Putting chronic fatigue syndrome's myths to bed

A new campaign aims to raise awareness of a condition that many say doesn't exist

By Jessica Berthold

Respected researchers say it's a condition that can be as disabling as AIDS or multiple sclerosis. Its prevalence is greater than that of ovarian cancer, lung cancer or lupus. And yet, nearly 20 years after chronic fatigue syndrome was officially recognized as a legitimate medical condition, many internists still doubt whether it truly exists.

The CDC is trying to change that. Spurred by 15 years of research, the agency kicked off a campaign in November to raise awareness about how to spot and treat the disease, which brings exhaustion, aches and pain, and is diagnosed in only 16% of the 1 million Americans who have it. "This is a disease that is very difficult to diagnose and very difficult to understand and treat," said CDC Director Julie Gerberding, MD. "(It) has been shrouded in a lot of mystery and controversy."

Lucinda Bateman, MD, has no doubt that chronic fatigue syndrome is real. A general internist and founder of a fatigue consultation clinic in Salt Lake City, Utah, Dr. Bateman became acutely aware of CFS in the mid-1980s when she tried to determine why her once-healthy, happy sister seemed to be getting viral infection after infection without improving.

"When I left for medical school in 1983 she was fine, and when I returned four years later, she had developed chronic fatigue syndrome—though it didn't have a name at the

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time," Dr. Bateman said. "I was an eager young internist doing my internship and residency, and I started reading and attending conferences to figure out how to help her."

Dr. Bateman soon became known for her expertise, and physicians referred more and more CFS patients to her. A year after opening her specialty clinic in 2000, Dr. Bateman's sister died of complications from non-Hodgkin's lymphoma at age 50.

"I think that having chronic fatigue syndrome for 10-15 years may have increased her risk of developing the illness that killed her. We know that diagnosing and treating CFS early leads to better outcomes," Dr. Bateman said. "That is why people need to recognize, research and diagnose this disease, and stop arguing about whether it's real or not."

Diagnosis of exclusion

Nailing down the diagnosis of CFS is a long, frustrating process for both patient and physician, internists said. There is no diagnostic test or laboratory marker for CFS, so physicians must rule out other potential causes, like thyroid or neurological disorders, before they confirm the diagnosis. Since the main symptoms of CFS—fatigue, pain, headaches—are common to many other illnesses, the exclusion process means repeat visits, a lot of lab work, and a lot of time.

"Most patients don't come in as the classic case, where they developed a mononucleosis-like illness and then it progressed. They just come in and say they haven't been feeling well for months or years," said Julie Brady, MD, a general internist in Colorado Springs, Colo. who currently has four CFS patients. "A diagnosis can take anywhere from three to six months."

The criteria for CFS, according to the International Chronic Fatigue Syndrome Study Group Case Definition, include medically unexplained fatigue of at least six months that's not the result of other diseases or conditions. The fatigue continues despite rest, and leads to a significant reduction in social, personal, educational and job-related activities. At least four of several characteristic symptoms—like sore throat, muscle pain, joint pain, headache and memory impairment—must be present concurrently.

Questionnaires that can help identify and monitor CFS patients include the MOS SF-36, the CDC Symptom Inventory, the Multidimensional Fatigue Inventory, the McGill Pain Score, and the Sleep Answer Questionnaire. Most of these assessment tools are available through the Web site of the CFIDS Association of America at: www.cfids.org/treatcfs/impairment.pdf.

According to the CDC, clinical evaluation of patients with fatigue requires:

- ☐ a detailed patient history, including review of medications that may cause fatigue,
- ☐ a thorough physical examination,
- ☐ a mental status screening, and
- ☐ a minimum battery of lab tests.

Recommended tests include urinalysis, thyroid function and C-reactive protein.

Adding to the difficulty of pinning down CFS is the fact that the disease's clinical course and the severity of symptoms tend to vary considerably by patient. Symptoms often wax and wane, with patients remitting and relapsing repeatedly. CFS patients also often have co-morbid conditions. Fibromyalgia is the most common; other typical ones include depression, irritable bowel syndrome and interstitial cystitis. Patients with Gulf War syndrome also often meet criteria for CFS, or go on to develop CFS, according to a June 2005 study in the *Annals of Internal Medicine*.

In some cases, co-morbidities arise because people wait several years to see a doctor for CFS and develop other problems in the meantime, said Suzanne Vernon, PhD, team leader of the CDC's molecular epidemiology program and a chronic fatigue expert.

"By the time people are seen, they have been sick for a long time, so not only do they have chronic fatigue syndrome, they have depression; their blood pressure has gone crazy; they have orthostatic instability," Dr. Vernon said. "It becomes a cascade of events."

Dr. Bateman, the fatigue clinic founder, said she understands why such a tricky diagnostic process might make internists hesitant to embrace CFS.

"Internists are the most rigid about meeting diagnostic criteria, and that's good, but it can marginalize patients with atypical presentations," Dr. Bateman said. "Still, general internal medicine should be the home for management of these illnesses, because we know how to manage chronic illness and multiple problems."

A tough sell for some

Lawrence Edwards, MD, professor of rheumatology at the University of Florida in Gainesville, said he often encounters patients with persistent pain and fatigue. But he doesn't diagnose them with CFS

"To view it as a separate disease process rather than one that is associated with other medical problems or depression is beyond what we know scientifically," Dr. Edwards said. "I think there are a lot of ways to treat fatigue without raising it to the level of a disease process."

Several internists, who asked not to be named, expressed similar views. A commonly stated belief was that chronic fatigue syndrome is a catch-all term for another condition that hasn't been properly diagnosed—like a sleep disorder or clinical depression. Yet recent research on chronic fatigue syndrome patients indicates otherwise, according to Anthony L. Komaroff, FACP, a Harvard Medical School professor of medicine and CFS expert.

"There is a huge [body of] literature that demonstrates measurable biological differences in these patients compared to healthy people of the same age and gender, or compared to depressed people or people with other fatiguing organic illnesses like multiple sclerosis and lupus," Dr. Komaroff said. "Indeed, the CDC's research uncovering such biological differences was one of the reasons it decided to initiate a public education campaign. I think most practicing doctors aren't aware of this literature."

More than 4,000 published studies show that patients with CFS have underlying biological abnormalities, many of them centering on brain hormones and the autonomic nervous system, Dr. Komaroff said. In terms of clinical application, he identified three research areas as the most promising or cutting-edge:

- ☐ Evidence that the immune system is chronically activated, and that pro-inflammatory cytokine production is increased. "This has therapeutic implications because there are a number of biologic pharmaceuticals that counter the activation of the immune system and the effect of the production of pro-inflammatory cytokines," he said.
- ☐ Evidence that there is something wrong with energy metabolism and the oxidative electron transport chain in mitochondria.

CDC debunks CFS stereotypes

One of the most common and inaccurate stereotypes about chronic fatigue syndrome patients "is that this is a bunch of hysterical, upper-class professional white women who are seeing physicians and have mass hysteria," said Dr. Williams Reeves, CDC chief of the chronic viral disease branch, at an April 2007 media briefing. According to CDC research, facts about chronic fatigue syndrome include:

- ☐ At least 1 million Americans have CFS.
- ☐ Less than 20% of Americans with CFS have been diagnosed.
- ☐ CFS affects four times as many women as men.
- ☐ CFS is most prevalent among adults age 40-59.
- ☐ In the U.S., CFS is at least as common among Hispanics and African-Americans as whites.
- ☐ CFS appears to be more common in lower-income than affluent individuals.
- ☐ CFS results in $9 billion in lost productivity in the U.S. annually.
- ☐ CFS results in $20,000 annually in lost wages and income per family.