

CFS PHOENIX

'The Phoenix is A Mythical Bird That Rises From the Ashes of it's Own Destruction'

PHOENIX RISING: A CFS/FMS NEWSLETTER by Cort Johnson	March/April 2007, Vol II, No. 5/6
A Disease of Many Faces? Fatigue in CFS, FM, Multiple Sclerosis and Post- Cancer.	<u>Subscribe to PHOENIX RISING!</u>

Please send submissions, comments and/or clarifications to Phoenixcfs@gmail.com). Please check with your doctor before trying any treatments found in these pages.

Dr. Bateman Talks! - One of our most active CFS physicians (board member IACFS/CFSAC member, OFFER) Dr. Bateman has produced the best one shot overview of CFS treatment I've seen. A wonderful communicator Dr. Bateman tells us how she treats sleep, fatigue, pain, gastrointestinal ailments and more in this presentation. Complete with informative slides, lots of detail. First appeared in the Wisconsin CFS Newsletter Lifeline. Thanks to Pat Fero and David Thompson. Check out her exercise paper as well: <http://phoenix-cfs.org/Bateman%20Treatment%2007.htm>

A Handbook on "How to Apply for Social Security Disability Benefits If You Have Chronic Fatigue Syndrome (CFS/CFIDS)" - compiled by Kenneth S. Casanova - is available free from the Massachusetts CFIDS Association website. Users may download or print the entire handbook, or selected sections. This is a fantastic document. If you are trying to get disability be sure to get it. http://www.masscfids.org/html/announcement_disability_book.htm

CFS Movie now available on DVD from Immune Support. - Remember "I Remember Me"? It brought me to tears. It has Dr. Bell, Dr. Klimas and a lot of CFS patients. It's available from Immune Support for \$29.95. You get it by calling 1-800-366-6056 and mention Source Code EP042907 or visiting ImmuneSupport.com at https://www.immunesupport.com/shop/product.cfm/product_code/N0428

An Antiviral Blog - Follow Sue as she works through her treatment program - which includes Valcyte, the antiviral drug Dr. Montoya is testing in patients in the ongoing Stanford Drug trial - with Dr. Levine: <http://livewithcfs.blogspot.com/search/label/Valcyte>

'Like the Living Dead' A heartbreaking story of an Ohio woman with CFS. http://www.news-herald.com/site/news.cfm?newsid=18417684&BRD=1698&PAG=461&dept_id=21849&rfi=6

New CFSAC Members Announced - This looks like a strong team. To find out the new members of the new federal advisory board - <http://www.hhs.gov/advcomcfs/index.html>

CFSAC Bio's Part I - ImmuneSupport is starting a series telling us just who our federal representatives on the CFSAC are; the first bio is on Dr. Leonard Jason, one of our most dynamic researchers. <http://www.immunesupport.com/library/showarticle.cfm/id/8013>

SPECIAL FOCUS: DEFINING CFS

What is CFS? Is it a syndrome – a kind of general condition caused by many different factors, or is it a discrete disease with a unique pathology? Are the general abnormalities that cause CFS at play in other diseases or are they unique to CFS? In this section of Phoenix Rising we look at the possible connections between CFS and FM, multiple sclerosis and others.

CFS AND Multiple Sclerosis: One Hand Washing the Other - A Similar Disease Model in Fatigued MS Patients?

D. T. Kasatkin and N. N. Spirin. 2007. Possible mechanisms of the formation of the Chronic Fatigue Syndrome in the clinical picture of Multiple Sclerosis. Neuroscience and Behavioral Physiology 37: 87-91.

Kos, D., Kerckhofs, E., Nagels, G., D'hooghe, M. and S. IJlsbrouckx. 2007. Origin of fatigue in multiple sclerosis. Neurorehabil Neural Repair doi:10.1177/154596830629893

Dr. Friedberg's poster in the IACFS conference ([click here](#)) indicated that while research into CFS has not increased over the past 10 years, research into other 'fatiguing' diseases has increased dramatically. In this paper we see evidence that these 'fatigue' researchers are not only aware of CFS research but are using it to guide their own inquiries. Note that, just as with CFS, 'fatigue' hardly describes the plethora of symptoms people with these disorders face.

Fascinatingly Kasatkin and Spirin state that studies indicate that 'CFS' occurs in a very high percentage of MS patients (75-93%!) and that the first signs of MS are often a CFS-like condition. For many people with MS, in fact, it's not the visual, speech, muscle or bladder problems that are most problematic but the overwhelming fatigue that often accompanies them.

The fatigue found in MS appears strikingly similar to that in CFS; it is usually exacerbated by mental or physical effort and is not substantially relieved by rest or sleep. Both MS and CFS patients often also suffer from sexual, sleep and cognitive problems and orthostatic intolerance. Both fatigued MS and CFS patients (but not unfatigued MS patients) often have altered heart rate variability and orthostatic intolerance. As with CFS, MS primarily affects people of working age.

Strikingly echoing statements made by Dr. Hyde regarding myalgic encephalomyelitis/CFS these authors observed that the 'protean clinical manifestations' of MS depend on where the central nervous system abnormalities (plaques) are located.

Intriguingly, not all MS patients suffer from fatigue and the fatigue in MS is not correlated with symptom severity in other areas. This suggests two central nervous problems are at play in MS, one which causes fatigue and one which causes the muscular and other problems. The question, of course, is whether the fatigue causing processes in these disorders is the same.

Similar Source of Fatigue in MS and CFS? These authors believe the fatigue in MS probably involves decreased serotonin- and norepinephrine-regulated nerve transmission in the brainstem and basal ganglia. They noted that this model of fatigue was developed for CFS. We saw Dr. Kuratsune and the Japanese research team highlight serotonin neurotransmission at the 8th IACFS Conference.

They also believe that impaired carnitine transport into the mitochondria results in impaired muscle energy production in MS - a defect that has also been seen in CFS. The Japanese research group believes impaired carnitine transport is at the heart of many central nervous system abnormalities in CFS.

These researchers also believe that pro-inflammatory cytokines (IL-1, ILI-6, TNF-a, TFN-7) cause fatigue in MS by disrupting normal hypothalamic (HPA axis) functioning - another scenario proposed in CFS.

Some aspects of the fatigue in MS and CFS at first appear to be different. Inhibited nervous system conduction in demyelinated nerve fibers appears to contribute to the fatigue found in MS but not in CFS. These authors report, however, that this reduced nervous system activity does not appear to be due to the nerve demyelination per se but to altered sodium channel functioning (channelopathy) on the nerves. In 1999 Chaudhuri and Behan posited that a nervous system channelopathy caused the symptoms in CFS ([click here](#)). Increasing evidence suggests a channelopathy also plays a role in CFS ([click here](#)).

Research Findings: These theories are interesting but what about research findings? Do MS and CFS display similar central nervous system abnormalities? A recent paper by Kos et. al. indicates that in some cases they do. They include:

- ✚ MS and CFS patients have to recruit more areas of the brain than normal in order to complete a task, a process which is believed to induce fatigue.
- ✚ Increased fatigue has been correlated with brain atrophy (gray matter volume loss) in MS - a process that also occurs in fibromyalgia and CFS patients.
- ✚ EEG studies indicate fatigued MS and CFS patients display decreased cortical inhibition and prolonged cortical normalization times during TMS (transcranial magnetic stimulation). CFS patients also
- ✚ Reduced cerebral glucose metabolism has been observed in fatigued MS patients and a subset of CFS patients also displayed reduced glucose uptake.

Increased rates of HHV-6 activation are found in both diseases, and another herpesvirus, EBV, is suspected in both.

We have seen how research into another disease may be able to inform CFS and vice versa. Perhaps funding for CFS is not as low as we might think. Could the researchers studying the fatigue in MS also be studying CFS?

A subset of post-cancer patients also exhibit a kind of fatigue (central fatigue) that extends both to the physical and cognitive realms. The way they describe their symptoms is startlingly familiar.

CFS AND POST-CANCER PATIENTS

"I Had a Mind Like a Steel Trap, and I Ended Up With a Colander for a Brain", Outakes From a New York Times Article.

That was not a CFS patient speaking; that was a 'recovered' cancer patient; her cancer was gone but her brain was fried in the process. It is remarkable how much these people sound like CFS patients: "One woman reported finding five unopened gallons of milk in her refrigerator and having no memory of buying the first four. A second had to ask her husband which

toothbrush belonged to her. At a family celebration, one woman filled the water glasses with turkey gravy. Another could not remember how to carry over numbers when balancing the checkbook."

"Children arrive at birthday parties a week early. Wet clothes wind up in the freezer instead of the dryer. Prosthetic breasts and wigs are misplaced at the most inopportune times. And simple words disappear from memory: "The thing with numbers" will have to do for the word "calculator."

Someone should make a list of the many different terms being devised to describe the unusual cognitive difficulties people with different diseases have; there's 'brain fog' (CFS), 'fibro fog' (fibromyalgia) and now there's 'chemo-brain' in post-cancer patients.

"Chemo brain is part of the language now, and just to have it acknowledged makes a difference," said Anne Grant, 57, who owns a picture-framing business in New York City. Ms. Grant, who had high-dose chemotherapy and a bone marrow transplant in 1995, said she could not concentrate well enough to read, garbled her sentences, and struggled with simple decisions like which socks to wear.

There are not a small number of chemo-brain patients. About 15 percent or roughly 360,000 breast cancer survivors have cognitive problems. Intriguingly, given the obvious gender bias in CFS, breast cancer survivors have led the fight to gain recognition for their problems. What places women at increased risk for these diseases? The issue of gender has, amazingly enough, hardly even begun to be explored in CFS.

The impaired post-cancer community is facing many of the problems the CFS community has and still is facing. They have struggled to get recognition: "Until recently, oncologists (physicians) would discount it, trivialize it, make patients feel it was all in their heads," said Dr. Daniel Silverman, a cancer researcher at the University of California, Los Angeles, who studies the cognitive side effects of chemotherapy. "Now there's enough literature, even if it's controversial, that not mentioning it as a possibility is either ignorant or an evasion of professional duty."

Research into post-cancer disability has had a strong focus on psychology and ancillary issues (e.g., is it really menopause?). The physiological changes occurring in these women are just beginning to be charted, but the breast cancer lobby is smart, well organized and effective - and they're going to keep punching away at this. As they do, it'll be interesting to see what they can tell us about CFS and what we can tell them about their problems.

In fact, at least two 'CFS' researchers are currently involved in elucidating the post-cancer fatigue state. Ian Hickie and Andrew Lloyd's interest in fatiguing disorders such as hepatitis C infection actually predated their interest in CFS. Dr. Lloyd believes central nervous abnormalities may be producing the fatigue and other symptoms in CFS, post-cancer disability, cholestatic liver disease and other fatiguing disorders.

Goldstein, D., Bennett, B, Friedlander, M., Davenport, T., Hickie, I. and A. Lloyd. 2006. Fatigue states after cancer treatment occur both in association with, and independent of, mood disorder: a longitudinal study. BMC Cancer 6:240.

This study found that a remarkably high percentage of breast cancer patients had significant fatigue (48%) and psychological distress (33%) in the year or so following their cancer treatment using radiation or chemotherapy. Fatigue and mood disorder were to some extent linked; most

mood disorder patients had significant fatigue but a substantial number of fatigued patients did not have a mood disorder.

Their distress proved to be long-lived; about 60% of women with these problems at 10 months still had them at 24 months. Interestingly it was more difficult for these women to shake the fatigue than it was to shake their psychological distress.

Their fatigue was not related to their menopausal status or to the type of treatment they received. This is amazing; some women had chemotherapy, some did not; some had radiation with tamoxifen, some did not - it didn't matter. Whatever process was triggered did so irrespective of the specifics of the treatment.

Researchers have found one cause of post-cancer fatigue; rather astonishingly it was anemia and was treated with erythropoietin. CFS patients also display a form of anemia but erythropoietin treatment does not usually resolve their symptoms. The study data indicated that neither anemia nor menopause could account for the CFS patients' symptoms in this study.

Dr. Lloyd has pointed out that fatigue and mood disorders are really central nervous system symptoms. The direct trauma occurring in the patients receiving radiation treatments, however, was limited to the breast tissue. The Dubbo studies have lead Dr. Lloyd to suspect that an infection in the periphery (the body) appears to cause central nervous system damage in CFS patients as well. How a peripheral injury ends up causing some sort of 'brain damage' is, of course, one of the real conundrums of CFS.

What systems are effected in both cancer and infection patients? The immune and stress response (HPA axis) are and these researchers posit that either or both of these systems play a role in the mysterious problems these patients face. Both, fo course, are primary fields of study in CFS

CFS AND FIBROMYALGIA

CFS and FM share more than similar symptoms, some laboratory findings and a high degree of co-morbidity; they are similar in an existential sense as well; researchers are unclear about how to define each disease and they question if prior definitions have at times led them astray.

In this section Dr. Winfield first gives us a short history of fibromyalgia and a new paradigm, Dr. Yunus then produces a new paradigm for CFS and FM and we close with a talk on the state of FM research and treatment by Dr. Clauw, a gifted communicator.

J. Winfield 2007. Fibromyalgia and related central sensitivity syndromes; 25 years of progress

A Short History of Fibromyalgia - Like CFS, FM has had a long history in the medical community. The diffuse aches and pains of FM were first called "muscular rheumatism" about 400 years ago. Based on the erroneous belief that FM was caused by a fibrous muscular inflammation FM was called fibrositis in the early 1900's. Stress-related injuries during World War II led to FM being characterized as 'psychogenic rheumatism' for several decades. The term fibromyalgia ('muscle fiber pain') was proposed in 1976.

Dr. Yunus re-oriented FM research in 1981 with a seminal article that distinguished between 'trigger' and 'tender' points, indicated that poor sleep and fatigue were an essential part of

FM, and identified the female gender bias. Three years later he began to identify the interrelationships between fibromyalgia and other diseases of increased sensitization, a concept which has come to dominate the field. The idea that FM was due to muscular inflammation was definitively rejected in Dr. Yunus's 1989 study.

Like CFS fibromyalgia has had a difficult time gaining acceptance as a legitimate disorder. Despite significant research breakthroughs, Dr. Winfield states that the view of fibromyalgia in the medical profession is not significantly different now than it was 30 years ago. Most clinicians still believe that fibromyalgia has a psychological basis and many refuse to treat it. CFS patients will understand Dr Winfield's dismay as he notes that

"Medical school curricula still give 'short shrift' to this group of illness, and medical house staff continue to adopt the outdated opinions of their professors. It is as if the huge body of scientific literature on the central mechanisms underlying chronic pain had been published only in Sanskrit. I hope the appellation "CSS" for fibromyalgia and related syndromes will redirect our attention to the fact that these are their own sensory disorders analogous to and infinitely more complex than disorders of sight and hearing."

CFS patients very rightly bemoan the inappropriateness of the name for their disease but they are not alone. Fibromyalgia (FM) seems like a 'good name' - it's scientific sounding, but like CFS it is misleading. Dr. Clauw believes that FM is characterized by 'global problem(s) with sensory processing not just pain'. Just as CFS patients don't have just fatigue, FM patients don't have just pain. Instead they have many sensory problems and, of course, experience fatigue, unrefreshing sleep, cognitive problems, etc. The bulk of the evidence also suggests that the pain that is present is not due to a problem in the muscle fibers as the name implies but to a problem in the central nervous system.

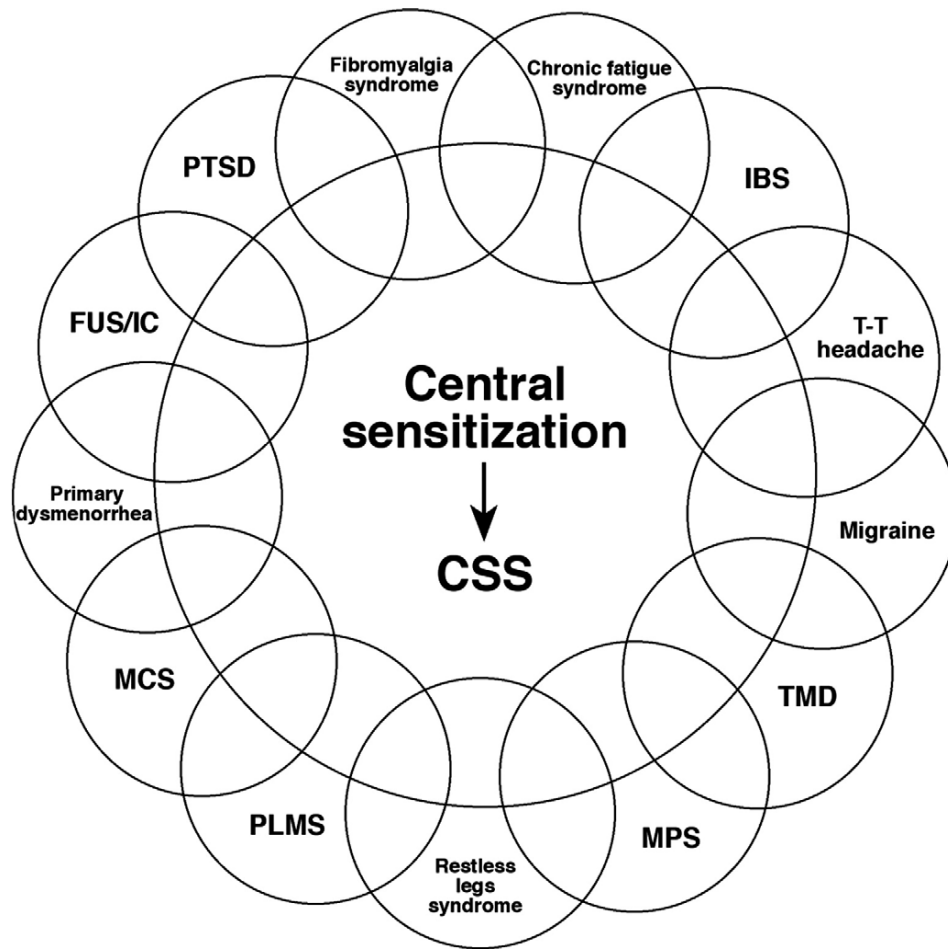
A better name will be very helpful for CFS but note how much trouble FM has had and still has achieving legitimacy even with its impressive sounding name. A bad sounding name hurts, but a better sounding name is obviously not a panacea.

Redefining CFS and FM and MCS and IBS and TMJ and.....

M. Yunus. 2007. Fibromyalgia and overlapping disorders: the unifying concept of Central Sensitivity Syndromes. Semin Arthritis Rheum, In press; xx:xxx.

Called the father of our modern view of fibromyalgia Dr. Yunus wrote a seminal paper twenty-five years ago differentiating fibromyalgia patients from healthy controls, among the first to validate FM as a real disease.

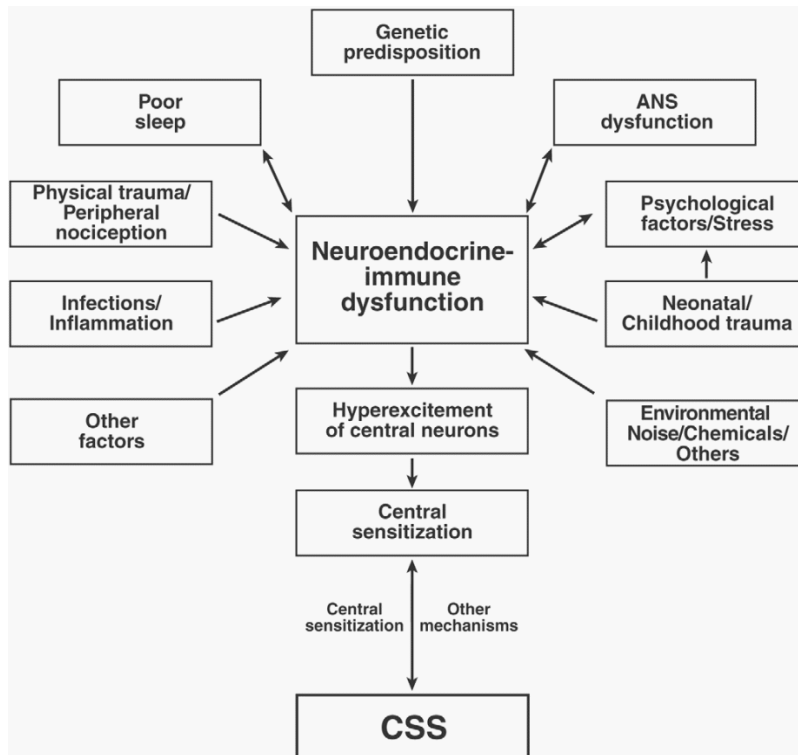
Dr. Yunus is trying to bring a similar clarity to a wide range of disorders, several of which still labor under a psychological (mis)interpretation. He believes that FM and CFS and 10 other disorders (irritable bowel syndrome, temporal mandibular disorder, migraine, post-traumatic stress disorder, multiple chemical sensitivity, restless leg syndrome, myofascial pain syndrome, etc). each result from a hyper-excitement of the neurons in different parts of the brain. Most are currently called "functional somatic syndrome", a term he believes is neither accurate nor explanatory. He instead proposes that these disorders should be called "Central Sensitivity Syndromes" or CSS.



The Process: The process of central sensitization appears to begin when an injury causes nerves to send signals to nerve terminals in a part of the spinal cord called the dorsal horn. Once these terminals are stimulated they produce neurotransmitters/neuromodulators (substance P (SP), NGF) that over time appear able to increase the activity and sensitivity of the nerves leading to the brain in some individuals. Through a process called neuroplasticity it is believed this chronic hyper-excitation alters the functioning of parts of the brain (thalamus, hypothalamus, limbic system, somatosensory cortex) involved in evaluating pain and other sensory stimuli. Studies have found abnormalities in these areas in both FM and CFS.

According to Dr. Yunus, in order to be classified as a central sensitivity syndrome, a disorder must display hypersensitivity to either pain, fatigue, chemicals, noise, etc. and it must co-occur with increased frequency in other central sensitivity syndromes; i.e. people with FM must have increased rates of CFS and vice versa.

Indirect Evidence For CFS: Direct evidence for CSS in CFS is largely lacking. Dr. Yunus notes, though, that brain imaging studies show CFS patients display decreased blood flows to many of the regions of the brain believed involved in CSS. CFS patients also display a surprising number of abnormalities common to many of these disorders including increased sympathetic nervous system activity, decreased parasympathetic nervous system activity, mild hypocortisolism, increased rates of mood disorder, an infectious trigger, poor sleep, and a genetic predisposition to the illness. Dr. Yunus's chart of the biopsychosocial mechanisms contributing to CSS is, in fact, quite similar to some produced for CFS.



Symptomatically, CFS shares several similarities with the broad group of CSS disorders; all evidence increased rates of pain, sleep problems, fatigue and mood disorder. CFS and FM, of course, have many similarities; both are characterized by post-exertional fatigue, mental fatigue and cognitive problems, muscle and joint pain, and both disorders can be triggered by an infectious event.

A Common Immune Component: Interestingly, infection and inflammation are known to trigger many CSS. In a process similar to that proposed in MS, Yunus believes that cytokines and other inflammatory substances produced during infection begin the process of central sensitization through their stimulation of the pain producing nerves.

The Most Common 'Disorder'? As a group Yunus believes that CSS is the most common problem physicians face on a day to day basis - they simply aren't aware of it.

AN UPDATE ON FM

Clauw, D. 2007. Fibromyalgia: update on mechanisms and management. Journal of Clinical Rheumatology 13; 102-109.

The State of FM Knowledge by Daniel Clauw -- This summary is liberally supplemented with my observations on CFS - they were not in Dr. Clauw's paper. There is much debate among both CFS and FM researchers about how to define these diseases. Since 1990 FM has been defined by the presence of widespread pain. The emphasis on discrete tender points in FM is now believed to be a mistake; researchers now understand that 'the entire individual is tender'. Dr. Clauw believes that the definitional mistake of concentrating on muscle tender points has put too much focus on the muscles and driven attention away from the primary locus of the disorder - the central nervous system.

Early Mistakes Prejudice Future Research: The association FM and CFS have come to share with mood disorders in the public's and medical community's minds may in good part be due to inaccurate definitions. Early analyses of the tender points in FM, for example, indicated that they were increased in females with high anxiety, depression and distress. This led to tender points to be rather memorably (and unfortunately) viewed as a kind of 'sedimentation rate for distress', and for the disease itself to be viewed as a kind of psychological disorder. More sophisticated studies have shown, however, that this group of patients is not characteristic of FM and that mood disorders do not contribute to or play a role in the severity of FM (or CFS). In this case an inaccurate definition inadvertently helped prejudice an entire generation of physicians and researchers.

An inaccurate definition has also led to perceptions that FM was an overwhelmingly female disease. If FM is defined using the 1990 criteria the patient population is dominated by women (>90%) but if indices of chronic widespread pain are used - as Dr. Clauw believes they should be - then the gap between the sexes declines markedly (60-40%).

Stereotypes Reinforce Past Errors: Dr. Clauw noted that gender stereotypes have also played a significant role in who gets diagnosed with FM. It turns out that male FM patients are almost invariably diagnosed as having osteoarthritis because as Dr. Clauw notes, that if you do enough x-rays or MRIs at some point you will find something wrong. He joked that he could tell who the male FM patients were simply by determining who had the most x-rays. Unfortunately their misdiagnosis meant that they missed appropriate treatments for their disorder; FM patients do not do respond well to the anti-inflammatories used to treat arthritis.

Hope For the Future: Dr. Clauw is very encouraged by the results of gene polymorphism (mutation) studies. This work has advanced enough in FM for Dr. Clauw to predict that in 5-10 years that we'll have gene chips that will be able to identify, based on mutations in the genes involved in neurotransmitter activity, people who will be at risk for developing FM. Familial studies in CFS are just getting underway, but familial studies in FM indicate that first degree relatives of people with FM have an 8 times increased risk of getting FM. This is a far higher risk than found in other 'familial' diseases such as lupus or rheumatoid arthritis.

Once the genetic risk factors for chronic widespread pain are identified, Dr. Clauw believes they will be very helpful in treating the disorder.

"There probably will be 20 or so genes that end up predicting ... where someone is on this continuum of pain processing. But where I think it's going to be incredibly useful in 5-10 years is to figure out what drugs to give people"

Neither FM nor CFS, of course, are all due to genetics; some sort of biological event is needed to translate a predisposition to a disease to the harsh reality of a chronic disease. How this happens is obviously the next big step in FM research. CFS researchers appear to have the edge on FM researchers in this instance. Two research groups, the Dubbo research group lead by Dr. Lloyd and a Chicago research group lead by Dr. Taylor, are attempting to determine what goes wrong as patients infected with various pathogens come down with CFS.

While FM research has come a long way, FM, like CFS, still has a long way to go before its legitimacy is fully realized. Dr. Clauw echoes Dr. Winfield's dismay at the slow state of FM acceptance when he states

"The research showing strong biologic underpinnings is equally strong in this spectrum of illness (FM) (as opposed to mood disorder), but most physicians and the lay public are not yet aware of these findings. This will likely change rapidly in the next few years as new drugs are approved specifically for fibromyalgia and the companies marketing these drugs will do a thorough job of educating both physicians and patients about these conditions."

Until then, though, these patients are shunned... in our current health care systems. Everyone is averting their eyes... Rheumatologists don't want fibromyalgia... none of the subspecialties want this. So there has never been an advocacy campaign like the psychiatrists and other mental health professionals mounted to legitimize psychiatric conditions."

Conclusion: Is CFS allied with these disorders? Do they share a similar pathology? Are closely related parts of the brain affected in each? Researchers of different stripes have been vying to claim CFS as theirs for years. The infectious trigger often found in CFS and immune-related symptoms led researchers to first posit a chronic viral disorder. Later, psychiatrists noting several similarities between CFS and depression, posited it was a unique form of mood disorder. CFS's similarities to nervous system diseases lead Chaudhuri and Behan to posit it resulted from a neurological channelopathy (ion channel problem). Now Dr. Yunus proposes it is one of many Central Sensitivity Syndromes.

Who is right? Could they all be right? These scenarios do not, after all, appear to be mutually exclusive; CFS could be caused by a chronic viral or other condition affecting parts of the brain associated with mood disorders and fatigue and pain.

We know that something happens to a subset of post-cancer, heart disease, hepatitis, liver disease and multiple sclerosis patients that causes them to have severe problems with cognition and fatigue. If the medical community looked closely at these patients, would they find that they typically have the same cognitive problems, unrefreshing sleep, joint and muscle pain, post-exertional fatigue and symptoms upon standing as CFS patients? Just as a subset of rheumatoid arthritis and lupus patients come down with FM, do a subset of multiple sclerosis and liver disease and post-cancer patients come down with 'CFS'? It could be that these fatigued, pain-ridden and cognitively challenged patients have a great deal to tell each other.

WEBSITE UPDATE

Dr. Bateman Talks! - This is the best one shot overview of CFS treatment I've ever seen. A wonderful communicator Dr. Bateman tells us how she treats sleep, fatigue, pain, gastrointestinal ailments and more in this presentation. Complete with informative slides, lots of detail. First appeared in the Wisconsin CFS Newsletter Lifeline. Thanks to Pat Fero and David Thompson: <http://phoenix-cfs.org/Bateman%20Treatment%2007.htm>

