

IDENTIFICATION AND TREATMENT OF CHRONIC INFECTIONS IN CFIDS, FIBROMYALGIA SYNDROME AND RHEUMATOID ARTHRITIS: SUPPORT FOR ANTIBIOTIC REGIMENS

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Chronic Fatigue Immune Dysfunction Syndrome (CFIDS) is characterized by a number of chronic (>6 months duration) signs and symptoms that do not resolve with rest. Among these are disabling fatigue, intermittent fevers, joint and muscle pain and loss of joint mobility, impairments in short-term memory, headaches, skin rashes, diarrhea, coughing, nausea and gastrointestinal and breathing problems, diminished vision and other signs and symptoms. Other chronic illnesses, such as Fibromyalgia Syndrome (FMS), Gulf War Illness (GWI), Rheumatoid Arthritis (RA), Inflammatory Bowel Disease, among others, also show many of these same signs and symptoms, suggesting that there may be some overlap in the underlying causes of these conditions or at least in the factors that may result in sickness (morbidity) or illness progression.

Although the causes of chronic illnesses are for the most part unknown, the complex signs and symptoms that evolve in many CFIDS, FMS, GWI and RA patients may be due, in part, to systemic chronic infections (bacteria, viruses, fungi). Such infections can follow acute or chronic chemical or other insults (viral, environmental, trauma, etc.) that have the potential to suppress the immune system [1, 2]. Thus these illnesses probably evolve over time as a multistep process that may require multiple toxic exposures, including infections that can be causative for the illness in some patients, cofactors for the illness (not causative but important to morbidity) in others or opportunistic in immune-compromised patients. Chronic infections that are usually held in check by our immune systems can take hold if they can avoid immune surveillance and penetrate and hide in various tissues and organs, including cells of the Central and Peripheral Nervous Systems [3]. When such infections occur, they can cause many of the complex signs and symptoms seen in CFIDS, FMS, RA and GWI, including immune dysfunction [2]. Changes in environmental responses as well as increased titers to various endogenous viruses that are commonly found to be expressed in these patients have been seen in CFIDS, FMS and GWI. If infectious agents are involved, few can produce the complex chronic signs and symptoms found in these patients.

One type of airborne infection that has received renewed interest of late as an important cause, cofactor or opportunistic infection in these disorders is represented by various primitive classes of bacteria [3]. These microorganisms, principally *Mycoplasmas* and other bacteria (*Chlamydia*, *Coxiella*, *Brucella*, *Borellia*, etc.), although not as well known as other agents in causing disease, are now considered important emerging pathogens in various chronic diseases and may also be important cofactors in some illnesses, including HIV-AIDS and other immunodeficiency disorders, skin diseases and some autoimmune diseases [3].

As chronic illnesses such as CFIDS, FMS, GWI and RA progress, there are a number of accompanying clinical problems, particularly increases in autoimmune signs and symptoms seen in some patients. These include acquiring most but usually not all of the classical signs and symptoms of Multiple Sclerosis (MS), Amyotrophic Lateral Sclerosis (ALS or Lew Gehrig's Disease), Lupus, Graves' Disease, RA and other complex autoimmune diseases. Although it is not proven, such usually rare autoimmune responses are at least consistent with certain chronic infections, such as mycoplasmal infections, that penetrate into nerve cells, synovial cells in joints and other cell types. It is proposed that these autoimmune signs and symptoms are caused when intracellular pathogens, such as mycoplasmas and other bacteria, escape from cellular compartments. Some microorganisms like mycoplasmas can incorporate into their own structures pieces of host cell membranes that contain important host membrane antigens that can trigger autoimmune responses [1], and they can also mimic host cell antigen structures [3]. Thus patients with such infections may respond immunologically to microorganism antigens as well as their own membrane antigens, producing unusual autoimmune signs and symptoms.

MICROORGANISMS CAUSE MORBIDITY IN MANY CFIDS, FMS, GWI AND RA PATIENTS

Most microorganisms like *Mycoplasmas* are not considered as important human pathogens when they are found at superficial sites, such as the oral cavity or gut, but some species, such as *M. fermentans*, *M. penetrans*, *M. pneumoniae*,

M. genitalium, *M. pirum* and *M. hominis*, among others, have the capacity to penetrate into the blood circulation and colonize various tissues, and these cell-penetrating microorganisms have been closely associated with various human diseases [3]. Do such infectious agents actually cause CFIDS, FMS, GWI or RA? Probably not on their own, but microorganisms like *Mycoplasma*, *Chlamydia*, *Brucella*, *Coxiella* and other bacteria and some viruses appear to be important in causing chronic illness progression, causing patient morbidity, or exacerbating the major signs and symptoms seen in patients with chronic illnesses.

If certain microorganisms are associated with chronic illnesses, is there any evidence for microorganism infections in CFIDS, FMS, GWI or RA patients? The answer is YES. In ~60% of CFIDS, ~70% of FMS and ~50% of GWI and RA patients examined we and others, principally Dr. Daryl See, formally of the University of California College of Medicine, Irvine, and Eli Mortechnai of Medical Diagnostics of New Jersey, are finding strong evidence for mycoplasmal blood infections that can explain much if not most of the chronic signs and symptoms found in these patients. In our studies on GWI, a CFIDS-like illness [4], we have found mycoplasmal infections in the blood of about one-half of over 200 patients, and these patients were found to have principally one infectious species of mycoplasma, *M. fermentans* [4-6]. However, in about 60% of the >200 civilians with CFIDS and FMS that we have examined we are finding a variety of pathogenic mycoplasma species, such as *M. fermentans*, *M. penetrans*, *M. pneumoniae*, *M. genitalium*, *M. pirum* and *M. hominis*, in their white blood cells [6]. The tests that we use to identify mycoplasmal infections, Forensic Polymerase Chain Reaction and Nucleoprotein Gene Tracking, are very sensitive and highly specific. These tests are a dramatic improvement over the relatively insensitive serum antibody and other tests that are currently being used to assay for systemic infections.

ANTIBIOTIC TREATMENTS FOR CHRONIC ILLNESSES

When microorganism infections are identified in blood fractions of subsets of patients with CFIDS, FMS, GWI or RA, these patients can be treated as medical not psychological or psychiatric patients, just like any other patients with blood infections. This does not mean that psychological or psychiatric problems are not important in some chronic illness patients. But if such infections are important in these disorders, then appropriate treatments with antibiotics or other medications that suppress chronic infections should result in improvement and even recovery. This is exactly what has been found [7, 8].

The recommended treatments for mycoplasmal blood infections require long-term antibiotic therapy, usually multiple 6-week cycles of doxycycline (200-300 mg/day), ciprofloxacin or Cipro (1,500 mg/day), azithromycin or Zithromax (500 mg/day) or clarithromycin or Biaxin (750-1,000 mg/day). Multiple cycles are required, because few patients recover after only a few cycles [4-6], possibly because of the intracellular locations of the infections and the slow-growing nature of these microorganisms. We now recommend that patients who have been diagnosed with blood infections receive continuous antibiotics for at least 6 months before using the 6-week cycles of treatment. Although patients starting such therapy usually have Herxheimer reactions and feel initially worse due to die-off or release of toxic materials from damaged microorganisms, they eventually stabilize and then slowly begin to recover. Unfortunately, the treatment requires long term therapy and recovery is usually very slow. Patients that have been sick for many years are unlikely to recover within a year of therapy.

The clinical responses that are seen are not due to placebo effects, because administration of some antibiotics, such as penicillins, resulted in patients becoming more not less symptomatic. In addition, they are not due to immunosuppressive effects of some of the antibiotics, because other antibiotics that do not cause immune suppression are also effective but only if they suppress the chronic infections. Some patients recover to a certain point and then fail to continue to respond to the recommended antibiotics, suggesting that other problems, such as viral infections, environmental exposures and other toxic events also play an important role in these illnesses, and may even play a predominant role in some patients.

What results for chronic illnesses like CFIDS have been obtained with antibiotics? Although a majority of patients diagnosed with chronic blood infections appear to benefit from antibiotic therapy, many patients respond and have some alleviation of most signs and symptoms but do not fully recover. A 3-year follow-up of antibiotic therapy in the Shasta CFIDS Association of Northern California is instructive. According to Sharon Briggs, R.N., a majority (~80%) of patients from the Shasta CFIDS Group that were confirmed with mycoplasmal infections recovered from 50-100% of their pre-illness health within this time period, and even some patients who did not test positive showed benefit from antibiotics. Similar to other therapies for chronic illnesses, not every patient benefited from antibiotic therapy, and the time required for recovery was quite variable.

Do chronic infections explain illnesses like CFIDS? It is unlikely that there is only one or even a few explanations for complex chronic illnesses like CFIDS. Rather, these illnesses are probably due to a combination of multiple toxic exposures, chemical and biological, in combination with genetic susceptibility (immune systems and/or detoxification systems) that determines whether a person becomes chronically ill. These considerations probably also play an important role in determining who will recover to various extents on different types of therapy. In addition, recovery can be complicated by patients over-dependence on drugs, such as certain antidepressants or other drugs that can suppress portions of the immune system.

COMPLEX ROLE OF TOXIC EXPOSURES IN CHRONIC ILLNESSES

The treatment recommendations for CFIDS, FMS, GWI and RA patients with chronic pathogenic mycoplasmal infections are similar to those used to treat Lyme Disease, caused by other slow-growing intracellular bacteria that are difficult to identify and treat. Interestingly, those patients that slowly recover after several cycles of antibiotics are generally less environmentally sensitive, suggesting that their immune systems may be returning to pre-illness states. If such patients had illnesses that were solely caused by psychological or psychiatric problems or by environmental or chemical exposures, they should not respond to the recommended antibiotics and recover their health. In addition, if such treatments were just reducing the autoimmune responses, then patients should not maintain recovery after the treatments are discontinued.

The treatments of chronic illnesses that are due to toxic exposures from chemical or radiological agents are quite different from the treatment of chronic infections [1]. The treatment of chemically exposed patients usually involves removal of offending chemicals from the patient's environment, depletion of chemicals from the patient's system and treatment of the signs and symptoms caused by chemical exposure(s). Chemically exposed patients are often extremely sensitive to a variety of commonly encountered chemicals, including perfumes and air fresheners, petrochemical fumes, chlorine, cleaning solutions and solvents, among others. They are also very sensitive to certain foods, and special diets are often necessary, and in some cases direct skin contact with certain substances can cause strong cutaneous reactions. Therefore, an important part of treatment for chemical exposures requires limiting exposures to a variety of common chemicals and gradual removal of the toxic chemicals [9, 10].

VITAMIN / NUTRITIONAL / SUPPLEMENT RECOMMENDATIONS

To be successful a comprehensive approach to the therapy of chronic illnesses must be undertaken with each patient [8]. In addition to treatments like antibiotics or removal of toxic agents, these patients often have nutritional and other deficiencies that must be corrected. For example, these patients are often depleted in vitamins B, C and E, among others, and certain minerals. Unfortunately, patients with chronic illnesses often have poor absorption. Therefore, high doses of some vitamins must be used, and others, such as vitamin B complex, cannot be easily absorbed by the gut, so sublingual *natural* B-complex vitamins in small capsules or liquids should be used instead of oral capsules that are swallowed. General vitamins plus extra C, E, CoQ-10, beta-carotene, folic acid, bioflavoids and biotin are best. L- cysteine, L-tyrosine, L-carnitine, malic acid and especially flaxseed oil are reported by some to be useful. Certain minerals are also often depleted in these patients, such as zinc, magnesium, chromium and selenium, and these should be supplemented as well. One problem with taking these supplements is that they cannot be taken at the same time as antibiotics because they may inhibit antibiotic uptake.

There are also other considerations [8]. Antibiotics deplete normal gut bacteria which can result in over-growth of less desirable bacteria. To supplement bacteria in the gastrointestinal system *Lactobacillus acidophilus* tablets are recommended. One product is a mixture of *Lactobacillus acidophilus*, *Lactobacillus bifidus* and other bacteria with FOS (fructooligosaccharides) to promote growth of these "friendly" bacteria in the gut.

A number of natural remedies that boost the immune system can be useful in the therapy of chronic illnesses. Among these are whole lemon/olive extract drink or an extract of olive leaves with antioxidants, plant extracts or purified plant products and milk proteins such as whey. These products are especially useful during or especially after antibiotic therapy has been completed. Although these products appear to help some patients, their clinical effectiveness in various chronic illness patients has not been carefully evaluated. They should be used during therapy to boost the immune system or especially after antibiotic therapy in a maintenance program to prevent relapse of illness [8].

FOR FURTHER INFORMATION

The Institute for Molecular Medicine can test patients for evidence of mycoplasmal and other infections of the types that worsen human diseases like CFIDS, FMS, GWI and RA. Blood samples can be sent to the Institute for Molecular Medicine for mycoplasma and other testing. The website for further information is: www.immed.org.

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