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Open Your Mind to the Possibilities: L.A. Conference Explores the CFIDS Brain

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The chronic fatigue and immune dysfunction (CFIDS) brain was on display as 250 persons with CFIDS (PWCs) and physicians gathered in Los Angeles to share and learn about this mysterious syndrome. "The Medical Neurobiology of Chronic Fatigue Syndrome (CFS) and Fibromyalgia (FM)" conference, held May 7-9, 1993, marked the fourth annual CFIDS conference organized by Dr. Jay Goldstein, director of the CFS Institute in Anaheim, California. As in the past, veteran clinicians and researchers in the CFIDS movement spoke and this year many new faces were seen at the podium.

The majority of the speakers were from Dr. Goldstein's southern California research circle. The collaboration of these scientists is to be lauded as one of the most promising developments in CFIDS research. No one person can solve a mystery as intricate as this one, and Dr. Goldstein is to be commended for coordinating this effort.

It was remarkable to see theories evolve over the three days – if you were

confused by a presentation on Friday, it would usually make sense by Sunday evening. As a newcomer to CFIDS and CFIDS conferences, it was exciting to see the how pieces of this intricate puzzle are beginning to come together through symposiums such as this.

1. Brain Scans

The most talked-about technology at this conference was Dr. Ismael Mena's single photon emission computerized tomography (SPECT) scanning. Nearly every researcher referenced the UCLA director of nuclear medicine's work as a breakthrough in CFIDS study and it appears that the SPECT scan is becoming a leading instrument to validate CFIDS theories and research, if not a diagnostic tool. Conventional brain scans such as magnetic resonance imaging (MRI) and computerized tomography (CT), which emphasize brain structure over function, do not always show distinct differences between CFIDS patients and controls. SPECT scanning, which examines brain function by measuring cerebral blood flow (CBF), shows profound dysfunction in the CFIDS brain. "CBF and cerebral function are directly equated, so that when CBF is diminished, cerebral function is also diminished," stated Dr. Mena.

"We are seeing a pattern of distribution of blood flow that is quite different from the uniform pattern of distribution that we see in the normal individual," continued Dr. Mena. CFIDS "is characterized by a diminution of CBF and diminished uptake of HMPAO (a radioisotope used to follow CBF), primarily in the right hemisphere, extensively involving the frontal and the temporal lobes and denoting an extensive projection of the limbic system in this area, primarily of the hippocampus in the anterior dorsal right frontal lobe ... The study of CBF and its relationship to cerebral function appears to be a very powerful biological marker for CFS."

Cerebral hypoperfusion (reduced blood flow) is the most common finding in the CFIDS brain, and researchers associated it with nearly every CFIDS symptom. Dr. Goldstein linked it with most limbic system and exercise-related irregularities. However, he could not link blood flow patterns with treatments that improve CFIDS symptoms. "Changes in blood flow, at least in certain kinds of therapy, were not related to how the person felt," he said. "The response to treatment as seen on brain SPECT is not simply [a function of] increasing the blood flow. Changes during treatment may be epiphenomena rather than involved in the causality of how the treatment works."

Recently, Dr. Goldstein has been using ophthalmic drops to treat CFIDS symptoms. As a basis for this treatment modality, Dr. Arthur Charap, of the University of California at Irvine, remarked that drugs administered in the eye will often behave very differently than the same drugs administered elsewhere in the body. The abundance of blood vessels in the eye allows the medicine to be carried into the bloodstream very quickly, so improvement can be seen within 5 to 30 minutes after administration.

Dr. Curt Sandman, from U.C. Irvine has correlated the degree of cerebral hypoperfusion with cognitive dysfunction. "The areas of the brain that Dr. Mena has found so sensitive to CFIDS are also the areas that seem to absorb most of the variance for the neurocognitive deficits. So, there is some consistency here between what we are finding with the localization of neurocognitive function in the areas Dr. Mena has found to be so sensitive."

Toxic chemical exposure (TCE) has been implicated as a potential "Agent X" for CFIDS. In Dr. Gunnar Heuser's study, 100 percent of 60 CFIDS patients who traced the cause of their syndrome to TCE presented diffuse abnormalities on the SPECT scan. (See "Chemical Exposures" later in this article.)

Dr. Michael Goldberg, a UCLA pediatrician, is beginning to use SPECT scans to diagnose children suspected of having CFIDS. He found CBF to be variable in his patients and, based on this finding, hypothesized that some attention deficit disorder (ADD) patients are being misdiagnosed, and should actually be diagnosed with CFIDS. (See "Children with CFIDS" later in this article.)

Ottawa, Canada researcher Dr. Byron Hyde finds SPECT scans to be potent enough to alter the diagnosis of CFIDS (or M.E. – myalgic encephalo-myelitis -- as he prefers). "What we're going to tell the insurance companies from now on is not M.E., which they won't pay for, and not CFS, but major acquired brain dysfunction. And that is what these people actually have."

The difficulty with using SPECT scans as a diagnostic tool lies in their inaccessibility to most physicians. To get an accurate SPECT scan reading, a brain-dedicated scanner which uses either the ¹³³Xenon or the HMPAO radioisotope to measure CBF is needed. At this time there are only four such facilities in the United States. This situation should change very soon, as at least three companies are now offering software compatible with the SPECT scanners currently in hospitals across the country. This new software will enable physicians to do the ¹³³Xenon scans that Dr. Mena discussed at this conference. In a recent conversation, Dr. Mena estimated that within six months this technology will be widespread enough to be useful as a diagnostic tool for CFIDS.

MRI scans are unable to reliably show CFIDS-related brain defects, according to Drs. Stephen Lottenberg, Anthony Komaroff and Gunnar Heuser. However, Dr. Christopher Gallen presented a new type of brain scan which combines MRI (an anatomical scan) with the SQUID (Superconducting QUantum Interference Device) scan, a functional scan of electromagnetic fields. This magnetic source image (MSI) scan gives an extremely accurate picture of the brain's function. These electromagnetic fields are extremely subtle and must be differentiated from all the other electromagnetic "noise" in the environment. Trying to find the correct signal is like "listening to the footsteps of ants walking on soft ground in the middle of a rock concert," according to Dr. Gallen, but this technology permits the researcher to isolate these minute signals.

MSI technology has been created with very stringent criteria for finding dysfunction. Because of this, Dr. Gallen and his team at the Scripps Institute estimate that they miss up to 30 percent of impaired people. In his very preliminary data, 50 percent of CFIDS patients show brain dysfunction with the MSI, primarily in the frontal, parietal and temporal lobes. Integrative and learning difficulties are often implicated by the MSI findings in CFIDS. Gallen stressed that more research needs to be done in this area before conclusions can be drawn, and that lack of funding alone has prevented these studies from being done.

Positron emission tomography (PET) scans measure glucose metabolism in the brain, another functional measure of brain activity. Dr. Lottenberg of U.C. Irvine has been able to "quantitatively evaluate brain function, especially for those who have more subtle findings that aren't as visually apparent" on MRI scans. "PET scanning is considered to be one of the gold standards in terms of evaluating whether there are functional problems that are causing [dysfunction]."

Finally, proton spectroscopy can be used to discover primary metabolic abnormalities in the brain, said UCLA's Dr. Bruce Miller. This technique uses the tools of MRI scans to discover the chemical composition of tissues.

2. The Limbic System

"I still believe that the mechanism of virtually all the (CFIDS) symptoms stems from limbic system dysregulation in a neural network or an immuno-neuroendocrine network that involves the brain and the entire body." -- Dr. Jay Goldstein

Dr. Goldstein's limbic dysfunction theory received considerable support at this conference. The limbic system includes the hippocampus, amygdala, orbitofrontal cortex and hypothalamus and it regulates most bodily functions. Any type of stress on the limbic system upsets homeostasis, which can result in the symptoms of CFIDS, stated Dr. Goldstein. Limbic dysfunction has been implicated in multiple chemical sensitivities (MCS), vertigo, sleep disorders, memory problems, poor vision, fatigue, pain and weight gain.

The nasal passages are a direct link to the limbic system. Dr. Iris Bell of the University of Arizona is researching toxic exposure and its effect on the brain. MCS is a syndrome where smelling toxic chemicals causes symptoms including headache, nausea and dizziness. MCS may result from "kindling" of the amygdala, a limbic system structure. Kindling is the ability of a stimulus to cause a reaction after repeated exposure to the agent. Because there is no blood-brain barrier in the nasal passages, limbic structures (e.g., the amygdala, olfactory bulb and hippocampus) can become easily kindled. This may result in CFIDS-type symptoms including memory loss, irritable bowel and migraine headaches. (See "Chemical Exposures" later in this article.)

Dr. Samuel Whitaker addressed vertigo in CFIDS. The U.C. Irvine otologist studied 11 CFIDS patients with vertigo and found them all to have a viral condition of the inner ear called "endolymphatic hydrops." The primary balance defect was central integration, which is related to limbic dysfunction. In a central integration defect, a person is unable to compensate for the disparity between what they see and what their inner ear is telling them about balance. Endolymphatic hydrops is probably a result of the reactivation of viruses caused by the dysregulated immune system in CFIDS.

Irritable bowel syndrome (IBS) plagues both CFIDS and fibromyalgia (FM) patients. Chronic abdominal pain is experienced by up to 70 percent of FM patients and may be a cousin of FM syndrome, according to UCLA's Dr. Emeran Mayer. IBS is related to hyperalgesia (an excessive sensitivity to pain) and central nervous system dysfunction. Dr. Mayer stated that in the study of IBS, "there are a lot of examples of neuropathic pain" and anomalies have been reported in the mid-brain, hippocampus, spinal column and other areas mediated by the hypothalamic- pituitary-adrenal (HPA) axis.

Other physicians identified defects in the HPA axis as well. Drs. Russell Poland and Anthony Komaroff noted a down-regulation of the HPA axis in CFIDS patients. Dr. Komaroff, of Brigham and Women's Hospital in Boston, hypothesized that a central defect in the HPA axis prevents the immune system from shutting down, and results in the constant immune activation which makes PWCs feel sick. Dr. Komaroff lent support to Dr. Goldstein's limbic dysfunction theory said, "In summary, I rather like the model Dr. Goldstein has put forward, that a final, common pathway to this illness may be limbic dysfunction theory, as triggered by a whole variety of different phenomenon."

Dr. Charles Lapp, of the Cheney Clinic in Charlotte, NC, presented a study done with his partner, Dr. Paul Cheney, on neuroendocrine responses to exercise. The differences between patients and controls also seem to support an HPA axis defect.

3. Exercise Intolerance

It is widely documented that exercise is an exacerbator of CFIDS symptoms. Drs. Mena

and Goldstein presented a series of SPECT scans which showed extreme hypoperfusion (reduced blood flow) in the brain following exercise. There appeared to be "holes" where blood would normally be flowing -- the degree of hypoperfusion was astonishing. Even 24 hours later, cerebral blood flow was severely reduced.

Cerebral hypoperfusion is not the only result of exercise intolerance. Drs. Lapp and Goldstein referenced irregular tidal volume rates common in PWCs. Hyperventilation and shallow breathing are frequent results of exertion. Normal controls breathe irregularly at the start of exercise, but respiration becomes regular over time. Dr. Lapp reported that PWCs breathed more regularly than controls at the outset, but during exercise their breathing was more variable. Dr. Goldstein concurred, "This phenomenon has never been described before in any population and, as of now anyway, we think that it's a diagnostic marker for CFS."

Neuroendocrine responses were often reversed or blunted in the Cheney-Lapp study. Cortisol, epinephrine, norepinephrine, DHEA levels and body temperature normally rise with exercise, but PWCs were found to have lower than expected measures of all of the above. Dr. Goldstein related this phenomenon to limbic dysfunction, as altered levels of interleukins and nitric oxide (NO) can result in altered neuroendocrine responses to exercise.

Dr. Lapp and Dr. Kathy Sietsema reported that PWCs reached anaerobic threshold much sooner than predicted. Anaerobic threshold (AT) is the point at which a healthy person becomes completely fatigued and cannot exercise any longer (commonly called "hitting the wall"). In the Cheney-Lapp study, PWCs continued exercising beyond the point of AT. Dr. Cheney has hypothesized that PWCs normally perform above AT in everyday activity due to a metabolic injury, and therefore are more accustomed to performing at this level than controls.

UCLA's Dr. Sietsema compared the current diagnosis of CFIDS with a Scandinavian disorder commonly diagnosed in the 1950s and 60s. Vasoregulatory asthenia was characterized by a reduction in exercise capacity, elevated heart rate and higher cardiac output. Dr. Sietsema found that a subset of PWCs had exercise-related dysfunctions that were consistent with the diagnosis of vasoregulatory asthenia.

4. Virology

Dr. Hyde, the Canadian researcher who has historically been one of the strongest supporters of PWCs and their cause, presented evidence that CFIDS may be caused by a retrovirus or an enterovirus, the family of viruses to which the polio virus belongs. The suspected CFIDS epidemics in the early 20th century had strong ties to the polio epidemic. Many California medical personnel who worked with polio patients contracted a CFIDS-like illness in 1934. Although this epidemic was uncharacteristic of poliomyelitis, it was diagnosed as polio due to lack of alternate diagnoses.

Hyde expressed concern with the U.S. and Canadian emphasis on funding herpesviral research to the detriment of retroviral and enteroviral research. "I am not suggesting that this disease is caused by polio or its variants ... [or] by a retrovirus. But we have ample concern from looking at these [viruses] that no research is being done seriously, [that is] funded by the Canadian or United States government, in these areas of major concern." (Eds. note: The NIH is currently supplementing the Association's funding of Dr. Sidney Grossberg's retroviral research. Please see "The Elusive CFIDS Retroviruses," pg. 2.) If a virus is causing this syndrome, then it is a "perfect virus," stated Dr. Hyde. He described a perfect virus as one elusive enough that it is not killed, but not so hazardous

that it kills the host. Thus, the virus can live and propagate indefinitely in the host. This infection would produce the immune activation which is responsible for many CFIDS symptoms. "As long as the cell is at rest ... it can do what it wants. As soon as you put it under stress, under work -- whether it's cognitive work or physical work or sensory work makes no difference -- that cell doesn't function."

If, in fact, one or more viruses are responsible for causing CFIDS, they have so far been extremely elusive. University of Southern California's Dr. John Martin has been working to identify a so-called "stealth virus" in CFIDS, which he feels is probably hiding in the limbic system. "A virus causing damage at such a critical site in the body, even though it may not be an overt infection, could cause devastating clinical changes," declared Dr. Martin.

Polymerase chain reaction (PCR) technology has been a cornerstone of Dr. Martin's CFIDS research. "PCR has represented a revolutionary breakthrough in the detection of very small amounts of virus. It also has the potential to fish out unknown viruses and to proceed along the path of identifying and characterizing new viruses."

Martin has cultured a virus which, although still unidentified, has a genetic sequence unlike any known virus. As yet, however, Martin has been unable to link this novel retrovirus to the cause of CFIDS. "There could be multiple causes, distinct illnesses, of which virus-positive people may be a subset." (Eds. note: For a history of CFIDS retroviral research, please see "The Elusive CFIDS Retroviruses" by Kim Kenney, pg.2 of this issue.)

5. Immune Defects

Up-regulation of the immune system has been well-documented in the CFIDS literature. Although the lymphocytes of the immune system are behaving as though an infectious agent is present, it is unknown whether this activation is a result of an infectious agent (such as the "mystery" virus Dr. Martin discussed) or an immune system gone awry. That this immune activation is responsible for many CFIDS symptoms has been accepted by most researchers and physicians.

Stress, in any form, places undue pressure on the immune system, stated Dr. Goldstein and Dr. Catherine Rivier of the Salk Institute in La Jolla, CA. Stress can cause dysregulation of homeostasis and immune activation. In a normal immune system, interleukin (IL)-1 is produced in response to a stressor. In CFIDS, IL-1 may be obstructed, resulting in a blockage of corticotropin releasing factor (CRF), an immunosuppressor. If CRF is not released, the immune system will remain activated indefinitely.

Effects of alpha interferon (α -IFN) on the central nervous system were explained by Dr. David Saphier, of Louisiana State University. α -IFN is released by the leukocytes in response to an infectious agent and alters the internal clock, inhibits HPA axis activity and causes fatigue and loss of appetite.

Dr. Nancy Klimas and her team at the University of Miami have been able to accurately predict 88 percent of CFIDS patients and 86 percent of controls with a mathematical model of immunologic parameters. This model combines levels of activated T-cells and CD4 inducers of cytotoxic T-cells with natural killer (NK) cell count and function. Although she has been able to predict a high percentage of PWCs, it cannot be considered statistically diagnostic, as 95 percent of a given population must have a certain

characteristic to approach statistical significance. Dr. Klimas emphasized that the all-encompassing nature of the CDC definition may hinder any quest for statistical significance. Because this definition is a "clinical umbrella," there is considerable question whether all CDC-defined CFIDS patients are suffering from the same disorder. Lymphocytes in the blood are responsible for recognizing foreign antigens, initiating the immune response, producing cytokines to fight the invader and causing immunosuppression.

In a normal population, 20 percent of lymphocytes are active at any given time. "In CFS, up to 80 percent of the cells are working -- they flip-flop that ratio," said Dr. Klimas. In addition, she stated that these lymphocytes and cytokines are so upregulated that they cannot be driven any harder. It is as if they have been pushed as far as they can go and the immune system is completely exhausted. (Eds. note: See pgs. 48-50 of the Spring 1991 issue of The CFIDS Chronicle for a more detailed explanation of lymphocyte activation in CFIDS.)

Dr. Klimas also presented a potential genetic marker for determining susceptibility to CFIDS. This would explain why some children and siblings of PWCs also have CFIDS, while spouses rarely get sick. (Eds. note: For a report on the poster presentation from the 1992 Albany research conference related to this topic, please see pgs. 64 and 69 of this issue.)

6. Cognitive Breakdown

A difficulty with creating new memories is the primary cognitive deficit in CFIDS, stated Dr. Sandman. When asked to predict how well they will do on a test of memory, PWCs have high expectations of their performance, but normally fall short of prediction. And as the amount of information increases or distractions occur, their memories become even less reliable, more so than depressed patients or controls. (See "Is CFIDS Depression?" later in this article and the August 1991 CFIDS Chronicle Physicians Forum for more on this topic.)

Information processing deficits can be seen in the EEG, a very crude measure of electrical activity in the brain. "There is a distinctive fingerprint in the EEG. The striking finding was a very early attentional component where information may be processing, and [PWCs] may not be consolidating this information well because something is being perturbed in the early information processing stage." By linking the EEG activity with memory deficits as seen on psychological assessments, Dr. Sandman can "separate normal controls from CFS patients 100 percent of the time."

Dr. Klimas found that "cognitive complaints correlate with specific immune abnormalities and disease severity and not with depression." Neopterin, an immune activation marker, correlated with the degree of cognitive dysfunction, as did T- and Bcell response. Levels of peripheral cytokines circulating in the bloodstream were not related to cognitive functioning, as expected.

A new questionnaire to determine the extent of cognitive problems in CFIDS was presented by Dr. Linda Miller Iger, a neuropsychologist in Laguna Beach, CA. This inventory is printed in this issue of The CFIDS Chronicle on pages 73 and 74. In order to get a statistically accurate sample, Dr. Iger needs to obtain a large number of completed questionnaires.

Dr. Keh-Ming Lin of UCLA's department of psychiatry presented a cross-cultural study of American and Chinese patients with CFIDS-type symptoms. He found that the Chinese diagnosis of neurasthenia correlates with the western diagnosis of CFIDS and

postulated that the primary difference is a cultural one; CFIDS or CFS are the preferred terms in western society while neurasthenia is favored in China.

7. Children with CFIDS

Michael Goldberg correlated a subtype of attention deficit disorder (ADD) with CFIDS. In the past, children with ADD were automatically assumed to be hyperactive. In the early 1980s, pediatricians began defining attention deficit hyperactivity disorder (ADHD), to differentiate it from so-called "ADD-quiet" children, who did not present with hyperactivity. Dr. Goldberg has found that ADD-quiet children overlap with children with CFIDS. "I believe that the majority, if not potentially all, of those children without hyperactivity may be representing manifestations of CFIDS," hypothesized Dr. Goldberg.

"Lab [tests] on these children," he continued, "are quite variable. Often what I look for is some evidence of immune dysfunction, a number of elevated viral titers [and] an extremely low sedimentation rate. We're picking up low natural killer cell counts on some of these children; but, as is typical with adults, there really is no consistent lab pattern at the moment. In this light, I think you'll see where I'm beginning to increasingly look upon the value of the SPECT scan and the work I've been doing with Dr. Mena." Dr. Goldberg has found that the hypoperfusion seen in SPECT scans of ADD-quiet children parallels that of children diagnosed with CFIDS.

Dr. Goldberg has had success treating children with CFIDS with Kutapressin. However, he has had difficulty finding children who will comply with the repeated injections that this treatment protocol requires.

8. Fibromyalgia

Fibromyalgia (FM) syndrome and CFIDS have many common symptoms, such as muscle and joint aches, irritable bowel syndrome and sleep disorders. Dr. Muhammad Yunus, from the University of Illinois-Peoria, presented evidence that CFIDS and FM are overlapping syndromes, with the primary difference being that PWCs have more cognitive problems than FM patients, and FM patients have more musculoskeletal tenderness than PWCs. (Eds. note: See The CFIDS Chronicle, Sept. 1992, pp. 53-58 for Dr. Yunus' comparison of CFS and FM.)

Like CFIDS, FM often leaves patients depressed, but Dr. Yunus pointed out that "the prevalence, or frequency, of depression ... is no more in FM than in other chronic pain groups, such as rheumatoid arthritis." On a number of neurohormonal tests, depression and FM fell on opposite ends of the scale. For example, in FM (and in CFIDS) there is profound hypocortisolism, whereas depressed patients have an abundance of cortisol. There is also a shortage of serotonin and norepinephrine in FM. Both of these neurotransmitters have been implicated in pain syndromes. This deficiency "would be quite compatible with the notion that these people have a decreased global pain threshold," said Dr. Yunus. (See "Sleep Disorders" in this article for other implications of serotonin inadequacy in FM.)

9. Is CFIDS Depression?

Researchers who have attempted to categorize CFIDS as an affective disorder were widely and loudly criticized at this conference. Drs. Komaroff, Lottenberg, Mena, Poland and Sandman presented data which showed CFIDS to be unlike depression on a variety of tests. Government researchers were censured for attempting to link the two disorders.

Dr. Komaroff led the charge: "The abnormality of the HPA axis that has been demonstrated many times in patients with major depression that leads to a hyperactive axis ... is not found in CFS. The group at NIH who looked for this, and I think they were looking to find the same thing in CFS; [found] that there is a down-regulated, or hypoactive, HPA axis."

Dr. Komaroff used SPECT scans to compare CFIDS, depressed and AIDS- dementia patients with healthy controls. When examining cerebral blood uptake, an objective measurement of dysfunction, CFIDS and AIDS patients were similarly and more severely impaired than depressed patients or controls, who had similar levels of uptake. However, when individual researchers counted the number of defects (a subjective measurement based on the researcher's perspective which does not consider the severity of the defects), CFIDS and depressed patients had the same number of problems, while AIDS patients had the most defects and controls the fewest. This subjective measurement could not statistically differentiate between PWCs, HIV-infected or depressed patients, but all three were very different from controls. Komaroff hypothesized that "objective measurements of intensity in each [cerebral] region might demonstrate quantitative differences in regional tracer uptake in patients with CFS, depression and HIV" and noted that these studies "are now underway."

A similar study using PET scans corroborated Dr. Komaroff's results. Dr. Lottenberg found that PWCs had more metabolic defects than depressed patients and often presented with PET scans in direct opposition to those with a major affective disorder. PWCs did have some overlap with both AIDS and depressed patients in regard to affected areas. As in Komaroff's study, CFIDS and HIV patients were more severely affected than depressed patients, with HIV patients demonstrating the largest number of regional defects. Dr. Lottenberg hypothesized that the overlap with depression may be a result of becoming depressed following acquisition of CFIDS. He also stated that the overlap with HIV patients, suggests "some kind of viral effect on the brain."

UCLA's Russell Poland also agreed with Dr. Komaroff's assessment when he stated that a major difference between PWCs and depressed patients is apparent in the regulation of the HPA axis. Depressed patients show a hyperactive HPA axis, while PWCs present with an extremely down-regulated HPA axis.

The extreme lateralization of hypoperfusion to the right hemisphere is a hallmark of CFIDS. In contrast, Dr. Mena has found that "in depression, there seems to be no significant difference between the left and right hemisphere." On SPECT scans of patients who develop depression following the onset of CFIDS, "the CFS pattern is the dominant pattern, not the depression pattern."

Dr. Sandman compared CFIDS and depressed patients on memory function. Because PWCs often become depressed following the onset of CFIDS, he assumed that these two populations would have similar profiles, but found that they differ significantly. Compared to depressed patients, PWCs make six times the number of errors on tests of memory, they consistently overestimate their performance on tests (depressed patients consistently underestimate their performance), they can't create new memories efficiently and they become less efficient as the amount of information increases. (See "Cognitive Breakdown" earlier in this article.)

The results Dr. Sandman found are "extremely sensitive and extremely specific, achieving diagnostic levels of about 90 percent. So, this constellation of symptoms is very effective for separating CFS patients from depressed patients and controls."

10. Sleep Disorders

Drs. Lottenberg, Yunus and Poland compared sleep disorders between CFIDS or FM and depressed patients and all found different profiles on a variety of tests. Although sleep disturbances are common to all of these disorders, sleep deprivation seemed to help depressed patients, but only made PWCs and FM patients feel worse, according to Lottenberg and Yunus. In the sleep laboratory, Dr. Yunus has seen that "by depriving people of their deep sleep, one can cause FM."

Dr. Poland hypothesized that alpha-wave (light sleep) intrusion in delta-wave sleep (deep sleep) may cause CFIDS symptoms. Serotonin, which modulates sleep, is also deficient in FM, and may be the cause of a similar alpha-intrusion in FM, according to Dr. Yunus. Compared to the serotonin deficiency noted in depressive and anxiety disorders, the deficiency in FM seems different and may be caused by altered serotonin receptor subtypes.

The alpha-wave intrusion in deep sleep results in non-restorative sleep. Up to 80 percent of growth hormone (GH) is secreted during deep, non-rapid eye movement (nREM) sleep. GH is responsible for repairing and refreshing the body. Prevention of GH secretion, caused by alpha- intrusion, has been shown to result in FM-type pain, stated Dr. Yunus. Dr. Poland also noted a lower level of GH in CFIDS.

Dr. Poland felt very strongly that more studies need to be done on sleep patterns in CFIDS. Studies of sleep disorders in depression have been extensive, and the same studies need to be done in CFIDS and FM. "It's very clear that there's considerably less available in terms of being able to understand what is going on in these two processes" compared to depression.

11. Chemical Exposures

Toxic chemical exposure (TCE) and multiple chemical sensitivity (MCS) often produce CFIDS-like symptoms. UCLA's Dr. Gunnar Heuser and Dr. Iris Bell of the University of Arizona presented evidence that environmental toxins may be one trigger for CFIDS. In some cases, MCS can develop after only one exposure to a toxic chemical. Because there is no blood-brain barrier in the olfactory (smelling) system, olfactory nerves can transport toxins directly to the limbic system. According to Dr. Bell, this lack of a bloodbrain barrier is responsible for rapidly sensitizing limbic system structures to chemicals which can cause seizures and CFIDS-like symptoms.

TCE frequently begins with a flu-like illness soon after exposure to an offending chemical. Dr. Heuser explained how TCE can develop into "fibromyalgia, which can go on for a long time with mild temperature elevations [and] night sweats; [patients] will not recover or feel recovered when they have slept, they ... cannot exercise anymore because they become fatigued" and they often complain that they "become confused" easily. Even years after a chemical exposure, TCE patients demonstrate lowered natural killer (NK) cell function and hypoperfusion on the SPECT scan.

The primary complaint of TCE patients is debilitating fatigue. Dr. Heuser suggested that physicians might want to consider the possibility that their CFIDS patients have a chemical exposure in their history. "In my mind, many of my patients fit the description [of CFIDS]. Not only that, I have seen patients who had gone to Dr. Goldstein and had been diagnosed as having CFIDS and it is discovered along the way that they had chemical exposure in their background. Then they come to me to be evaluated and they present [with TCE]."

12. What Causes CFIDS?

If this question ever had even a hint of a singular answer before, it was shattered at this conference. The overriding answer to this question was "anything and everything." Viruses were mentioned as a potential cause more than once, but they were never hailed as the one complete answer. Even John Martin, discoverer of a novel virus which may be associated with CFIDS, agreed that there may be many causes of this syndrome, a virus being only one of them.

Other leading candidates presented were toxic chemicals in the environment, stress on the limbic system, an unknown infectious agent, a genetic susceptibility to immune activation, sleep disorders and the list goes on.

One thing that was conceded was that most CFIDS symptoms are caused by upregulation of the immune system and the inextricable limbic system dysregulation.

Whether this is a cause of the syndrome or the effect of an unidentified agent is unknown. However, as Dr. Klimas stated, the triggering agent for this hyperactivity "absolutely cannot be answered without longitudinal data," that is, knowing the patient before and after illness.

UCLA's Dr. George Solomon suggested that the only logical way to study such a varied complex of symptoms, as in CFIDS, is through a psychoneuroimmunological approach. Psychoneuro-immunology (PNI) views the body as a single integrated system, where one factor can potentially influence and affect all other parts of the body. PNI is "concerned with complex multi-dimensional interactions between the immune system and the central nervous system," according to Dr. Solomon's abstract. Taking a systemic approach, such as this one, may be the only way to unravel the mystery of a disease as complex as CFIDS.

13. References

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