

HEALTHwatch™



IN THIS ISSUE

Insulin Potentiation Therapy: A New Approach to Treating CFS & FM.....	1
New Developments in the Management of FM	1
Research News Briefs	2
Pro Health to Match CFIDS Research Contributions	3
Dr. Komaroff's Recommendations for CFS Care	4
Neurotoxins: Diagnosis and Treatment Info for CFS, FM and other 'Mystery Illnesses' (Part Two)	6
Drug News Briefs	11
Research Shows Phosphoglycolipids Protect Cells and Fight Fatigue	15
Achieving Effective Results with Guaifenesin	16
Methionine for Mercury Detoxification	17
Research Study Shows Superior Absorption of Coral Calcium.....	18
Yeast Overgrowth Wreaks Havoc on Immune System.....	19

INSULIN POTENTIATION THERAPY: A NEW APPROACH TO TREATING CHRONIC FATIGUE SYNDROME AND FIBROMYALGIA



Dale Guyer, M.D.

An exclusive interview with Dale Guyer, M.D.

Dale Guyer, M.D., is a holistic family physician and Director of the Advanced Medical Center in Zionsville, Indiana, where patients are offered a unique blend of traditional and alternative therapies incorporating a mind-body-spirit approach for a variety of health issues, including Chronic Fatigue Syndrome and fibromyalgia.

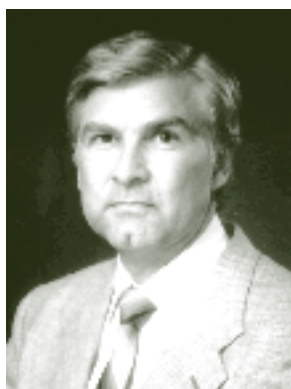
Healthwatch (HW): Thank you, Dr. Guyer, for taking the time to provide us with information about this innovative new therapy for the treatment of Chronic Fatigue Syndrome and fibromyalgia in patients in which chronic viral infections act as an instigating component. Can you tell us a bit about this therapy, how you have initiated this treatment approach and its overall effects?

Dr. Guyer: One of the challenges practitioners have encountered in the treatment of Chronic Fatigue Syndrome and Fibromyalgia Syndrome (CFIDS/FMS) are the frequent appearance of chronic infections, which invariably come along for the ride in CFIDS sufferers. These infections are often viral or atypical bacteria, or both, and are often found to be the causative etiology of ongoing chronic illness by virtue of their ability to systematically unravel immune system function and derange the internal terrain leading to biochemical homeostasis alterations.

A common historical feature of many individuals is the flu-like illness that never went away. These patients will usually relate that they felt reasonably well until they acquired this flu-like illness and since that time they have felt achy, tired, run down, and exhausted. Sometimes secondary symptoms may be present such as sore throat, lymph node tenderness, "brain fog," and depression. Laboratory testing on these patients will tend to find high antibody levels to

continued on page 10...

NEW DEVELOPMENTS IN THE MANAGEMENT OF FIBROMYALGIA SYNDROME



I. Jon Russell, M.D., Ph.D.

Editor's Note: Following are key highlights from the presentation I. Jon Russell, M.D., Ph.D., made at the American College of Rheumatology 2002 Annual Meeting.

By I. Jon Russell, M.D., Ph.D.

I. Jon Russell, M.D., Ph.D., is Associate Professor of Medicine at the University of Texas Health Science Center and is also Director of the University Clinical Research Center. Dr. Russell is an internationally recognized and respected researcher and clinical practitioner caring for patients with musculoskeletal pain disorders including fibromyalgia.

Epidemiologic data indicate that Fibromyalgia Syndrome (FMS) affects at least 2% of the general population in the United States

continued on page 12...

RESEARCH NEWS BRIEFS

NEUROTOXIN DISCOVERED IN CHRONIC FATIGUE SYNDROME

Research sponsored by the National CFIDS Foundation was formally announced at the International Symposium on Toxins and Natural Products in Okinawa, Japan in November 2002 by Dr. Yoshitsugi Hokama. The research, for the first time, discovered ciguatoxin, a potent neurotoxin, in the blood of Chronic Fatigue Syndrome patients. "Chronic ciguatera poisoning has already been suggested as a scientific model for Chronic Fatigue Syndrome (CFS)," stated Dr. Hokama.

Ciguatoxins are potent, heat stabile, non-protein, lipophilic sodium channel activator toxins and are recognized as some of the most potent biological toxins known. They produce dramatic neurological manifestations, such as peripheral sensory or motor symptoms (including paresthesias, pain, burning, tingling, numbness), central symptoms such as headache, autonomic dysfunction and also affect multiple body systems (gastrointestinal, immune, hepatic, cardiovascular) and the muscles. Many CFS patients in the study had higher levels of the toxin than the patients with cancer, hepatitis or acute ciguatera poisoning.

Gail Kansky, President of the National CFIDS Foundation, said, "We believe this to be a significant breakthrough. CFS, which has come to include myalgic encephalomyelitis, is a very severe illness that has not received adequate funding or appropriate medical attention. Although there are still many unanswered questions and much work to be done, research efforts will ultimately turn the tide in the understanding of this disease and allow patients to receive appropriate medical therapies. We are indebted to Dr. Hokama and his colleagues."

STUDY CAPTURES CYTOMEGALOVIRUS DORMANT IN HUMAN CELLS

Princeton scientists have taken an important step toward understanding how cytomegalovirus infects and lies dormant in most people, but emerges as a serious illness in transplant patients, some newborns and other people with weakened immune systems - including those who suffer with Chronic Fatigue Syndrome and fibromyalgia. The virus, called human cytomegalovirus, enters the bone marrow and can hide there for a lifetime. Until now, however, scientists had not been able to study the virus in its latent stage because it infects only humans and does not readily infect or become dormant in laboratory strains of bone marrow cells.

In a study published in November 2002, Felicia Goodrum, a postdoctoral fellow, and Tom Shenk, a professor of molecular biology at Princeton University, demonstrated a laboratory system for studying the virus in its latent stage. They showed they could establish a latent infection in freshly collected bone marrow cells and then retrigger an active infection. They drew on their system to discover a set of genes that the virus uses in its latent state and that may give the virus its great capacity

for stealth. Knowing what genes the virus uses to hide and re-emerge could give pharmaceutical companies targets for designing drugs that disrupt those mechanisms. "So you could dream that some day in the future we could clear the virus from a person and not just treat the symptoms that occur when the virus re-emerges," said Shenk.

CLINICAL DEVELOPMENT MILESTONE IN CHRONIC FATIGUE SYNDROME THERAPY

Hemispherx Biopharma, a leading company in the experimental stage development of immune based therapies primarily addressing the diseases of HIV/AIDS and Chronic Fatigue Syndrome, announced in December 2002 that its Phase III, pivotal study in Chronic Fatigue Syndrome (CFS) is fully enrolled. The phase III pivotal study is rigorous in design and includes multi-center, randomized, double-blind and placebo-controlled components. As a fully enrolled program, it is the first Phase III clinical study ever successfully implemented in CFS, either in North America or Europe. The experimental immunotherapeutic, Ampligen®, is being given to more than 230 severely debilitated patients who have enrolled in the experimental program at multiple sites across the U.S. (described more fully at www.hemispherx.net). All 230 patients must meet rigorous medical and laboratory criteria in order to qualify.

Historically, four other multinational pharma companies, and two internationally recognized research institutes, including the National Institutes of Health (NIH), ceased product development at an earlier or Phase II level, because their experimental drugs were not shown to be statistically different from placebo in terms of improving physical performance or quality of life.

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PRO HEALTH TO MATCH CFIDS RESEARCH CONTRIBUTIONS

By K. Kimberly Kenney

The path to a cure for CFIDS is charted one step at a time. Each study takes us a bit further along that path, answering some questions, raising new ones. The mysteries that continue to puzzle scientists who've been studying CFIDS for years are now piquing the curiosity of researchers just entering this critical field of exploration. And, together, we're making progress. But clearly, there is an urgent need for more effective treatment options, a definitive laboratory marker, and a cause.

This is a pivotal time for CFIDS science. Driving relevant, cutting-edge research is at the heart of The CFIDS Association of America. In effect, the Association acts as a "scientific venture capitalist," identifying gaps in current knowledge, providing seed money for promising pilot projects and enabling investigators to gather the data they need to successfully compete for larger grants.

To that end, I'm pleased to announce that the Association will fund two new studies this year with more than \$155,000 in grants.

One study will be conducted by Theodore C. Friedman, M.D., Ph.D., division of endocrinology at the UCLA School of Medicine.

Friedman's study, "Decreased Cerebral Blood Flow and Orthostasis in Chronic Fatigue Syndrome", will look at the possible causes behind the decreased blood flow to the brain that occurs in some people with CFIDS. This phenomenon could be due to a decreased ability to produce a hormone called renin. Renin, made in the kidneys, stimulates the production of other hormones that help conserve salt in the body. Without enough salt, blood flow to the brain may be impaired – resulting in the onset of a number of CFIDS symptoms. A preliminary study found defects in the renin production mechanism of 19 of 21 people with CFIDS.

Another study conducted by Giris Jacob, M.D., DSc, director of the Jacob Recanati Autonomic Dysfunction Center in Haifa, Israel, will examine the possible link between a persistently overactive immune system and CFIDS. His team will study 50 patients who have recently suffered from flu-like illnesses and have felt fatigued for at least three months, providing a rare opportunity to look at people just developing CFIDS – as well as some who may recover.

Jacob will test the patients for the levels of cytokines – proteins produced by the immune system – in their blood. In particular, the scientists will test levels of interleukin 1 (IL-1), interleukin 6 (IL-6) and tumor necrosis factor (TNF)-alpha. The study also will look to test the hypothesis that overactive immune systems are responsible for problems with the autonomic nervous system (ANS). Finding a link between the two body systems may lead to future studies that improve both the diagnosis and treatment of CFIDS.



Both projects were chosen using a peer-review process that began with the evaluation of 37 letters of intent and 11 full applications.

Since 1987, The CFIDS Association has provided more than \$3.8 million in research grants and is the nation's largest not-for-profit source of funds for scientists studying CFIDS.

We're proud that Pro Health shares the Association's commitment to accelerating the progress of CFIDS research and are grateful for their equally solid commitment to raising the funds that, in turn, will help make ground-breaking research possible.

Your tax-deductible donation to The CFIDS Association will be matched, dollar for dollar, by Pro Health. So, please give as generously as possible. Please make donation checks payable to The CFIDS Association of America and send to:

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New research promises better diagnostic tools, new directions for treatment and an end to this devastating illness. Please support CFIDS research today.

*K. Kimberly Kenney
President & CEO
The CFIDS Association of America*

DR. KOMAROFF'S RECOMMENDATIONS FOR CHRONIC FATIGUE SYNDROME CARE



Anthony Komaroff, M.D.

By John W. Addington

John W. Addington is a medical researcher, a patient rights paralegal, and a CFS patient. As a free lance writer, he regularly publishes on topics relating to CFS and FM.

Persons with Chronic Fatigue Syndrome (CFS) can be thankful that Dr. Anthony Komaroff is on their side. To begin with, he is a staunch advocate of the disorder's legitimacy. He is also a Professor of Medicine at Harvard Medical School, the Senior Physician at

Brigham and Women's Hospital, and the Editor-in-Chief of Harvard Health Publications. Thus, Dr. Komaroff has the right clout to influence others to accurately understand this disorder.

Dr. Komaroff has put that clout to good use in his role as member of the U.S. Department of Health and Human Services CFS Coordinating Committee. Aided by Komaroff, a particularly noteworthy accomplishment of that committee was the identification of CFS funds that had been misallocated for other purposes by the Centers for Disease Control. The committee's work led to the restoration of those funds for CFS research as originally designated.

RESEARCH

Dr. Komaroff publishes and lectures widely on research that he and other experts have conducted regarding CFS. His own CFS research has addressed immune dysfunction, viral involvement, allergies, and nervous system problems including cognitive difficulties and hormonal imbalances. Dr. Komaroff explains that "the most exciting area of research in the past 5 years has been the many studies finding neuroendocrine [hormone related] abnormalities in CFS. These studies provide further evidence of a biological process involving the central nervous system in CFS."

DISTINGUISHING OTHER AILMENTS

When it comes to patients with fatigue, Dr. Komaroff advises doctors to be concerned about making the proper diagnosis. In fact only two to five percent of patients who complain of fatigue to their doctors actually have CFS. Others problems that should be ruled out are anemia, hypothyroidism and hidden malignancies. In some cases, Dr. Komaroff believes simply overworking can be the cause of fatigue.

Psychological problems should also be considered. This is because, as Komaroff notes "depression and anxiety

appear to be the most common underlying causes...of chronic fatigue." Thus, this Harvard expert on fatigue says that doctors "should carefully evaluate the possibility of an underlying primary psychiatric disorder in any patient with fatigue." (As will be seen below, however, this does not mean that Komaroff believes that CFS is really just a manifestation of a psychological problem.)

DRUG THERAPY

Dr. Komaroff is frustrated that the current state of CFS research has only yielded therapies of limited value. Nonetheless, since tricyclic drugs such as amitriptyline (Elavil) have helped in a number of cases he feels patients should consider their use. "In the very low doses we use, these medicines help improve the quality of sleep and thereby improve some of the symptoms of CFS," Dr. Komaroff states.

Although Dr. Komaroff recommends tricyclics, drugs normally used for depression, it is not an endorsement by him of the assertion that CFS is a form of depression. A reason Komaroff sees for the distinction is the difference in time and dosage required for tricyclics to benefit CFS as opposed to depression. Thus, Dr. Komaroff notes that with CFS the "rapid effect and the low doses used (relative to doses used in the treatment of depression) are not consistent with an effect on an underlying depression."

Other CFS symptoms can be addressed with medications as well. For pain and headaches, Dr. Komaroff feels nonsteroidal anti-inflammatory drugs (aspirin, Ibuprofen, naproxen, etc.) may be the best bet. In patients with anxiety or panic problems, anxiolytic drugs (Buspar, Klonopin, Paxil, etc.) can be used. Regarding hypotension, Dr. Komaroff explains, "some patients with fatigue after long periods of standing improve with added salt or fludrocortisone, but none has completely recovered [using these treatments]."

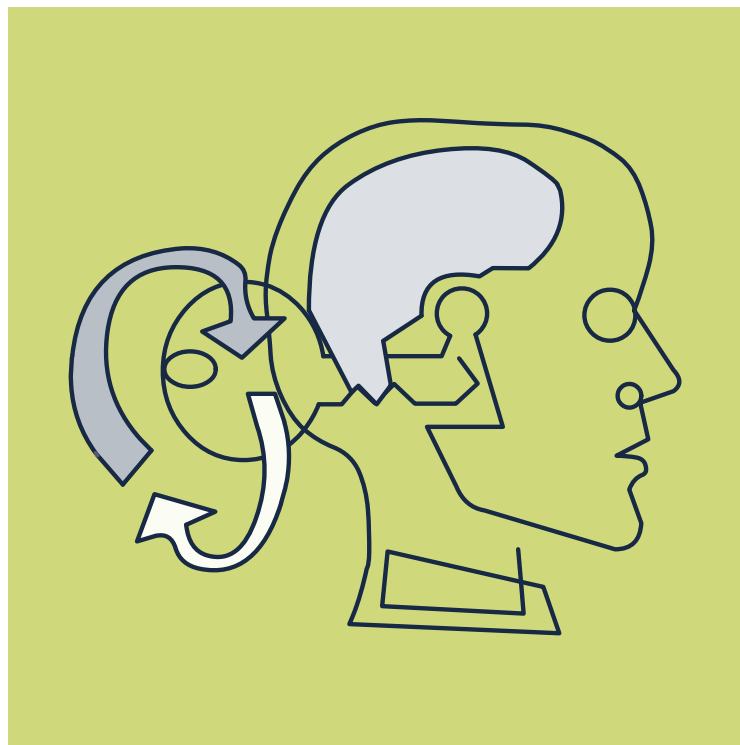


Although research seems to support viral activity in a portion of CFS patients, studies on antiviral medications have not proven the merit of this therapy. Likewise, no drugs have been able to relieve the immune system dysfunction often seen with CFS. Further, Dr. Komaroff thinks the side effects of hydrocortisone weigh against its use in counteracting diminished cortisone levels.

COGNITIVE BEHAVIORAL THERAPY & EXERCISE

Dr. Komaroff recognizes the benefits of cognitive behavioral therapy (CBT) with some patients. A British doctor, Michael Sharpe, has studied cognitive behavioral therapy and its implications for CFS extensively. He explains that CBT is "based upon the hypothesis that inaccurate and unhelpful beliefs, ineffective coping behavior, negative mood states, social problems, and pathophysiological [abnormal functioning] processes all interact to perpetuate illness. Treatment aims at helping patients re-evaluate their understanding of the illness and to adopt more effective coping behaviors."

CBT therapists encourage patients to modestly increase their activity, even including light exercise. Dr. Komaroff explains that "the diagnosis of CFS can encourage an unnecessarily restricted level of physical activity that leads, in turn, to deconditioning and further physical dysfunction. Graded, modest, regular physical activity is encouraged and found to be beneficial." He also cautions, however that, "the success of [CBT] therapy is very therapist-dependent."



PSYCHOLOGICAL ISSUES

That Dr. Komaroff acknowledges the value of cognitive behavioral therapy is no indication patients have just imagined their symptoms. Komaroff commented on this issue in a special issue of *The American Journal of Medicine* devoted

to CFS. He said, "there is now considerable evidence of an underlying biological process in most patients who meet the CDC definition of chronic fatigue syndrome."

Continuing, Dr. Komaroff stated that recent research "is inconsistent with the hypothesis that chronic fatigue syndrome involves symptoms that are only imagined or amplified because of underlying psychiatric distress symptoms that have no biological basis. It's time to put that hypothesis to rest and pursue biological clues...in our quest to find answers for patients suffering from this syndrome."

Research that Dr. Komaroff has personally been involved in has helped to distinguish CFS from depression. In a recent study, Komaroff and his associates compared the cognitive functioning (thinking ability, memory, language skills) and psychological symptoms of depressed patients and patients with CFS. While both groups had symptoms of depression as well as cognitive problems, the researchers found that, "the depressed patients were significantly more impaired overall compared to CFS patients." Thus, Komaroff and his associates concluded that the cognitive difficulties experienced by CFS did not appear to relate to depression but rather were more "consistent with...brain alterations."

CONCLUSION

Dr. Anthony Komaroff's dedicated research efforts have brought us further in understanding the exact nature of this perplexing malady. His sage treatment guidelines have also proven their value. Just as remedial for many CFS patients, however, has been Dr. Komaroff's respect for the legitimacy of the ailment. With his help, the battle against CFS is a little easier. ■■

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NEUROTOXINS: DIAGNOSIS AND TREATMENT INFORMATION FOR CHRONIC FATIGUE SYNDROME, FIBROMYALGIA AND OTHER "MYSTERY ILLNESSES" (PART TWO)

By Patti Schmidt

Patti Schmidt is an award-winning writer and PWC (Person with CFIDS), a former CFIDS support group leader, co-founder of the Greater Philadelphia CFIDS Alliance, and is an officer of the Board of Directors of the CFIDS Association of America. Ms. Schmidt has written about a wide variety of topics relating to coping with the disease and seeking out effective treatment.

The first part of this two-part series explained how two scientists, Maryland family practice physician Ritchie C. Shoemaker and EPA neurotoxicologist H. Kenneth Hudnell, developed their "neurotoxin-mediated illness" theory explaining why many multisystem illnesses like Chronic Fatigue Syndrome (CFS), Multiple Chemical Sensitivity (MCS), fibromyalgia (FM), Sick Building Syndrome (SBS) and Lyme Disease are making people sick these days. Hudnell and Shoemaker believe they have both a biomarker for neurotoxic illness and an effective treatment. (The first part of the article can be read online at <http://www.ImmuneSupport.com/library/showarticle.cfm/id/3990/>.)

The first article also detailed the clinical trials in which they tested the theory; the new, simple, inexpensive way they test for neurotoxins; and described their treatment protocol, which features an effective, FDA-approved prescription medicine that flushes toxins safely away. The two became convinced that many of these illnesses are neurotoxic when clinical trials found their treatment for Pfiesteria - cholestyramine (CSM) - also helped many of those patients improve. Pfiesteria, the toxic dinoflagellate Pfiesteria piscicida, is the cause of many major fish kills and fish disease events all over the Eastern seaboard, especially North Carolina and Florida.

As part of my research for this series, I agreed to go through Dr. Shoemaker's diagnostic and treatment protocols. I've been ill with CFIDS, FM, Irritable Bowel Syndrome (IBS) and a few others for more than 20 years, so I had little hope that his treatments would "cure" me. But CSM, often prescribed to lower cholesterol levels, has a long safety record, so it probably wouldn't hurt me, either. But then Dr. Shoemaker's diagnostic process found something unexpected, putting a whole new spin on things; and suddenly, the world was a very different place for me.

THE DIAGNOSIS

Dr. Shoemaker's office is located in Pocomoke City, Maryland. First I sat in a medium-sized, cheerful front office and filled out medical information and insurance forms. Within



H. Kenneth Hudnell, Ph.D.

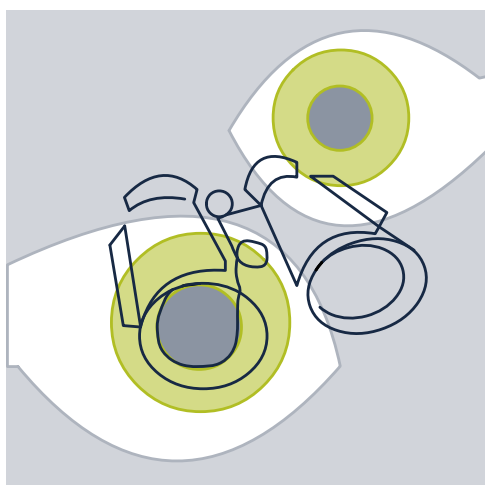
Ritchie C. Shoemaker, M.D.

minutes, I was led to a small, clean exam room. I took out my notebook and a tape recorder. Dr. Ritchie Shoemaker entered the room suddenly. He read my medical history and health questionnaire and it was immediately clear from his comments that the challenge of figuring out and treating these diseases is what drives him. We spent the next two hours going over my history, symptoms and his theories. (See part one for theory details.) To help me visualize how his theory works, he begins drawing on a roll of white paper stretched taut on the patient's examining table between us.

Some of Dr. Shoemaker's questions are a bit odd, including, "Have you ever felt a sudden, sharp pain like a lightning bolt or a feeling like an ice pick stabbing you?" But odd or not, once while driving to work years ago, I got an intense pain in my heart and thought I was having a heart attack. I detoured to my physician's office just minutes away and was diagnosed with costochondritis, an inflammation of the ribcage's costochondral joints. I know FM patients often experience that. Do I have light sensitivity or a metallic taste in my mouth, he asked? Yes, I'm sensitive to light, I told him, and the weird tastes I get sometimes in my mouth seem more like either mayonnaise or pennies to me. He checked 'yes' for that one, too. Shoemaker hears complaints of strange tastes often from his neurotoxic patients. He asked me a group of hypothalamic-related questions: Do I ever have mood or appetite swings, profuse sweats, night sweats or an inability to control my body temperature? All of them, I say. Divide 7 into 91, he said, looking for how I handle numbers. I was surprised and a little humbled when I couldn't do it, even after he gave me extra time. Most neurotoxic patients have these symptoms, too.

Do I suffer from excessive thirst, frequent urination or a susceptibility to static electrical shocks? Yes to all three, I answered, especially the shocks. But I'm curious: what do

those things have in common? Is a tendency to give people electrical shocks tied to illness somehow? What do all of these things signify? Shoemaker answered the shock question first: Hormonal deficiencies cause neurotoxic patients to lose water, and as salt becomes more concentrated in their blood, sweat glands respond to protect the blood from excessive salt by excreting it in sweat. In fact, cystic fibrosis patients are diagnosed by the amount of chloride in their sweat, and often neurotoxic patients have even more chloride in their sweat than cystic fibrosis patients. The salty sweat dries on the skin, making it a very large, efficient conductor of electricity. I'm happy to know why this happens, but I had no idea it had anything to do with my health problems.



As he examined me, then has an assistant take 12 vials of blood, he answered my other questions. He ordered several tests, including levels of ACTH (adrenocorticotrophic hormone), cortisol and ADH (antidiuretic hormone). He also wanted to know my osmolality (the amount of salt in my blood). He also tested for MSH (melanocyte-stimulating hormone) and leptin levels (see part one of this series for a detailed description of how MSH and leptin effect patients with neurotoxic illness); ordered an HLA-DR by PCR (human immune response gene testing, done by polymerase chain reaction); and tested for androgen levels, including total testosterone, androenedione, dehydroepiandrosterone sulfate (DHEA-S), and MMP-9, the enzyme that delivers inflammatory elements from the blood

into the brain, lung, heart and joints. He also ordered a Tumor Necrosis Factor (TNF) level test; a plasminogen activator inhibitor-1 (PAI-1) test; and a test to see if I have a Coag Negative Staph infection.

MMP-9 levels are increased by the immune system's response to biotoxins, and it delivers inflammatory elements into joints, lungs, heart and brain. Shoemaker's research shows that patients with high MMP-9 are often the ones who also have Unidentified Bright Objects (UBOs) on their MRIs. He believes it may be that UBOs come from ischemia (lack of oxygen), inflammation or from the same kind of demyelination that Multiple Sclerosis (MS) patients suffer from. But after treatment with Actos and CSM, MMP9 levels fall and UBOs disappear. Shoemaker believes every neurotoxic patient should know their MSH and leptin levels. Leptin initiates MSH production. The damage to the MSH production pathway (also known as leptin resistance) that's seen in neurotoxic patients is a marker for biotoxic illness. He says he answers the question, "How long will I be sick, doctor?" with this: "As long as your MSH is low, you'll continue to have symptoms." MSH controls peripheral cytokine production, thought to cause inflammation throughout the body. An MSH deficiency allows cytokine production to go wild. MSH also controls defenses in mucus membranes in the nose and GI tract, which is why Shoemaker tests for Coag Neg Staph, an opportunistic colonizer found in the deep recesses of the nose. In the gut, research has yet to define the mechanism that allows people to lose nutrients into stool, often referred to as "leaky gut," and which creates the IBS symptoms like bloating, gas and cramps, diarrhea and constipation that neurotoxic patients often suffer from.

MSH also controls pituitary function, which controls hormones. If you're deficient in MSH, you'll likely be deficient in ADH and prolactin, growth hormone, ACTH, LH (luteinizing hormone) and FSH (follicle-stimulating hormone), says Shoemaker. "Not all patients have all of these deficiencies, but it's unlikely that an MSH-deficient patient won't have at least one."

Luteinizing hormone plays an important role in controlling ovulation and in controlling the secretion of hormones by the ovaries and testes. Without androgens (male hormones like testosterone), the adverse effects of peripheral cytokines are multiplied. That dysfunction causes the rest of the hormones in your body to dysfunction, resulting in symptoms like low libido in both sexes; impotence in men and menstrual irregularities, endometriosis, sexual dysfunction and premature production of uterine fibroids in women. "Hormones may be why more women tend to get these illnesses," says Shoemaker. "It's a never-ending cycle that will continue until the source of MSH deficiency is corrected." When each of these feedback loops is damaged, each causes specific dysfunction. Lyme patients take Actos to correct the cytokine excess. Working backwards to correct the MSH deficiency, we need to remove the damage to the MSH production pathway. That means that we need to block excessive cytokine production, which comes from fat cells. Enbrel, a drug for Rheumatoid Arthritis, suppresses cytokine production, but not cytokines produced by fat cells. Only Actos does that. Actos also blocks MMP-9, excessive leptin production and turns on uncoupling proteins which burn fat directly. That process, which causes weight loss, also mobilizes fatty acids, reducing insulin resistance that in turn lowers the adverse effects of cholesterol, triglycerides and blood sugar, thus helping us avoid heart disease and diabetes.

"All of this cytokine chemistry goes for naught if the person is still exposed to toxins," warns Shoemaker. "Then, regardless of which treatment you try, cytokines will increase." In other words, you must get rid of all confounding variables that might also be making you sick. That means that Lyme patients have to be treated for Lyme before they can be treated for the neurotoxic effects of Lyme; that the SBS patient must be removed from further exposure; and that Coag Neg Staph must be removed from the nose.

But back to the office visit: the Coag Negative Staph test isn't pleasant. To get a sample from deep inside your nose where the Staph organisms hide,

he sticks a long Q-tip two inches up your nose. No one likes that test, but it's necessary because if it's a complicating factor, he must treat it first. Dr. Shoemaker also noted the results of a recent Complete Blood Chemistry, thyroid testing, and a few hormone tests like estrogen and estradiol that were ordered by my primary care physician, my gynecologist or a specialist. I asked what the significance is of sudden sharp pains, which he called neuropathic pains. "They reflect damage to nerves," Shoemaker replied. Many neurotoxic patients suffer from them, including CFIDS, FM and Lyme Disease sufferers. Light sensitivity, mood swings, sweats, and the other symptoms symptomatic of autonomic system dysfunction signify "hypothalamic neurotoxicity," otherwise known as CFIDS.

At the end of two hours, Shoemaker believes he has a complete picture of my medical history and previous diagnoses. He also notes my health questionnaire answers and the data from the physical exam. He asks about previous Lyme tests. All negative, I say. He frowns: do I know which tests were done? Find the reports, he says, because based on everything he's seen, he believes I have Lyme Disease. I'm shocked; I'm not sure what to think. Then I remember that the University of Pennsylvania had tested my spinal fluid while looking for reasons for cluster headaches a few years back. Isn't that a sure sign of being Lyme-free, I ask? "You cannot rely on test results alone to make a Lyme Disease diagnosis," explains Shoemaker. "Not the Western Blot, not the Elisa, not the PCR test of cerebral spinal fluid. Lyme Disease is now considered a clinical diagnosis, which means a physician has to look at a patient's symptoms in order to make a diagnosis." I didn't know that. My head is spinning. I doubted that I'd been misdiagnosed because I'd seen some of the best doctors in the field. How could they each have missed something so obvious? I can hardly wait to get home to do some research.

LYME DISEASE

Soon, genetic testing results confirm that Dr. Shoemaker was right about my genotype; additional results were also compatible with Shoemaker's preliminary diagnosis of Lyme Disease.

I had no confounding exposures, i.e., nothing else that would explain these symptoms. (The Lyme was probably what caused the CFIDS, FM, IBS and other illnesses.) In the meantime, my research confirmed that Lyme Disease was a clinical diagnosis, and that there were two scientific camps: one that believes that as little as a three week-long course of antibiotics would eradicate *Borrelia burgdorferi* (the bacterium responsible for causing Lyme Disease) and another that believes chronic Lyme Disease patients needed much longer antibiotic treatment. Naturally, insurance companies are in the short-term camp.

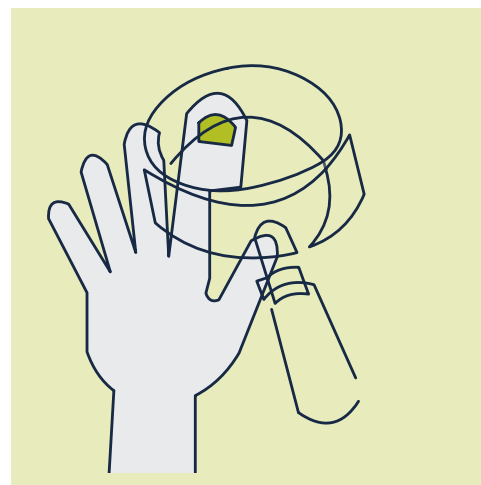
According to the LymeTruth organization's website (<http://www.lymetruth.org/>), serological tests may not detect up to 60 percent of cases of Lyme disease. In some areas, 100 percent of deer ticks harbor Lyme disease spirochetes. More than 50 percent of infected humans never notice a rash or a bite; I did have a rash in the 1980s that no doctor was able to diagnose, but it wasn't the typical "bullseye" rash Lyme patients get. I contacted several Lyme experts. One went over my medical history in detail with me, and we found 13 indications of Lyme Disease, including an incident of Bell's Palsy in 1977 and meningitis in 1986. A recent significant improvement while taking Amoxicillin was also an indicator - it's one of the best Lyme killers.

I had chronic Lyme Disease. It was probably why I first got CFS, and was also probably the reason for the last - and worst - of my many relapses, the one that finally knocked me out of the working world. Shoemaker was confident I had chronic Lyme Disease before he got the test confirmation because his research has shown that people with my specific group of symptoms, diagnoses and exposure (i.e., where I'd lived) all shared the same genotype, a "15-6-51," and a "1-5." (Differential association of HLA-DR genotypes with chronic neurotoxin-mediated illness: Possible genetic basis for susceptibility, R Shoemaker, presented Nov. 11, 2002 at the American Society of Tropical Medicine and Hygiene's 51st annual meeting. Abstract available at <http://www.chronicneurotoxins.com/learnmore/>

[latestAbstracts.cfm](#).) That research hadn't been available to my other physicians previously, so they never knew to run that test. The research is still preliminary as well.

But Shoemaker notes that it's not surprising that individual susceptibility to illness caused by toxins made by invertebrates is controlled genetically. The immune response genes, including HLA-DR, along with immunoglobulins and white blood cells called T cells, are only found in vertebrates. It's also not surprising that deficiencies of the immune response to those toxins result in illnesses in some patients with exposure, but not in other patients with the same exposure who don't have the same immune response gene defect.

"Basically, if you get bit by a tick and develop Lyme Disease, you will develop chronic Lyme Disease if you have those genes," says Shoemaker. The "1-5" genes also predict I would develop low MSH, which is why I have chronic pain and chronic fatigue, pituitary abnormalities and alterations in gut and nose function. "The '1-5' genotype will give you MSH deficiency regardless of which toxin you're exposed to, if you also have one of the genes for susceptibility to the toxin you're exposed to," says Shoemaker.



Shoemaker's current research is finding ways to replace MSH in MSH-deficient neurotoxic patients. (See his website at <http://www.chronicneurotoxins.com> for details.) He also says the Lyme tests that were done on me didn't meet CDC criteria. "No one would have diagnosed you with Lyme Disease [before]," he

said. That's because in 1994 a group of experts decided that you must have 5 of 10 bands present on the Western Blot Lyme test to be positive for Lyme. I didn't have all 10, but most "Lyme-literate" physicians would also consider some of the other symptoms I've had, like the meningitis, and diagnose me with Lyme anyway because research shows many Lyme patients don't have all 10 bands. "The difficulty is, the bands they chose were based on a European *Borrelia*, which guaranteed Lyme was rarely diagnosed," Shoemaker points out.

My local Lyme support group leader agreed with that assessment and told me that many patients still remain undiagnosed, just as I was. He also said he gets calls every week from patients previously diagnosed with CFIDS or fibromyalgia who find out they've had Lyme for some time. (See my sidebar for more information about how to determine if you've been adequately tested for Lyme Disease. If you have any doubts, make sure a "Lyme-literate" physician examines you and your health history in detail.)

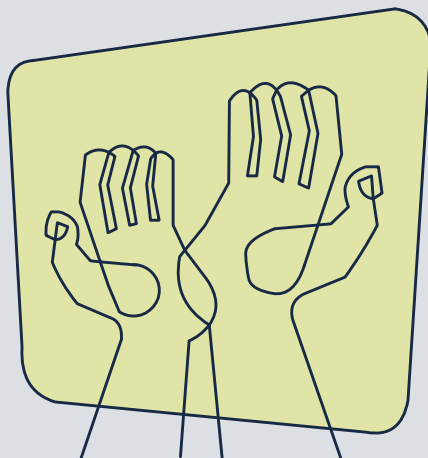
New Possibilities

Driving home from Shoemaker's office, there was a moment when I realized a new diagnosis opened up new treatment possibilities. Suddenly, the world was a very different place. At various points during the antibiotic treatment, if I experience a severe Jarisch-Herxheimer reaction (an immediate worsening of all symptoms while taking antibiotics, essentially a "die-off" reaction caused by a cytokine storm of TNF and MMP-9), Shoemaker will prescribe Actos to stem the tide. I'm instructed to call immediately if I start to feel much worse. Since Actos blocks cytokines, it's a pretreatment before taking CSM, which can also cause increased cytokines if the patient isn't adequately pretreated.

Actos is a drug usually given to diabetics. The difference between Shoemaker's approach to treating Lyme is that he'll give oral antibiotics, like the oral Amoxicillin I took, a chance to do the job, but if the patient is still having symptoms, then he uses the Actos/CSM protocol to give the antibiotics an even better chance. "The response of

a patient to Actos/CSM is predictable - if the Lyme organism is dead you'll improve," he says. "If there are still Lyme organisms actively circulating, however, then the patient must be treated with additional antibiotics, justifying the extra cost and risk." If still symptomatic after round two of antibiotics, then Shoemaker tries another CSM/Actos regimen. He's perfectly convinced that Lyme is both an infectious and a neurotoxic disease, so it makes sense to pulse these drugs alternatively, giving

"I'M ACTIVELY WRITING EVERY DAY, SOCIALIZING AND LIVING AN ALMOST-NORMAL LIFE. I'M CAREFULLY PACING MYSELF, FOLLOWING A STRICT DRUG REGIMEN AND OTHERWISE TAKING GOOD CARE OF MYSELF. I CAN'T BE SURE WHAT THE FUTURE HOLDS, OF COURSE. BUT I HAVE MORE HOPE OF RECOVERY THAN I'VE HAD FOR A LONG TIME."



the drugs a chance to work on both.

The first time we tried the CSM/Actos regimen, it didn't work - it made me feel worse slowly. Since I had been improving on Amoxicillin prior to that, a return to low energy, napping in the afternoon and all of the other symptoms I'd suffered didn't make me confident. But Shoemaker assured me that the return of

those symptoms meant I still had Lyme organisms circulating, so we switched to another antibiotic, Doxycycline. Within a few days, I felt better. Within a week, I was back to feeling great. I've been on the Doxycycline for almost a month now, and soon we'll try another CSM/Actos treatment. If the oral antibiotics don't continue to do the job, we'll try intravenous ones. If the antibiotics have done their job well, the Actos/CSM treatment will draw the neurotoxins out of my body, allowing it to heal on its own.

The other day for the first time in many years, I woke up feeling refreshed and energetic, ready to tackle the world at 7 a.m. What a difference from before, when I'd have to start the day slowly, hoard my energy and hope that I'd have enough to read or write a bit by noon or 2 p.m. Maybe I'd get a second wind later in the evening and be able to write, read or think a bit, but many days, I didn't have any energy at all and was unable to accomplish much of anything.

I'm not sure how 20 years of CFIDS has damaged my body, or what effect that damage will have on my Lyme Disease treatment. But I'm feeling better now than I have since - well, I can't even remember feeling this good, it's been so long. I've had so much energy, I moved into a new apartment recently and had everything organized within three weeks. I'm actively writing every day, socializing and living an almost-normal life. I'm carefully pacing myself, following a strict drug regimen and otherwise taking good care of myself. I can't be sure what the future holds, of course. But I have more hope of recovery than I've had for a long time. ■■

Editor's Note: To read this article (Part Two) in its entirety including the author's sidebar and complete references, please go to <http://www.ImmuneSupport.com/library/showarticle.cfm?id=4291>. Part One of this article was published in Healthwatch Volume XI, No. 4, 2002 and can be read online at <http://www.ImmuneSupport.com/library/showarticle.cfm/id/3990/>.

**INSULIN POTENTIATION THERAPY:
A NEW APPROACH TO TREATING
CHRONIC FATIGUE SYNDROME AND
FIBROMYALGIA**

An exclusive interview with Dale Guyer, M.D.
continued from page 1

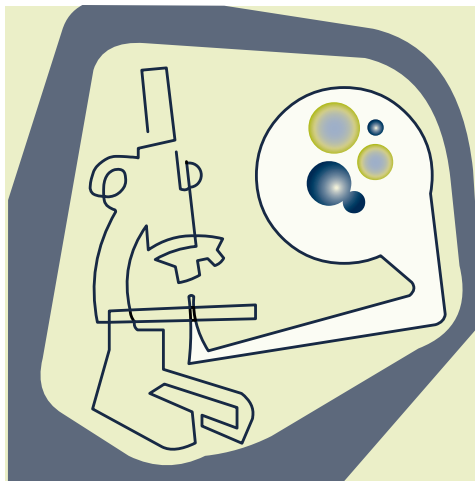
viruses such as CMV (cytomegalovirus), EBV (Epstein-Barr Virus), and HHV-6 (human herpes virus 6). This will usually be confirmed by follow-up testing utilizing PCR analysis. Secondary bacterial infections are not unusual to discover as well. They may include strains of mycoplasma, chlamydia, and streptococcus to name a few.

Generally speaking, successful treatment involves engaging a comprehensive or holistic approach to better understand the entire picture, which will lead to enhanced clinical outcomes. Paying attention to the balance of the endocrine or hormonal system, detoxifying the body of toxic heavy metals, treating chronic infections, boosting nutritional status, and correcting nutritional deficiencies will often go a long way to assisting many individuals to getting back on their feet and reestablishing their functional best. Unfortunately, there are many patients who are not helped by the best holistic treatments or have incomplete responses. These tend to be the "tough cases" in the field of physicians, like myself, who tend to specialize in CFIDS/FMS treatment. As would be expected it can be frustrating for the patient who just wants to get back to feeling like they are experiencing a normal life.

During the last two years, we are seeing enormous success in treating these tough cases using a combination of Insulin Potentiation Therapy (IPT) and Low Dose Foscavir (LDF). To my knowledge, this approach has not been done elsewhere as of this time. Foscavir is an intravenous antiviral medication that is FDA-approved in the treatment of herpetic viral infections.

IPT has in recent years emerged as a viable option for cancer treatment in combination with low dose chemotherapy. Because of the potentiation effects of insulin, the dose of chemotherapy agent required is usually about one-tenth of a typical dose. Using this approach, the chemotherapy drug has higher selective

uptake in cancer cells inducing greater cell killing ability while sparing normal healthy cells. Obviously, since the required chemotherapy dose is so low, it is generally devoid of side effects. (For those interested in reading more about IPT treatment for cancer they should obtain a copy of Dr. Ross Hauser's new book, *Treating Cancer with Insulin Potentiation Therapy*.)



The idea for creating this unique therapeutic approach originated from seeing a film documenting the successful treatment of polio virus using IPT by its founder, Donato Perez Garcia, M.D., and in addition, the writings and medical experience of Dr. Jean-Claude Paquette espoused in his book, *Medicine of Hope: Insulin-Cellular Therapy*. (You can read this book online at http://www.iptq.com/medicine_of_hope.htm). So the idea was to utilize a combination of IPT, which by itself has antiviral and anti-bacterial activity, with Low Dose Foscavir to more effectively eradicate the viruses causing CFIDS/FMS. To date, the patients treated with this approach have been those who have been non-responders to the usual comprehensive treatments provided. Generally, we have utilized a series of 5-10 treatments depending on a patient's severity. In our experience, most patients notice an improvement within the first couple of treatments. The typical feedback from patients is that energy levels and physical stamina increase, overall mood and happiness are improved, and flu-like symptoms of achiness, sore throat, and lethargy resolve. Also important to note is that follow-up laboratory testing to evaluate viral levels in these patients also demonstrate improvements.

HW: This is a fascinating new treatment. Could you describe its basic administration?

Dr. Guyer: Generally this treatment occurs in three stages. An important component to remember is that the concurrent administration of insulin makes every other treatment work more effectively whether it be nutritional or pharmaceutical. So generally, we have patients take a series of oral supplements including Transfer Factor, and we then follow-up about 20 minutes later with a series of intramuscular injections using Kutapressin and Vitamin B12. Then the patient is given a low dose of intravenous insulin, and gradually over the next 20-30 minutes the blood sugar level will drift downward. Our goal is to see that the blood sugar gets down to about the mid-20's. At this point and time this is known in IPT circles as the "therapeutic window." This is the timeframe when cell membrane permeability is at its maximum, and cell uptake of the active medicines will be greatest.

At that point and time we initiate the administration of the IV antiviral medicine, and then we begin a reversal process by the administration of IV glucose. Doing this provides for a fairly rapid turnaround, and within a few minutes the patient is generally feeling normal and able to eat and drink. Generally we provide them with Gatorade to rebuild the blood sugars and a protein bar or snack to help provide additional calories. Their subjective feelings are usually the same as somebody who would for a very short-term time period experience hypoglycemia, and that is the sense of feeling sometimes lightheaded, hungry, and thirsty. This should not be confused with the historical notations of insulin coma induction often used in the 1930's and 1940's to treat chronic clinical depression. The patients using this modified IPT approach actually are quite conversant, alert, and oriented, and really do not report any feelings that are negative. The IV treatment with the medicine is continued for the next two hours.

On occasion, depending on a patient's needs, we will include other adjunctive therapies such as UVB, Ozone and intravenous IV nutrient therapies with a

high dose of Ascorbic Acid and Trace Minerals. The whole procedure can take anywhere from 3-5 hours depending on which medicines are administered as some of the antiviral drugs require a prolonged timeframe of administration. Generally, we would do the treatments once to twice weekly as needed.

HW: *How would you determine the best patient candidates to benefit from this procedure?*

Dr. Guyer: In my experience, these are often patients who have had a history of the flu-like illness I mentioned previously and subsequently complain of feeling chronically run-down, tired, physically exhausted, achy in the joints and muscles, and in general experience viral flu-like symptoms. In addition, on their laboratory analysis they tend to have high antibody levels to the viruses previously mentioned and often positive PCR analysis as well.

HW: *It would seem likely that other illnesses such as Hepatitis C, Lyme Disease, and even HIV may respond to this type of approach.*

Dr. Guyer: Yes, indeed there is currently a fair amount of collective experience with other practitioners utilizing IPT treatment and myself included showing some initial positive results. I think we are possibly too early into this process to predict the outcome for those illnesses with any certainty.

HW: *One question that is on almost every patient's mind when it comes to receiving treatment relates to insurance coverage. What has been the feedback on this topic?*

Dr. Guyer: Since the medicine administered (Foscavir) is FDA approved, the reimbursement individuals receive is generally very good. **HW**

If you are interested in learning more about this promising new treatment, visit Dr. Guyer's website at www.daleguyermd.com.

DRUG NEWS BRIEFS



PREGABALIN SHOWS BENEFITS FOR FIBROMYALGIA PATIENTS

Pregabalin appears to be effective and safe in treating patients with fibromyalgia, according to new clinical trial findings. It may also improve sleep quality, fatigue, and increase quality of life, research suggests. Leslie Crofford, M.D., from the University of Michigan, Ann Arbor, and colleagues presented their findings at the American College of Rheumatology (ACR) 66th Annual Scientific Meeting in October 2002. According to Dr. Crofford, the mechanism of action of pregabalin is "not completely understood," but it binds to calcium channels, modulating calcium influx, which results in analgesic, anxiolytic, and anticonvulsant activity. "Treatments for fibromyalgia are limited," Dr. Crofford told Medscape, "and pregabalin represents another treatment option compared to tricyclic antidepressants and serotonin reuptake inhibitors, which have also been shown to be useful in smaller studies," she said.

NEW DRUG SHOWS PROMISE AGAINST CANDIDA INFECTIONS

In the first large-scale trial of its kind, researchers have shown caspofungin, a new type of antifungal drug, to be as effective and less toxic than amphotericin B, the current standard treatment for candidiasis. Candidiasis is the fourth most common bloodstream infection detected in hospitalized patients, and causes death in 30 to 40 percent of cases. "Echinocandins," including caspofungin, are a new class of medication that will treat fungal infections by directly targeting the structure of the fungal cell wall. "This study represents the first comprehensive trial comparing echinocandin and polyene treatments for invasive fungal infections," said John Perfect, M.D., professor of medicine at Duke University Medical Center and senior author of the study published in the December 19, 2002 New England Journal of Medicine. "I consider the results of this trial to be an advance that may help change the way physicians approach the treatment of candidiasis. Caspofungin is a safe and effective treatment for a variety of candida species which frequently infect hospitalized patients."

MILNACIPRAN SIGNIFICANTLY IMPROVES PAIN AND FATIGUE IN FM

Cypress Bioscience Inc.'s drug milnacipran developed for treatment of Fibromyalgia Syndrome (FMS) was shown to provide statistically significant improvement of pain and fatigue symptoms in a preliminary analysis of the Company's Phase II clinical trial. The study evaluated the efficacy and safety of milnacipran for the treatment of pain and associated symptoms such as fatigue, depressed mood and sleep. Patients were asked to characterize their pain, fatigue, sleep and related symptoms several times each day on an electronic diary. Milnacipran-treated patients randomized to the twice a day dosing group (BID) showed statistically significant improvements in pain compared to those who received placebo. Of the 95 patients that had completed the trial as of the date of this analysis, 87 percent of all milnacipran-treated patients reported overall improvement, compared to 33 percent in the placebo group (p less than 0.001). Further, 36 percent of milnacipran BID-treated patients reported at least a 50 percent reduction in pain intensity, compared to 9 percent of patients who received placebo, a difference that was statistically significant (p=0.030, intent to treat analysis).

In addition, milnacipran-treated patients showed significant improvements in fatigue and depressed mood. "It is extraordinary to see such a significant improvement in symptoms in this patient population," said Dr. Daniel Clauw, Professor of Medicine, Division of Rheumatology; director, Center for Advancement of Clinical Research; and director, Chronic Pain and Fatigue Research Center, The University of Michigan and chairman of Cypress' Rheumatology Advisory Board. A final analysis of the trial, including all enrolled patients, will be available early in 2003. It should be noted that response rates and significance levels may change when the final analysis is performed.

NEW DEVELOPMENTS IN THE MANAGEMENT OF FIBROMYALGIA SYNDROME

continued from page 1

(approximately 5 million persons), and a similar prevalence seems to exist worldwide. Furthermore, it appears that 6% to 10% of all individuals in a medical physician's waiting room have FMS, so most physicians with active clinical practices can expect to relate to at least one patient with FMS daily.

BIOCHEMICAL ABNORMALITIES

The most dramatic laboratory abnormality, found in most FMS patients (>80%), is a consistently elevated, stable level of cerebrospinal fluid (CSF) substance P (SP). All of the 4 research groups that have studied the levels of this neuropeptide in FMS cerebrospinal fluid have found similarly elevated levels despite populations of patients from different ethnic backgrounds. Furthermore, elevated levels of CSF SP for patients who were not undergoing treatment did not fall spontaneously during a 1-year period. In addition, there are correlations of the CSF SP with the excitatory amino acids in the CSF of FMS patients. The biogenic amines [chemical compounds important in neurotransmission] that naturally regulate the release of substance P are deficient in the CSF of people with FMS. There also is growing evidence for abnormalities in the hypothalamic-pituitary-adrenal, gonadal, and growth hormone axes. It is possible that some or all of these abnormalities result directly from the recognized abnormalities in biogenic amines and neuropeptides. Finally, as with rheumatoid arthritis, the morning serum hyaluronic acid (HA) level has been found to be elevated in FMS, and the change in HA from midmorning to noon correlates with the patient's perceived severity of morning stiffness.

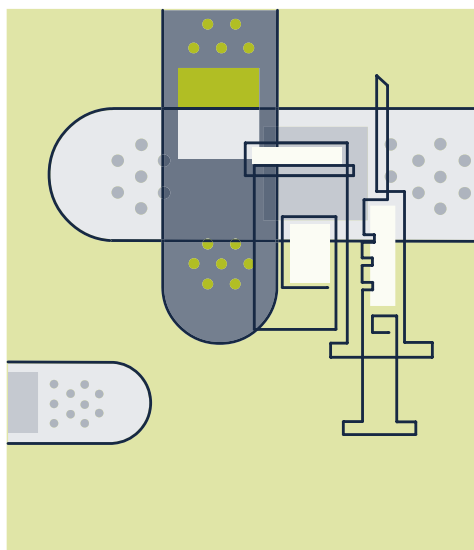
TREATMENT

The most common approach to treatment of FMS is multimodal and includes patient education, psychological support, physical modalities such as exercise, and medications. The perception that pain

medications, with their potential risks, are not indicated in FMS because it is a benign condition has now been countered by the documentation of objective evidence that FMS patients are actually experiencing the pain they describe. Medication therapy of FMS has variously involved over-the-counter preparations, analgesics, and antidepressants, but patients seldom achieve complete relief from any kind of monotherapy.

BENEFIT FROM NORMALIZATION OF SP?

Tizanidine is a relatively new, centrally acting, α_2 -adrenergic agonist that has been approved for the treatment of spasticity, such as that occurring in patients with multiple sclerosis or spinal cord injury. This agent is believed to act like norepinephrine by inhibiting polysynaptic pathways involved in the activation of motor neurons. Ono and colleagues have documented the effects of tizanidine and clonidine [The FDA has not approved these medications for this use at this time] on the in vitro release of SP from slices of rat spinal cord tissue. In this study, exposure of the cord tissue to 10 $\mu\text{mol/L}$ of clonidine or tizanidine significantly reduced veratridine-induced release of SP in vitro.



If tizanidine were to exhibit the same effects on human spinal cord tissue in vivo, it might be possible to document a reduction in the elevated levels of CSF SP in patients with FMS. This hypothesis was the basis for an open-label study

conducted by Russell and colleagues from the University of Texas Health Science Center in San Antonio. The study focused on a single biological outcome variable (change in CSF SP level with tizanidine treatment) as the primary outcome variable. Because it had been previously demonstrated that FMS CSF SP levels do not fall spontaneously (without treatment), it was accepted that any observed fall in CSF SP levels during medication treatment would represent a therapeutic effect.

The study enrolled 25 primary FMS patients who met the ACR classification criteria for that condition and 23 completed 8 weeks of on-therapy follow-up. Patients discontinued use of FMS medications for 2 weeks before their baseline assessment. Radioimmunoassay for SP was performed on CSF samples at baseline and on stable monotherapy at week 8. The tizanidine dose ranged from 4 mg at bedtime to 24 mg/d in divided doses, as tolerated. Secondary outcome variables measured at the same visits included serum HA levels and clinical assessments such as the Sleep Efficiency Scale (SES), the Stanford Health Assessment Questionnaire (HAQ), the Fibromyalgia Impact Questionnaire (FIQ), the Pain Visual Analog Scale (PVAS), the Tender Point Index (TPI), and the Average Pain Threshold by dolorimetry.

The average CSF SP level fell significantly ($P = .02$) with tizanidine therapy but did not normalize to below 20 fmol/mL . Among the secondary measures, the mean serum HA level fell numerically but that reduction was not significant. SES ($P = .02$), PVAS ($P = .01$), HAQ ($P = .01$), and FIQ ($P = .02$) scores improved but the others did not change significantly, and none of the clinical changes correlated with the decrease in CSF SP levels. Interestingly, several key clinical variables correlated with the smaller decrease in HA ($P = .03$ to $.04$). One subject left the study because of abnormal liver function and another because of hallucinations. Five patients experienced transaminitis, which responded to tizanidine dose reduction or discontinuation.

This was an open-label study so the influence of placebo on the clinical variables could not be assessed.

However, the primary outcome variable for the study was an objective laboratory test (CSF SP) that should be less subject to hopeful enthusiasm. The critical observation was that potent alpha2-agonist therapy significantly reduced the levels of CSF SP in this FMS cohort. This finding supports the hypothesis that excess CSF SP production in FMS is caused by recognized deficiencies of endogenous, caudally directed, inhibitory biogenic amines.

What is not known is whether the reduction in CSF SP in this study was achieved entirely by inhibiting afferent neuron production of SP or whether it included inhibition of SP production in brain and spinal interneurons as well. It is certainly possible that serotonergic activity [relating to serotonin as a neurotransmitter] would be additive or synergic with that of the tested alpha-adrenergic agent. Other inhibitory receptors may also be active in this regard. The secondary outcome measures in the reported study were also of interest. Tizanidine treatment of FMS patients was accompanied by significant improvement in the subject's perception of their sleep, subjective pain, and reported physical function. None of the secondary outcome measures from baseline to week 8 of tizanidine therapy correlated with the change in CSF SP levels. This may have been true because the levels of CSF SP did not actually normalize under the conditions of this study. It may be necessary to therapeutically reduce the CSF SP levels to normal because small increases could be sufficient to amplify nociception [pain sensations]. On the other hand, a trend toward falling serum HA levels correlated with improvements in clinical scores.

These findings suggest that serum HA may be a useful measure of clinical response to therapy in FMS. Thus, in this study, tizanidine was well tolerated and may be clinically useful in the treatment of FMS; however, transaminase levels should be monitored during continuous therapy.

INHIBITION OF SEROTONIN AND NOREPINEPHRINE

Zijlstra and associates from the Department of Rheumatology at

centers in Enschede and Rotterdam, the Netherlands, cooperated in a study that examined the benefits of the antidepressant venlafaxine for patients with FMS [The FDA has not approved this medication for this use at this time]. The mechanism of the proposed benefit of venlafaxine in FMS relates to its recognized inhibition of both serotonin and norepinephrine reuptake into neurons that have released them into a central nervous system synapse. The investigators alluded to a previous open-label trial that suggested benefit of this drug in 6 of 15 study participants. Wisely, the current investigators proceeded to a randomized, placebo-controlled trial. Ninety primary FMS patients who met ACR criteria were randomized to receive venlafaxine at 75 mg/d (n = 45) or placebo (n = 45) for 6 weeks. The sample size was reasonable, standard outcome measures were used, and the statistical analysis was appropriate. The only real difference in outcomes between the groups was that significantly more of the subjects in the venlafaxine group dropped out of the study because of adverse effects (P = .01).



Although venlafaxine inhibits the reuptake of both serotonin and norepinephrine, the differential ratios of the effects on these 2 biogenic amine receptors are known to vary with the dosage. In low doses, venlafaxine can behave like a selective serotonin reuptake inhibitor (SSRI), but at higher dosages it more effectively inhibits norepinephrine reuptake as well. The 75-mg/d dosage is in the low range and probably was primarily influencing serotonin. A previous study with a low dose of a different medication, the SSRI

fluoxetine, was effective for relieving anxiety, depression, and insomnia in FMS but not for the pain. A more recent study using substantially larger dosages was more successful with subjective pain.

USING A NOVEL ANTICONVULSANT

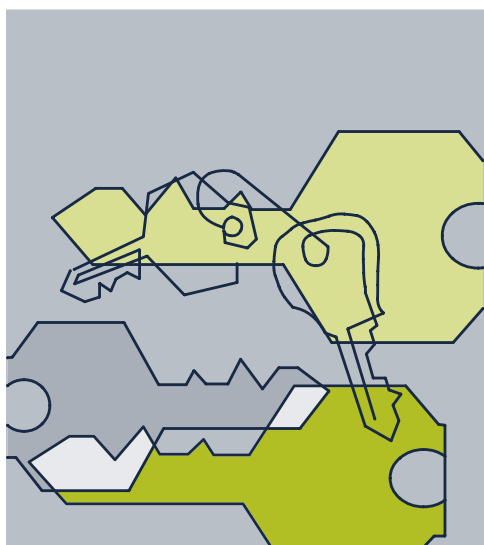
Pregabalin is a second-generation anticonvulsant agent similar to gabapentin but about 6-fold more potent. Because of their structural similarity to gamma aminobutyric acid [GABA], these drugs were believed to function as neural inhibitors; however, their mechanism of action may actually relate to inhibition of the preganglionic calcium-gated channel. In animal models of chronic pain, pregabalin has been found to be effective in raising the pain threshold, reducing allodynia, increasing slow-wave nonrapid eye movement sleep, relieving anxiety, modulating acute pain symptoms, and reducing colon-related pain.

However, it may also induce nocturnal myoclonus. An 8-week, multicenter, randomized, double-blind, placebo-controlled study by Crofford and coworkers from the University of Michigan, Ann Arbor, and colleagues from several other institutions evaluated the efficacy and safety of pregabalin in patients with FMS [The FDA has not approved this medication for this use at this time]. Patients diagnosed as having primary FMS completed a 1-week baseline phase before the 8-week, fixed-dose treatment phase. A total of 529 patients were randomized to receive placebo, 150 mg/d, 300 mg/d, or 450 mg/d of pregabalin.

Patients used an 11-point numeric rating scale to measure and record their pain level in a daily pain diary. Secondary outcome measures were assessed with the Short Form McGill Pain Questionnaire (SF-MPQ), the sleep quality diary, the Medical Outcomes Study (MOS) Sleep Scale, the Multidimensional Assessment of Fatigue, the Patients' Global Impression of Change (PGIC), the Clinical Global Impression of Change (CGIC), and the 36-Item Short-Form Health Survey.

Patients treated with the highest dose,

450 mg/d, of pregabalin experienced significant improvement in the end point mean pain score ($P < .001$) compared with those receiving placebo and were more likely to experience a 50% reduction in pain from baseline to end point ($P = .003$). Likewise, the mean SF-MPQ and visual analog scale pain scores were both significantly improved at each follow-up visit and at the end point for this treatment group compared with placebo. For patients receiving either 300 or 450 mg/d, other variables, such as the mean sleep quality, fatigue, and CGIC and PGIC scores at end point were improved significantly. Patients in all treatment groups demonstrated significantly improved MOS-Sleep Index scores.



In total, 48 patients (9%) withdrew from the study because of adverse side effects (most commonly dizziness and somnolence) and 44 (8%) because of poor efficacy. This study represents an important achievement in the field of FMS and specifically for patients with FMS for several reasons:

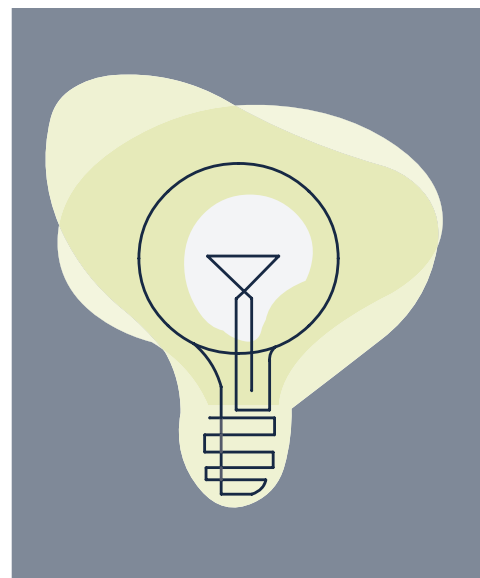
- A new medication in the therapeutic armamentarium [tools and resources] for FMS offers an additional option for patients who have experienced intolerance to earlier medications.
- This drug expands by one the classes of drugs that have demonstrated benefit in the management of the central neuropathy of FMS.
- Although it is not necessarily true that other members of the anticonvulsant family of drugs will be helpful for this

condition, researchers who pioneer the development of designer drugs now have another model to consider.

- The drug is backed by a major pharmaceutical house with the resources to carry it through the FDA to achieve an indication.
- An FDA-approved indication will provide a form of legitimacy to the FMS diagnosis that will promote better acceptance of the disorder, in part, because there is an accepted efficacious treatment the physician can use when the diagnosis is made.
- The usual process of pharmaceutical marketing will require clever advertisements and continuing medical education programs that will also inform physician prescribers how to properly diagnose FMS.
- Pharmaceutical marketing programs, particularly the new trend toward direct patient marketing, will raise awareness of the disorder among patients with undiagnosed conditions, nonphysician health care professionals, politicians, and the general public.
- Education programs will require additional discussion of other agents of different classes that have been found to be effective for FMS, and these other agents will become better known.
- Profits from the success of one drug on the market indicated for FMS will encourage other companies to risk creative entry and investment in the field.

SUMMARY

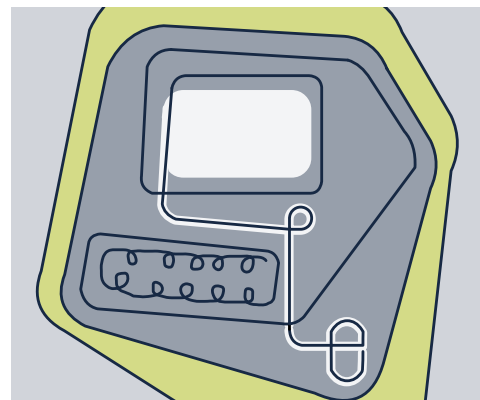
Fibromyalgia is a common syndrome of widespread soft tissue pain that is substantially underserved by the medical profession and the pharmaceutical industry. This field of inquiry and patients with FMS would be better served by an improved understanding of the biologic and physiologic processes responsible for the symptoms of FMS. The finding that elevated levels of CSF SP in FMS respond to a potent alpha-adrenergic agonist drug (tizanidine) provides encouragement to try other similar interventions, including combinations of drugs with recognized separate inhibitory activity at specific sites in the



pathogenesis of FMS. Finally, another trial found that the investigational agent pregabalin improved many of the typical symptoms of FMS. Thus, two therapeutic agents with different mechanisms of action may now be added to the FMS therapy armamentarium.

Some important questions have yet to be addressed. What kinds of biochemical and physiologic changes predispose individuals to developing the disorder, and how have these rendered patients susceptible to FMS? Can these changes be manipulated by psychological or psychophysiological interventions? Which steps in the nociceptive process might be altered to produce clinical benefits? The 2002 American College of Rheumatology (ACR) meeting provided a number of key answers to critically important questions. Undoubtedly, the 2003 ACR meeting will prove equally rich in ideas. **HW**

The entire text of this report including the complete list of scientific references can be read at: <http://www.medscape.com/viewarticle/445110>.



RESEARCH SHOWS PHOSPHOGLYCOLIPIDS PROTECT CELLS AND FIGHT FATIGUE

Phosphoglycolipids [also known as glycopospholipids] are essential for the structure, function and regeneration of all biological membranes. Healthy cells have fluid membranes rich in lipids that enable proper cell-to-cell communication. Preventing loss of membrane integrity and the resulting loss of cellular energy may be accomplished, in part, by replacing the damaged lipids. Protecting cell membrane integrity is believed to enhance cellular health, energy, and efficient metabolism.

Three recent human clinical studies have concluded that a multi-nutrient formula rich in phosphoglycolipids significantly reduces fatigue among patients. One of these studies included cancer patients undergoing chemotherapy; in addition to improvements in fatigue, they also reported reduced vomiting, nausea and diarrhea. Animal studies of phosphoglycolipid-rich formulas showed 20% greater preservation of mitochondrial function, nerve function and DNA among animals receiving supplementation. It is important to note that delivery of intact phospholipids through cell membranes is crucial for repair to take place.

HUMAN FATIGUE RESEARCH STUDY

A scientific study¹ was conducted to determine whether fatigue, as defined by the Piper Fatigue Scale (PFS), could be significantly relieved by use of a phosphoglycolipid-rich dietary supplement [Propax™ with NT Factor™] in a targeted sampling of the general population (mean age=50.3 years). Sixty four (64) subjects completed the self-reported PFS and were admitted to the study when their self-reported sign/symptom severity scores were converted to fatigue scores and rated as high moderate to severe fatigue. The PFS has been shown to accurately reflect the multifactorial nature of fatigue through statistical factor analysis and clinical studies.

Using the Piper Fatigue Scale, there was a 33% reduction in fatigue after eight weeks of supplementation. The PFS rates fatigue from a score of 0 (no fatigue) to 10 (severe fatigue). The average initial fatigue score for the group before treatment was reported as severe (mean score=7.9± 0.82 SD, range=6.4-9.9). After the fourth week of supplementation, the average fatigue score was rated as moderate (mean=6.1±1.66 SD, range =2.6-9.5) (p<0.0001). At the eighth week of supplementation, the final average score was rated as moderate (mean=4.7±2.01 SD, range=1.5-9.4) (p<0.0001). In this self-reported study, dietary supplementation significantly reduced fatigue as measured by the PFS. While this pilot study did not compare the study product with a placebo, the response generated in the initial survey was significant enough to warrant further investigation in an expanded, controlled study utilizing a placebo.

HUMAN MITOCHONDRIAL STUDY

Research conducted at The Institute for Molecular Medicine in Huntington Beach, California² evaluated the effects of NT Factor™ on mitochondrial function in an elderly population (average age 69 years, n=20). Mitochondria of peripheral blood cells were isolated using flow cytometry and stained with fluorescent reducing dye Rhodamine 123. Involvement of mitochondrial function in 8 weeks reached levels normally seen in early middle age. Continued use maintained improved levels. Patients' fatigue improvement as measured by the published Piper Fatigue Scale correlated with increased mitochondrial function. A washout period caused function to return to near baseline indicating a need for continued use. Dosing during the study was 3 tablets twice daily. All statistical measurements were considered significant.

HUMAN CHEMOTHERAPY RESEARCH STUDY

The effect of Propax™ with NT Factor™ has been documented in a double-blind, crossover placebo-controlled, randomized study on cancer patients undergoing chemotherapy.³ Thirty-six patients with cancer were enrolled in the 12-week pilot study. The consumption of the recommended daily dosage of Propax™ with NT Factor™ (12 tablets and 3 softgel capsules) resulted in an improvement or no change or worsening in chemotherapy-related side effects of fatigue, nausea, impaired taste, diarrhea, general tiredness, constipation and insomnia. These results were assessed by the Quality of Life (QOL) questionnaires completed by patients and nurses participating in the study.

Fatigue is one of the most common complaints in cancer patients, in addition to the numerous adverse reactions associated with the administration of chemotherapy. The results of this pilot study, both open-label and double-blinded placebo-crossover in design, indicate that patient perception of benefit with multi-nutrient phosphoglycolipid supplementation to chemotherapy is significant in reducing fatigue and other chemotherapy-induced toxicities.

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ACHIEVING EFFECTIVE RESULTS WITH GUAIFENESIN

Paul St. Amand, M.D., Assistant Clinical Professor of Endocrinology at Harbor-UCLA believes guaifenesin therapy can significantly help fibromyalgia (FM) patients combat their symptoms and lead normal, healthy lives.

Dr. St. Amand's theory of the medicinal effects of guaifenesin for FM is based on the premise that excess calcium and inorganic phosphate compounds accumulate within cells to produce a state of hyperpermeability. This condition allows excess fluids, ions and other unwanted substances to flow into cell mitochondria, disrupting normal cell function, including production of ATP, the body's energy source. Dr. St. Amand believes these factors cause the body to experience an energy deprived state, in which widespread bodily functions are disrupted. Dr. St. Amand also feels a possible genetic defect in FM patients may be responsible for the abnormality in natural phosphate excretion, thus resulting in the buildup of these chemicals and subsequent symptoms.

WHAT IS GUAIFENESIN?

Guaifenesin is a common component of many cold and cough remedies that helps loosen and liquefy mucous. It is a safe medication that may even be used by children. Derived from a tree bark extract called guaiacum, it was first used to treat rheumatism during the 16th century. Twenty years ago, the extract was synthesized, pressed into tablets and named guaifenesin. Today, there are many formulations of guaifenesin available, the most popular being extended release tablets that deliver both immediate and long lasting effects.

THE ST. AMAND GUAIFENESIN PROTOCOL

Guaifenesin is regarded by Dr. St. Amand as the most potent drug to date for treating FM. In Dr. St. Amand's guaifenesin protocol, a physician maps the location, size and degree of hardness of swellings or lesions within muscles, tendons and ligaments all across the body. The map serves as a baseline for future comparisons during guaifenesin treatment. Patients also make note of variations in the amount of pain and fatigue they experience, and the combined input is used to determine the proper guaifenesin dosage and to confirm the regression of the disease.

The initial goal of guaifenesin treatment is to exacerbate the patient's symptoms. Dr. St. Amand stresses that the worsening of FM symptoms, or the appearance of new symptoms indicates that disease reversal has begun. Dosage generally begins with 300mg (one-half tablet) of time released guaifenesin twice daily for one week. If symptoms have not worsened, the dosage is increased to 600mg twice daily. As treatment continues and the reversal process progresses, periods of less intense symptoms appear. As time passes, these periods cluster into days and weeks and lesions begin to clear. He has also reported a 60% increase in phosphate excretion and a 30% increase in oxalate in patients' urine, indicating that the offending compounds are effectively being removed from the body.

SALICYLATES

An important part of Dr. St. Amand's protocol focuses on the avoidance of salicylates. In nature, salicylates are manufactured by plants as a defense against bacteria and fungi. Aspirin and other herbal or plant based products contain salicylates or salicylic acid. Any product containing salicylates can completely block the benefits of guaifenesin. The human body easily absorbs salicylates through the skin and intestines, so patients taking guaifenesin must be wary of medicines, supplements, lotions, cosmetics and even garden plants which can neutralize guaifenesin treatment.

RESEARCH

In 1995 the only double blind, placebo controlled study of guaifenesin in FM was conducted by Robert Bennett, M.D. and fellow researchers at the University of Oregon¹. Time released guaifenesin treatment (600mg twice daily) was administered to 20 female FM patients. Results showed guaifenesin was no more effective at relieving symptoms of FM than placebo. However, according to Dr. St. Amand, there may have been some flaws in the study that resulted in the poor results. He cites these key points in refuting the study findings:

1. The study was conducted before anyone knew the signs of reversal are not apparent if the subject has uncontrolled reactive hypoglycemia. At the time, the frequency of reactive hypoglycemia was relatively unknown.
2. The complete range of salicylate containing products and their capacity to block the effects of guaifenesin was not well known during the study. Also, each patient seems to have a different sensitivity to products containing salicylates.
3. Inadequate dosage may have been a factor. St. Amand reports that only 20% of his patients improve with a 300mg dose of time released guaifenesin twice daily, while at 600mg (time released) twice daily, 70% of patients improve.

Dr. St. Amand points out that guaifenesin treatment is trying. As the disease reverses, patients feel symptoms intensify and new or dormant symptoms can surface. This causes some patients to doubt their progress during the initial stages of treatment; however, Dr. St. Amand reports that as good days begin to accumulate, patients will have more confidence and strength to go on with treatment. Guaifenesin is not a cure for FM; the underlying condition that caused the build up of phosphates remains, and will return if the patient ends therapy. Therapy is a long term commitment but may offer significant rewards.

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METHIONINE FOR MERCURY DETOXIFICATION

Studies have shown the protective effects of Methionine in animal models against mercury, lead and atrazine (an herbicide). Methionine is an essential sulfur amino acid and is listed on the FDA's "generally regarded as safe" list. It was once used in soy-based baby formulas to provide adequate Methionine nutrition for infants.

Methionine is a critical component of tissue development, growth and tissue repair for all humans – no matter what the age. Methionine functions as an antioxidant (free radical deactivator) and helps neutralize toxins. It serves as a principal source of sulfur that the body needs to replenish daily. Sulfur is used for mucous production and detoxification.

MERCURY, THE ENVIRONMENT AND HUMAN TOXICITY

Mercury is a shiny, silver-white, liquid metal, or if heated, a colorless, odorless gas. Unfortunately, mercury is one of the primary pollutants in our environment. It enters the air during mining, burning coal and waste, and from industrial manufacturing.¹ It then falls from the atmosphere through precipitation and is deposited into rivers and lakes where it is absorbed by fish. While pollution spreads this metal throughout the environment, mercury can also be found in our homes and even in our teeth. Amalgam dental fillings contain mercury as do thermostats and thermometers, lighting, and electrical equipment.²

SYMPTOMS OF MERCURY TOXICITY

If someone is exposed to large amounts of mercury it is possible that they may develop mercury toxicity. Common symptoms of mercury toxicity include fatigue, sluggishness, and low energy. Other health problems may include headache, neuromuscular pain and stiffness, poor concentration and memory, while affecting organs and body systems like the brain, lungs, kidneys and liver. Additionally, mercury may impair immune system and enzyme function, inhibit inflammatory processes and alter metabolic pathways.³

According to a Center for Disease Control and Prevention (CDC) report⁴, chronic exposure to mercury can result in "a variety of manifestations of central nervous system toxicity," that is, high levels of mercury in your brain and spinal cord may cause memory loss, mental illness, and changes in or loss of hearing, vision, or taste. The CDC states mercury toxicity should be considered as a probable cause in cases where neurologic symptoms like these are of unclear etiology.

MERCURY TOXICITY RESEARCH

A study conducted at the Uppsala University Medical School in Sweden⁵ reported that chronically ill patients contain abnormal levels of mercury within their cells. Of the 25 chronically ill participants, the researchers determined that 12 had Chronic Fatigue Syndrome. After a three-week

period in which patients were not allowed to supplement with trace elements and vitamins, blood samples were taken and analyzed for cellular levels of mercury. Levels exceeding the detection limit (0.5 ug/g dry weight) were found in 14 patients and in 5-15% of their red blood cells. For the studied granulocytes (another red blood cell) 20 of the 25 patients displayed detectable mercury levels in 10-30% of the cells. The researchers concluded that all of the patients had an elemental profile suggesting a heavy metal burden that had influenced their health.

Another study presented at the International Symposium on Functional Medicine⁶ tested sensitivity to metals such as mercury and lead using a method of testing known as MELISA (Memory Lymphocyte Immuno Stimulation Assay). Of patients with Chronic Fatigue Syndrome, 45% showed mercury hypersensitivity and 49% showed lead hypersensitivity. When the metal burden was removed from the body (in many cases by removing mercury-containing silver dental fillings), 77% of patients reported improved health.

HOW METHIONINE WORKS

Methionine supports mercury removal by promoting the body's natural detoxification processes. Methionine suppresses and neutralizes toxic chemical activity, and functions as a chelator, a binding agent that deactivates and removes toxic metallic substances by altering their molecular structure. This process inhibits transport of mercury throughout the body, including the brain and central nervous system, where mercury may have its more harmful effects.

Methionine also promotes healthy levels of homocysteine, a toxic byproduct of the methylation process that, if left unchecked, may cause serious health problems.

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RESEARCH STUDY SHOWS SUPERIOR ABSORPTION OF CORAL CALCIUM BY HUMANS

Coral Calcium has been receiving much media attention as the widely preferred source for readily absorbable and accessible calcium in the body. The following study was undertaken to evaluate in humans whether mean intestinal absorption of coral-derived calcium (incorporated into crackers) might be comparable or even superior to mean intestinal absorption of calcium carbonate-derived calcium.

SUBJECTS & METHODS: Twelve normal subjects (6 men and 6 women) participated in the study. The subjects were divided into two groups; subjects of one group ingested coral-added crackers first (group A) and those of the other group ingested calcium carbonate-added crackers first (group B). After a subsequent 3-d wash-out period, the groups received the study regimens on a cross-over design. An additional group (group C) served as a control not ingesting crackers. Each 12-g piece of coral-added cracker contained 75 mg of calcium and 36 mg of magnesium. Calcium and magnesium contents of a 12-g calcium carbonate-added cracker were 75 and 6mg, respectively. Each subject ingested seven pieces of either cracker each time in this study since, according to Harvey et al¹, oral ingestion of 500 mg of calcium suffices for adequate evaluation of intestinal calcium absorption by measurements of urinary calcium excretion. The calcium intake and magnesium intake after the ingestion of 7 coral-added crackers were calculated to be 525 and 252 mg, respectively, and those after ingestion of 7 calcium carbonate-added crackers to be 525 and 42 mg, respectively.

RESULTS: Calcium absorption: The group receiving coral-added crackers and that receiving calcium carbonate-added crackers were practically comparable with respect to urinary calcium excretion during 2-h pre-ingestion. Mean urinary calcium excretion after the ingestion of coral-added crackers was greater than that after calcium carbonate-added crackers by four determination methods. Significant intergroup differences were noted in urinary calcium excretion during 4-h post-ingestion, increase in urinary calcium excretion (mg/dL OF) during the latter half of the post-ingestion observation period, and increase in urinary calcium excretion (A from control mg/mg Cr) during 4-h post-ingestion. However, significant difference was demonstrated for the first half of the post-ingestion observation period.

These findings were generally in line with the conclusions from absorption studies on calcium citrate [as found in coral calcium] versus calcium carbonate by Harvey et al¹ and Nicar and Pak² that calcium citrate was better absorbed. The males exhibited better calcium absorption from coral-derived calcium as compared with the females, though the subject sample sizes were small. Meanwhile, the increase in urinary calcium excretion during the subsequent 2-h period determined for reference, showed a plateau with no appreciable difference between the two cracker regimens. It was thus considered appropriate to assess the responses by

analyzing two consecutive 2-h post-ingestion urine samples for the comparison based on urinary calcium excretion.

DISCUSSION: The assessments of calcium absorption from supplemented crackers demonstrated a better absorption of coral-derived calcium than that of calcium carbonate-derived calcium on the average. A laboratory study in rats to explore the ability to utilize calcium derived from Ryukyuan coral which contains calcium and magnesium at a ratio of about 2-to-1 has been reported by Suzuki et al³. The investigators calculated the calcium balance from excretions in the feces and urine during the last 3 days of a 4-week rat feeding trial using coral. They concluded that the efficiency of calcium utilization was satisfactorily greater with coral-derived calcium as compared to calcium carbonate-derived calcium, although the difference observed did not attain a level of statistical significance. Suzuki et al also described that their concurrent test with a fivefold increase in dietary magnesium intake (i.e., 0.25% as against 0.05%) demonstrated a marked increase in urinary calcium excretion; hence, a better calcium absorption in the group fed on high-magnesium (0.25%) diet.

The present study was conducted under conditions with a higher rate of magnesium content (6-fold difference) as compared to the above two laboratory studies of Suzuki et al, viz. a magnesium content of 36mg (0.3%) per 12-g coral-added cracker versus a magnesium content of 6 mg (0.05%) per 12-g calcium carbonate-added cracker. While Suzuki et al have given no account of the high efficiency of calcium utilization from coral in their article, it would be reasonable to assume that the high magnesium content has some bearing upon the intestinal absorption of calcium when viewed together with consideration of the present human trial data. However, it is of importance to mention that problems such as coral calcium solubility in gastric acid, absorption from the intestine and reabsorption from the renal tubules per se should be discussed. Additionally, the potential involvement of magnesium and further basic studies are needed. The present data demonstrating the remarkably good absorption of calcium from coral containing calcium and magnesium in a ratio of 2-to-1 are of profound interest.

Study Authors: Kunihiro ISHITANI, Eiko ITAKURA, Shiro GOTO and Takatoshi ESASHI. Higashi Sapporo Hospital, Sapporo 003-8585, Japan.

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YEAST OVERGROWTH WREAKS HAVOC ON IMMUNE SYSTEM

Candida albicans is yeast normally found in small amounts in the warm interior membranes of the mouth, skin and digestive tract of healthy individuals. Typically, *Candida* does not cause any health problems as its growth is kept under control by the immune system and other "friendly" bacteria in the body. However, there are conditions that may disrupt the balance of bacteria and cause the overgrowth of *Candida*, producing an infection. This type of infection is called Candidiasis, and can range from superficial conditions such as sores in the mouth (oral thrush), vaginal yeast infections in women and diaper rash in infants, to dangerous invasive infections of the blood stream.

Candida infections occur when the immune system is weakened by disease, stress or medication. Other factors that may prompt *Candida* overgrowth include high blood sugar levels, excessive alcohol intake, use of birth control pills, low stomach acidity, and a poor diet high in fat.

Extended use of antibiotics can also play a significant role in the development of a *Candida* infection. Patients with medical conditions that require treatment with broad-spectrum antibacterial medications can have lower bacteria levels throughout the body, as antibiotics easily destroy friendly bacteria in the intestinal tract. Friendly bacteria are known as probiotics, and benefit the body by helping to digest protein and improve bioavailability and usage of vitamins and minerals. More importantly, friendly bacteria support the immune system by activating antibodies that protect the body from bacterial infection and disease.

If the balance of intestinal flora is upset and pathogenic yeast such as *Candida* becomes the dominant occupant of the intestinal tract, friendly bacteria may no longer effectively produce the antibodies and nutrients the body needs to be healthy. Once growth of *Candida* becomes unregulated and pathogenic it will begin to release large amounts of toxins that have harmful effects on tissues and organs, which in turn produces symptoms such as excessive fatigue, bowel and digestive problems, gas and bloating, food and mold allergies, skin rashes, depression and thyroid problems.

HOW IS CANDIDA TREATED?

According to the Mayo Clinic, a physician will typically prescribe an antifungal medication such as nystatin to lower levels of *Candida*. The normal course of treatment usually lasts about 10 to 14 days. However, prolonged treatment may result in the yeast becoming resistant to the medication. At that time, a drug called Amphotericin B (Amphocin) may be used when other antifungals are no longer effective. Safety may be an issue for some as certain antifungal medications may also have harmful effects upon the liver. As a result, a physician is likely to monitor liver function through blood tests, especially if the patient has a history of liver disease.

Modifying a patient's diet is also an important strategy in combating a *Candida* infection. As *Candida* thrives on sugar and simple carbohydrates, it is recommended that patients eliminate high sugar foods such as sodas, fruit juices, sweet desserts, high carbohydrate foods and other refined foods from their diet. Additionally, increasing levels of probiotic bacteria will also help reduce the amount of *Candida* and return the balance of intestinal flora to normal. Probiotic bacteria such as *Lactobacillus acidophilus* naturally produce inhibitory factors that limit the overgrowth of yeast. Probiotics can be most easily obtained by consuming sugar-free yogurt or by taking oral supplements.

Many integrative health care professionals utilize targeted transfer factors and/or natural egg-derived products containing transfer factor for powerful immune support by promoting a healthy digestive tract with targeted immune factors. These immune factors and humoral cofactors are formulated to provide the body with millions of naturally produced immunoglobulin that help support the immune system. Transfer factor proteins and humoral cofactors harvested from the yolks of immunized chicken eggs can provide the body with the information and nutrients it needs to promote normal immune function. The immune cofactors are isolated and purified using numerous rigorous techniques, and processed into a fine grain powder for consumption. Meticulous testing then ensures that the appropriate and effective levels of each immune factor are present.

In a study presented at the 10th International Symposium on Transfer Factor¹, Italian Researchers from the University of Bologna (Italy) tested two transfer factor (TF) preparations on 15 patients suffering from chronic mucocutaneous Candidiasis. The first preparation was an in vitro produced transfer factor specific to *Candida albicans* antigens, and the second included TF extracted from pooled buffy coats of blood donors. The researchers assessed cell-mediated immunity (CMI) of each patient using the leukocyte migration inhibition test (LMT) and lymphocyte stimulation test (LST). The aim of the study was to evaluate transfer factor treatment and the incidence of positive tests before, during, and after therapy.

Eighty-seven LMT evaluations were performed for each antigen dose, and researchers found 58.9% (33/56) of the tests were positive during non-treatment or non-specific transfer factor treatment, while 83.9% (26/31) were positive during specific transfer factor treatment. Only during specific TF treatment was a significant increase of reactivity against the *Candida* antigen noticed, when compared with the period of non-specific treatment. Clinical observations were also encouraging as all but one patient experienced significant improvement during treatment with specific TF. The researchers concluded orally administered specific TF increases the incidence of reactivity against *Candida* antigens.

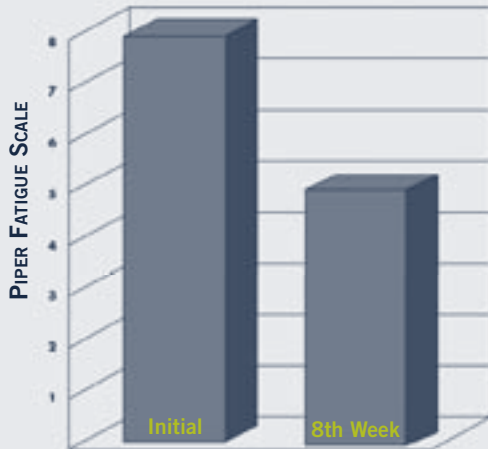
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