 tablets twice per day.[117] Currently in the US, there are many malic acid and magnesium preparations being sold. None of these have stood the rigors of medical testing to prove that they work. This is why only Super Malic can be recommended without reservation. The magnesium in Super Malic can encourage loose bowel movements, so it may be advisable to begin with one tablet three times a day, and eventually work up to a daily dose of 3-4 tablets three times a day, unless liquid stools develop. Increasing the dosage by one tablet per day every four to five days may be the best approach to use in the initial stages of treatment, when trying to establish an individualized dose response.

There seems to be a metabolic disturbance of the ability of the body to handle glucose in patients with FM.[117] Because of this, patients are started on Super Malic to help correct the metabolism disorder in conjunction with DHEA.

***Second Office Visit*:** After the patient has been on DHEA, magnesium, and Super Malic for three months and the inositol choline treatment, a challenge dose of intramuscular OT 10 units with lidocaine 1% 0.25 cc should be administered, unless the patient is sensitive to lidocaine or similar preparations. Within five minutes the patient should start to feel very warm and relaxed,

(Continued on next page)

Chart 2

Effects of Treatment Protocol on Fibromyalgia Symptoms

Category	BRX	ARX	P value	SE	Category	BRX	ARX	P value	SE
* Daily stiffness	7.4	4.5	0.0006		Excess anxiety	1.9	0.8	0.0004	
*Days feel good	0.8	3.3	0.001		Excess fatigue	2.6	1.8	0.0007	
*Do laundry	0.8	0.3	0.01		Exercise	1	2.9	0.002	
*Do shopping	1.6	1	0.03		Fever	0.4	0.2	0.03	
*Drive car	0.6	0.2	0.03		Flushing	1	0.6	0.03	
*Feeling in mornings	8.5	5.5	0.0007		Frequent urination	1.5	1.4	0.4	
*Felt Depressed	6.1	2.9	0.001		Hands change color	1.1	0.4	0.006	
*How much pain	7.5	4.5	0.0006		Headaches	1.7	1.1	0.001	
*How tired	8.8	5.3	0.0001		Impaired concentration	1.4	0.9	0.07	
*Make beds	1.1	0.6	0.07		Insomnia	2	1.2	0.007	
*Miss work per week	3.1	1.4	0.004		Irritability	1.4	0.6	0.006	
*Nervous/anxious	6.6	2.5	3e-05		Joint pain	2.3	1.3	0.0003	0.6
*Pain with work	7.2	4.8	0.007		Joint swelling	1.3	0.6	0.002	0.5
*Prepare meals	1	0.8	0.15		Leg cramps	1.4	0.6	0.005	
*Vacuum a rug	1.4	1.2	0.2		Loose stools	1	0.7	0.04	
*Visit friends	1.3	0.6	0.01		Loss of reason	1.3	0.2	0.0008	
*Walk blocks	2.1	1.7	0.025		Memory loss	1.5	0.5	0.00002	
*Wash dishes	0.9	0.7	0.19		Muscle pain	2.6	1.7	0.0002	0.6
*Yard work	1.3	1.9	0.005		Nasal congest.	1.4	1	0.02	
Abdo. cramping	0.8	0.4	0.03		Nervousness	1.6	0.9	0.005	
Anger	1.4	0.4	0.0007	0.4	Numbness	1.1	0.8	0.04	
Awaken tired	2.5	1.4	0.001		Pain keeps awake	1.6	0.7	0.0002	
Back pain	1.9	1.4	0.04		Pain w/ exercise	2.5	1.9	0.03	0.8
Blurred vision	0.8	0.07	0.3		Palpitations	0.8	0.3	0.02	
Brittle nails	1.4	0.8	0.01		Panic attack	0.9	0.2	0.003	
Burning on urination	0.5	0.2	0.05		PMS	1.3	0.6	0.01	
Chest pains	1	0.5	0.05		Poor sleep	0.2	1.2	0.001	
Climb stairs	1.4	1	0.05		Restless legs	1.8	0.8	0.0003	
Constipation	0.8	0.4	0.02		Short of breath	1	0.7	0.1	
Depressed	2.1	1.6	0.01		Sounds in ears	1.1	0.04	0.006	
Dizziness	1.1	0.7	0.02		Stiffness	2	1.3	0.002	0.5
Dry/itch eyes	1	0.08	0.13		Tender skin	2	1.2	0.01	

and within 20 minutes he should notice a reduction of pain. Once satisfied that the patient has responded to OT, the patient can then start an oral dose of 10 units each morning. An upper limit of 40 units daily has been established for this therapy. Oral OT tablets were developed at Belmar Pharmacy in Lakewood, Colorado, and have been shown to be biologically active (unpublished data). Oral oxytocin tablets should be taken in the morning.

Observations at the office have also indicated that patients who smoke have not responded as well to the OT therapy. This is presumably because the chemicals in cigarette smoke may block OT receptors.

At the second office visit, repeat blood work should be done to monitor hormone and mineral blood levels for those patients that are receiving replacement therapy. Chart 2 is a list of symptoms most often seen in fibromyalgia. These were monitored over a 3-6 month basis. Symptoms were listed as not present equaling zero; mild symptoms equal one; moderate symptoms equal two; and severe symptoms equal three. Symptoms were assessed before treatment and after 3-6 months of treatment. In order for a symptom's improvement to be considered statistically significant, the p-value had to be less than .05. Hence below joint pain before treatment was 2.3. After treatment it was 1.3. The p-value was .0003. The interpretation would say that reduction in joint pain was statistically significant. Blurred vision had a p-value of .3 and was not felt to be statistically significant.

BRX means before treatment and ARX means after 3-6 months of treatment while SE is standard error. Those items with asterisks are included in questions on the Fibromyalgia Impact Questionnaire.[223] This questionnaire works as an instrument to assess the current health status of a woman with FM. It is a self-administered instrument that measures physical functioning, work status, depression, anxiety, sleep, pain, stiffness, fatigue, and well-being. When the score for this questionnaire is added up for before treatment (55.6) as compared to after treatment (30.9), p-value (.0000003) is found to be very statistically significant.

Consider Carefully

An increased desire for intimacy — a feeling all too rare for many FM/CFIDS affected women — is often found lacking during the office visit. Chronic illness imposes a real mix of limitation, experienced by both the injured and the well partner. It is as though personal identity and sense of purpose take up new residence in the background, as the disease and all that entails takes over. In addition, most families affected by FM/CFIDS illness also suffer financial embarrassment, due either to mounting medical bills, or to the sick partner's inability to work, or both. Adding the sick partner's chronically low or non-existent libido to this picture for both partners is a challenge at best, but striving to accomplish this can be absolutely devastating when perhaps the single most powerful ingredient for establishing and maintaining closeness has simply been removed.

This is a very private and understandably sensitive issue. However, we feel a responsibility to address the problem because so many women injured by FM/CFIDS are affected; yet, embarrassment and fear of further rejection prevent most from discussing it with treating physicians. It is important to realize that there are true physical reasons for this lack of desire, and that most women injured by FM/CFIDS share this problem. Although medical opinions may differ as to the actual causes, the end results are essentially the same. No longer desiring to be intimate with a partner represents yet another insult from the illness, because it affects the well partner deeply, and it can affect the security of the marriage directly or indirectly.

For this reason, finding a treatment program with the potential to restore a healthy desire for intimacy, while at the same time reducing pain and increasing mobility, has seemed like an answered prayer to many chronically ill women.

Overall, FM/CFIDS patients who are involved in this particular regime seem pleased. However, as with any therapy involving medications, side effects do exist, and should be researched before treatment is initiated. Although the information provided in this paper is accurate, it should by no means be considered complete.

The reported benefits from patients for this therapy include a reduction of both pain and fatigue. Although still in the early stages, the above outlined interactive OT -Hormonal-Nutrient Treatment Protocol provides an exciting new alternative to the traditional methods of FM/CFIDS treatment. Generally, mainstream medicine is geared toward treating symptoms. Because of time constraints, physicians may be more interested in reducing the severity of symptoms than identifying the cause. As identified earlier in the text, traditional methodology is now being challenged, as more and more FM/CFIDS affected patients regain control over their lives and make a commitment to take an active role in their own recovery. As with anything else, it is important to conduct your own research, and decide on your own, what seems

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to be the most reasonable approach for your personal treatment. Following are the side effects that have been associated in the medical literature with DHEA, inositol, OT, malic acid, and magnesium.

***DHEA Side Effects*:** An increase in DHEA has been known to cause increased hair growth on the head, legs, underarms, and pubic area. This is not normally considered to be a problem, because a decreased level of DHEA has usually created a reduction of hair growth in these areas. This increase in hair growth can be witnessed by increased itching of the scalp and skin. The itching is actually secondary to the hair growth. In addition, an increase of facial hair has been noted on rare occasions.

Because DHEA can also stimulate oil glands to increase oil production, an increase in acne may be seen.[224] These side effects as listed are the natural effects of this hormone, so anytime an excess of DHEA is present, an increase in these areas can be expected.[133,135,165] An increase in muscle mass and a slight increase in the fat mass around the abdomen has also been observed (clinical observation). If DHEA is taken at night, it can cause insomnia. This can be due to the fact that it is a neuroexcitatory hormone of the brain.[225-230]

Although DHEA is capable of increasing thermogenesis,[170] patients receiving this hormone who normally complain of being hot all the time have reported feeling comfortably cooler. This would suggest that DHEA might play a role in helping to control the thermal settings of the brain which determine whether a patient is too hot or too cold.

The combination of thyroid hormone supplementation, DHEA, and injectable estrogen given to the same patient at the same time was noted to produce an overactive libido, to the extent the labia became painfully engorged. This extremely painful physical condition persisted for a period of 14-21 days (clinical observation).

***Oxytocin Side Effects*:** OT therapy helps to stimulate microcirculation, thereby increasing body temperature which can make some patients feel uncomfortably warm.[10,67,231] Still, complaints of cold hands and feet are usually diminished, as the patient experiences increased circulation in these areas. Correct dose regulation can alleviate tissues that get too warm. OT therapy increases circulation to the head and can produce headaches, but they usually disappear within a short time after starting treatment.

Patients with congestive heart failure or decreased renal function are not good candidates for OT therapy because of its propensity to cause fluid retention. OT may be given to a pregnant patient in her first or second trimester if she is having no signs of contractions. Six patients have now gotten pregnant while taking oxytocin pills. Oxytocin took away the nausea and vomiting of early pregnancy. Research shows that oxytocin receptors are mostly present in the uterus during the last few weeks of pregnancy. It has been requested that all patients stop using oxytocin during the last two months of pregnancy.[232,233] The symptoms of FM are the worst during pregnancy, and oxytocin by mouth stops the FM pain. By the last few weeks of pregnancy, most patients are well enough to stop oxytocin and the FM does not bother them much.

If a patient does not have enough DHEA or inositol on board at the time OT therapy is initiated, the addition of OT can actually cause agitation, rather than produce its normal calming effect. This would suggest that this patient is not ready to begin OT therapy and would probably benefit from increasing the amount of DHEA and inositol taken for a few months, before trying OT again. On the other hand, too much OT could theoretically cause patients to experience a psychiatric problem known as obsessive compulsive disorder. This is based on data from one study only.[234] In addition, an increase in the manic phase of patients diagnosed with manic-depressive illness is seen as a disorder of inositol.[191,193] This increase in the manic phase comes under quick control as soon as either the hormones or inositol are withdrawn.

Some patients have noted an increase in the size of breast tissue, sometimes necessitating a corresponding change in bra cup size. Increased breast and nipple tenderness have been reported by patients, while others report reduced breast tenderness before their monthly cycle. Patients have also reported greater sensation and sexual excitation when the breast is caressed.

***Malic Acid and Magnesium Side Effects*:** Gastric irritation can occur in the presence of malic acid.[117,235] Taking the nutrient with at least one eight-ounce glass of water seems to minimize this reaction, although some still find it necessary to experiment until an appropriate personalized dosage of malic acid is reached.

Magnesium is contained in Super Malic, and may cause problems with frequent loose bowel movements.[201,236] Many patients with constipation find this side effect of their therapy to be helpful. If liquid stools develop, reducing the Super Malic until t wo or three soft bowel

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movements per day are achieved seems to work well.

As previously described, this combination of preparations has been known to produce effects ranging from decreased fatigue and pain to clearer vision and improved thinking. Many symptoms are eliminated such as being lightheaded, irritable bowel syndrome, cramps, cold hands and feet, foggy concentration, and muscle pain. Other improvements include better circulation, better body temperature regulation, more energy, reduced skin sensitivity, and less agitation.

As these and other treatment modalities surface, hope looms on the horizon for both women and men suffering from FM/CFIDS-related illnesses. The future holds even more promise!

Source of Medication and Supplements

Belmar Pharmacy (Lakewood, Colorado) compounds a highly bioavailable form of DHEA as well as oxytocin. Both these hormones are available by prescription. Super Malic (Optimox Cooperation) is available without medical claims as a source of both malic acid and magnesium and can be purchased at your local pharmacy or health food store as an over-the-counter product. It can also be purchased through Belmar, along with inositol/choline and Mag 200. The medication is shipped directly to the patient after a prescription has been faxed to the pharmacy from the doctor's office.

Medications should be prescribed in the following amounts:

- DHEA: 50mg 1 qam #100 for DHEA levels less than 100mcg/dl; 25mg of DHEA for levels between 100-200mcg/dl
- Thyroid T3: 90, 120, or 150 mcg 1 qam #100 (This pill is sustained release)
- Oxytocin: 10 unit tab 1-3 tab qam #100
- Nitrostat: .3 mg slq 4-6hr #100; First dose should always be given in a doctor's office; Try giving a quarter or half tab first. Be sure to get a pill cutter at the pharmacy.

Belmar has all these products. Health food stores may have some of the supplements. Supplements should be prescribed as follows:

- Super Malic: 3-6 bid #180
- Choline-Inositol-Paba: 5 qam or (choline 1500mg/day, inositol 1500mg/dayand paba 500mg/day) #250
- Mag 200: 2 bid #120
- Creatine monohydrate: 2 tsp qam in juice #300 gms; creatine should only be started after oxytocin has been initiated
- MSM (methylsulfonylmethane): 500 mg 2 bid
- L-Arginine: 500 mg 2 bid
- Aurasol(aqueous colloidal gold): 3 tabs per day for one month then 3 tabs per week. This is for patients with a positive C-reactive protein.

About the Author

Dr. Jorge Flechas is a family practitioner in North Carolina who works with patients who have fibromyalgia (FM) and chronic fatigue and immune dysfunction syndrome (CFIDS). He has developed a new protocol for treatment of these illnesses using oxytocin (OT), dehydroepiandrosterone (DHEA) and some natural nutrients. He feels both diseases are most likely due to a neuroendocrine/metabolic disorder with chronic hypoxia, which causes abnormalities in the biochemistry of patients.

For more information about DHEA and Oxytocin therapy write to: Dr. Jorge D. Flechas, 80 Doctors Drive, Suite 3, Hendersonville, NC 28792. You can also call him at (828) 684-3233. Your phone call will be returned as a collect call as time allows.

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