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# Chronic Fatigue Syndrome

Is the cause physical or psychological?

hronic fatigue syndrome is almost as mysterious today as when cases of "yuppie flu" first surfaced in the 1980s. No infectious agent has been found to cause the illness, which is defined as six months of fatigue and at least four flulike symptoms. Some researchers argue that the disease is psychologically induced — perhaps even a form of "mass hysteria." Others are convinced it has a physical cause. The federal government is funding investigations into possible disturbances in the immune system and the brain. Surprisingly, new studies suggest minorities and blue-collar workers - not yuppies — are most likely to suffer the symptoms. The illness probably will turn out to be a complex interplay of biological, psychological and social forces, many experts agree.



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# Chronic Fatigue Syndrome

### BY SARAH GLAZER

## THE ISSUES

onica Meyer remembers the beginning of her chronic illness as a time of overwhelming stress. She had just been through a nasty divorce and was raising two children while working full time as a systems analyst. She landed in the hospital with a serious bladder infection. As she tells it, she never got well again.

Meyer returned to her job in Marin County, Calif., but felt so weak after an hour that she could not stand up. Her coworkers had to carry her out of the office. During a lengthy convalescence, her mother had to hand feed her.

Before her illness, Meyer,

53, was vivacious and energetic. But for the past 10 years she has been unable to work because of recurrent episodes of profound fatigue. A half-hour phone conversation can leave her so tired she has trouble completing sentences. In her most exhausted states, she says, she feels "retarded," unable to read or comprehend a newspaper.

Meyer's chronic tiredness and cognitive problems, and her occasional joint pain, were diagnosed as chronic fatigue syndrome (CFS), a mysterious, lingering illness with no known organic cause, but plenty of controversy within the medical profession. Many sufferers say their illness started with the flu or an infection. In others, the symptoms developed gradually, without a clear illness triggering it.

According to the Centers for Disease Control and Prevention (CDC), a CFS diagnosis requires a patient to have severe, chronic fatigue for six months or longer and at least four of the following symptoms: substantial impair-



Monica Meyer's chronic tiredness, cognitive problems and joint pain have been diagnosed as chronic fatigue syndrome. The condition forced her to stop working as a systems analyst 10 years ago.

ment in short-term memory or concentration; sore throat; tender lymph nodes; muscle pain; multi-joint pain; headaches; sleep which is not refreshing; and feeling extremely tired or out of sorts for at least a day or two after exertion. As many as 800,000 Americans have the condition, according to a recent DePaul University study. <sup>1</sup>

Federally funded researchers have been investigating possible organic causes since the 1980s, ranging from viruses and other infectious agents to abnormalities in the immune system and the brain. So far, they have failed to find a definitive answer.

Skeptics in the medical community suggest the condition is largely psychological. In her 1997 book *Hystories: Hysterical Epidemics and Modern Culture*, Princeton University humanities Professor Elaine Showalter suggested that CFS is a classic psychogenic epidemic, in which people unconsciously develop symptoms they learn about through the media or other patients. <sup>2</sup>

She describes CFS as a modern version of 19th-century hysteria, which "mimics culturally permissible expressions of distress." <sup>3</sup>

Meyer admits that she was "burning the candle at both ends" with activity and stress, and that the bladder infection "pushed my body over the edge. I believe there's an invisible line, and once you cross it, you never bounce back."

Today, Meyer carefully conserves her energy, depends on friends for grocery shopping and builds long periods of rest into her tightly restricted schedule. Like many CFS sufferers, she goes through cycles of feeling good, in which she exerts herself through exercise or sociability, and then crashes with exhaustion. These days she keeps track of her

energy level moment to moment, making sure to rest when anything tires her.

There is no known cure for CFS, so most doctors treat the symptoms, using a variety of approaches, including painkillers, sleep aids, blood pressure medications, anti-depressants and stimulants. However, in a CDC study in which recovery was defined by the individual patient, about half reported "recovery," and most of them said they had recovered within the first five years after the onset of the illness. <sup>4</sup>

Meyer has "tried everything" from New Age treatments like acupressure and homeopathy to mainstream treatments like anti-depressant drugs — all with little success. "The solution for me is just self-monitoring," she says. "I think the body just needs time to heal itself."

Robert Ferrari, a Canadian doctor in Edmonton, Alberta, specializing in rheumatology, says Meyer is typical of many patients he sees — perfectionists who led overly full lives. Ferrari believes CFS provides a socially acceptable means for overstressed people to drop out and restructure their lives, although they have no conscious desire to do so.

"Super-moms especially have a lot of stress. They don't listen to the clues that tell us when we should back off," Ferrari says. "Typical CFS patients tend to be super individuals. They can't just go to their boss and say, T've taken on a big project and now I want to drop it.' They cannot say to themselves either, 'Suddenly I can't handle it.' "

As for the widely reported cognitive problems, he points to studies finding that individuals subjected to psychological stress have a harder time completing cognitive tasks. As for the pain, he notes that people who keep a daily pain diary tend to magnify symptoms they might otherwise ignore.

Anthony L. Komaroff, a professor of medicine at Harvard Medical School, says his personal experience with hundreds of CFS patients has convinced him that the disease does have a physical basis. However, Komaroff admits, there is no "perfect test" that shows any single abnormality unique to all CFS patients that distinguishes them from healthy people — or from patients with other diseases.

In the mid-1980s, Komaroff went to the Lake Tahoe resort town of Incline Village, Nev., to examine the first modern reported rash of patients complaining of chronic fatigue symptoms in the United States. "Many had physical things wrong that no amount of suggestibility could cause," he says, including abnormal lab tests, difficulties with muscle strength and coordination and loss of intellectual ability. Particularly memorable, he says, were patients who had graduated near the top of their class the year before suddenly having below-average IQs.

David S. Bell, a pediatrician in rural Lyndonville, N.Y., had a similar experience in 1985, when he treated more than 200 adults and children for CFS. <sup>5</sup> "I knew many of the patients

### CFS in the U.S.

CFS is most common among women, Latinos, people in their 40s and skilled workers, based on a random sample of 18,000 Chicago adults. Nationwide, 800,000 people suffer from CFS, researcher Leonard Jason of DePaul University estimates.

## Prevalance rates of CFS (per 100,000 people)

By gender the state of the same	over si	
Men	291	
Women	522	
By race		
White	318	
African-American	337	
Latino	726	
Other	491	
By age		
18-29	315	
30-39	412	
40-49	805	
50-59	413	
Over 60	354	
By occupation:		
Professional	325	
Unskilled/semiskilled	486	
Skilled workers 70		
Nationwide	422	
Course Loomand & Jason et al	"4	

Source: Leonard A. Jason, et al., "A community-based study of chronic fatigue syndrome," Archives of Internal Medicine, 1999

before they got sick, and I do not feel they had mass hysteria or that this was a psychiatric illness," insists Bell, author of *The Doctor's Guide to Chronic Fatigue Syndrome*. "I believe it is a physical illness."

The conviction that there is a physiological explanation for CFS is shared by the CDC official investigating the

condition. Dr. William C. Reeves says CFS patients are not "whiners looking for excuses. These are people who had very successful lives, and those lives are ruined."

The disease can frustrate doctors, he says, because physicians "don't have a physical sign they can get into the billing system" or a drug that can fix it.

The CDC is financing research into possible immune system or brain dysfunction as a potential cause of CFS. "At its root, there's something wrong. We just haven't found it," Reeves says.

As scientists continue to search for a cause, here are some of the issues being debated:

## Is CFS a physical disease?

When CFS first came to public attention in the early 1980s, some researchers and doctors blamed the Epstein-Barr virus, the bug that causes infectious mononucleosis. The theory derived partly from the mysterious chronic fatigue outbreak in Incline Village, where two local doctors found that 75 percent of their patients had increased Epstein-Barr antibody levels. 6 However, the hypothesis was discarded after it was discovered that many healthy people also have such antibodies. About 95 percent of all adults over age 35 have been infected with Epstein-Barr, but many have no symptoms. 7

Since then, other hypotheses have cropped up, but researchers have yet to find a single cause or group of causes that would distinguish CFS from any other disease or explain CFS in all patients.

The most ardent skeptics say CFS is just the modern manifestation of such Victorian maladies as "nervous exhaustion," a set of socially acceptable symptoms victims learn about through the press, their doctors and other patients. According to some theorists, these patients manifest symptoms of tiredness and aches because they cannot admit they have psychological problems or are overwhelmed by stress.

Almost every cause blamed for CFS either is so common that it occurs in as many people with the syndrome as without, or the abnormalities are the result — not the cause — of the syndrome, says George E. Ehrlich, an adjunct professor of medicine at the University of Pennsylvania and chairman of the Expert Advisory Panel on Chronic Degenerative Diseases at the World Health Organization.

Studies have found that anywhere from 35-70 percent of patients with CFS also suffer from another mysterious disease, fibromyalgia. <sup>8</sup> It is defined by three months of widespread musculoskeletal pain and tenderness at 11 of 18 specific points on the body. Many doctors on both sides of the debate view CFS and fibromyalgia as virtually the same illness.

"I see both of these as iatrogenic diseases — caused by doctors," Ehrlich says. "Usually the symptoms cannot be verified by examination. On the whole, these are signs of social maladjustment — not diseases."

There's a tendency for the diagnoses to vary according to what kind of specialist sees the patients, skeptics point out. For example, rheumatologists look for musculoskeletal pain; gastroenterologists look for gastrointestinal problems. Depending on the study, 58 percent to 92 percent of patients with CFS also have irritable bowel syndrome — characterized by pain, constipation or diarrhea.

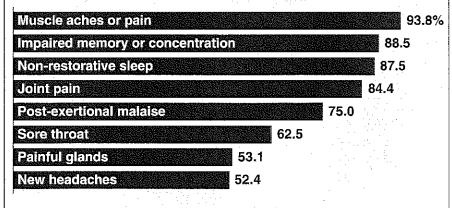
Harvard's Komaroff was an early champion of CFS as a disease with a physical basis. While he acknowledges researchers have yet to find a diagnostic test that can single out a CFS patient from healthy individuals, he says most studies find intriguing differences in many CFS sufferers.

"There are clear, statistically significant differences reflected in [CFS patients'] central nervous and immune systems . . . that are different [from healthy people] in the vast majority of scien-

## Pain and Memory Problems Are Common

In adition to suffering from at least six months of fatigue, most CFS patients also reported such classic symptoms as muscle and joint pain and impaired memory, according to Professor Jason's Chicago survey. Most of the sufferers had never been diagnosed with CFS, and most were receiving no treatment.

## Symptoms reported by CFS sufferers



Source: Leonard A. Jason, et al., "A community-based study of chronic fatigue syndrome," Archives of Internal Medicine, 1999

tific papers," he says. Unusual neurological patterns have been detected in high-tech magnetic resonance imaging (MRI) pictures of the brains of some CFS sufferers, he notes. Many also have unusually low blood pressure.

Since many CFS patients first contracted a flulike illness, some experts believe CFS is caused by an abnormality in the way the immune system responds to infection. For instance, the immune system may behave as if it must continue to fight an infection that is no longer there, causing the fatigue normally present when a person is fighting a virus. Or, the immune system activation might be sending distorted messages to brain cells — leading to fatigue, cognitive dysfunction and other symptoms of CFS. <sup>9</sup>

However, no single biological abnormality has cropped up in all CFS patients. In fact, symptoms can vary widely from patient to patient, making CFS appear to be several different diseases. Pediatrician Bell lists over 40 common symptoms. <sup>10</sup>

"Finding syndromes with overlapping symptoms and lab test abnormalities could reflect different expressions of the same underlying abnormality," Komaroff says.

Skeptics like Nortin M. Hadler, a professor of medicine and microbiology/immunology at the University of North Carolina, say they're not persuaded by any of the studies, because so-called abnormalities may simply reflect minor differences among healthy individuals rather than markers of biological sickness. "We're talking about metabolic variations that are slightly different, and some of them are things you'll have when you feel joy; some when you feel awful," Hadler scoffs. He dismisses reports that CFS patients show unusual patterns in their brain scans or their neuroendocrine or immune systems. Such patterns are "either very hard to reproduce" in subsequent studies, he says, or are more likely "a reflection of feeling ill" than a cause.

In the absence of convincing biological evidence, Hadler says, he con-

cludes that CFS patients are "psychosocially challenged." Others suggest that depression is a major factor among CFS patients.

However, after polling 18,000 Chicago residents, Leonard A. Jason, a professor of psychology and director of the Center for Community Research at DePaul University, disagrees. "The majority of people in our samples [who had CFS] did not have psychiatric disorders before getting CFS," he reports.

Jason is among a growing body of experts who think CFS is likely to be explained by an interplay of biological, psychological and social factors. "It could well be that having post-traumatic stress disorder or depression could bring about biological changes in the body so a person could be more vulnerable to having CFS or a variety of things," Jason says. "So, clearly, psychological disorders could be one more risk factor." But he doubts depression or any other psychiatric problem alone causes the phenomenon. <sup>11</sup>

Benjamin Natelson, a professor of neuroscience at New Jersey Medical School, estimates that 30-40 percent of people with CFS have co-existing psychiatric problems. But, he adds, when he treats his patients' psychiatric problems with anti-depressants, for example, they feel better, but most continue to have physical symptoms linked to CFS.

Natelson is currently researching two hypotheses about the cause of CFS: that some patients may have "a [mild] smoldering brain disease," or are in the early stages of heart disease. "When you ask early heart failure patients, what's their major problem, it's fatigue," he notes.

Anthony S. Russell, who heads the Rheumatic Disease Unit at the University of Alberta, Canada, doubts that CFS or fibromyalgia are organically based. When he asks both types of patients to rate their pain on a scale of 1 to 10, they almost invariably rate it as a "10" — extreme pain, he says. But the fibromyalgia patients with CFS don't act as if they're in excruciating pain. "These

patients are smiling, chatting, holding normal conversation," he says.

Russell believes that such patients simply represent a portion of the general population that has always suffered aches and pains especially keenly, without necessarily giving it a name. He points to British surveys showing that about 5 percent of the general population claim to suffer from chronic pain. <sup>12</sup> "But most never see a doctor because they deal with it," he says.

Skeptics often describe this exaggerated response to pain or fatigue as "symptom amplification" or "somaticizing" — essentially, a psychosomatic response that makes a patient feel pain or fatigue that is unwarranted by their physical condition.

However, two University of Washington researchers think CFS and fibromyalgia patients may have a physiological characteristic that makes them feel pain and fatigue more keenly than most people. After surveying the research on conditions in which fatigue or pain appear out of proportion to patients' physical exams, they concluded, "The most frequent and consistent objective finding in unexplained clinical conditions has been a decrease in pain threshold and tolerance." <sup>13</sup>

Lead author Leslie A. Aaron cites a variety of studies that may provide a biological clue to these patients' increased pain sensitivity. "Since 1990, there's been an impressive accumulation of data in basic science labs showing that individuals with fibromyalgia have increased substances known to carry pain signals to the brain," she says. In addition, some studies using EEG tests find that people with fibromyalgia respond to tactile and visual stimuli more acutely than healthy people. Still other studies find that these patients tend to have low blood flow to portions of the brain known to modulate pain transmission.

"This evidence strongly suggests that something is going on at the physical level," says Aaron, who thinks it's most

likely that physical and psychological phenomena interact in these patients to produce CFS symptoms.

## Is cognitive behavioral therapy (CBT) the best treatment for CFS?

According to a controversial recent British government report, the two most successful CFS treatments are CBT—a form of psychotherapy— and graduated exercise.

Psychologists use CBT to change a patient's mistaken beliefs, such as the conviction that exercise will make him sicker. Then the therapist helps a patient establish a sleep-and-activity routine and set goals for getting better. Graduated exercise aims to gradually increase a patient's aerobic activity, such as walking or swimming, on the grounds that inactivity makes patients physically and psychologically worse. <sup>14</sup>

Both conclusions generated controversy, especially from patients. First, some objected to CBT because it is used by psychologists, and thus implies the disease is "all in the mind." <sup>15</sup>

However, proponents claim it has successfully helped patients with other well-accepted diseases — like cancer and arthritis — return to normal, active lives. In addition, it doesn't require that the therapist question the biological basis of the sickness, they point out.

Pediatrician Bell says he uses CBT with his patients, but doesn't call it that. "I say, 'I know you're sick: I do think you should get out of the house and go shopping for an hour every day,' "he explains. "A lot of patients will say, 'If I do any activity, I will get worse.' The implication is the disease will get worse. What I'm trying to change is the last concept. Your symptoms may be worse for the next couple of days, but the disease does not get worse."

"Psychologically informed treatments are certainly the most effective management strategies to date," says Simon Wessely, a psychiatric epidemiologist and head of general hospital psychia-

## 'It Was Emotionally Devastating'

ome skeptics view chronic fatigue syndrome (CFS) as a disease of depressed housewives or employees looking for an excuse to get out of work. But several current and former members of a California CFS support group suggest a different pattern: ambitious professionals who strove valiantly to keep working despite feeling debilitated by a mysterious ailment.

After Julie Woodside, a former account executive, caught what felt like the flu, she continued dragging into work for several years, often working only part of the week and then spending the next three days in bed. "I spent a lot of time managing my fatigue instead of my work and covering up for my errors," she says, recalling that cognitive difficulties led her to make numerical mistakes in handling her clients' money.

"Chris" tried to keep his job as an information technology specialist for two years after getting a persistent flu, even though the number of days he made it to the office each week dwindled. "It was very rewarding work," he says. "I didn't want to give that up."

Steven D. Patterson, 43, managed to finish law school while suffering from symptoms including severe cramps, constipation, night sweats, flulike fatigue, food allergies and ringing in his ears. He wanted to keep his demanding job handling federal disaster assistance but was laid off, he believes, because his employer thought he was malingering.

Perhaps a sign of their desperation to find a cure and get their lives back on track is the willingness of many CFS patients to try treatments ranging from the occult to the alternative. Woodside spent her savings to travel to London for "polarity therapy" — which claims to heal people by manipulating their "energy" forces — after she heard of a woman there who could work miracles. The woman waved her hands around, claiming to marshal healing forces, but Woodside didn't feel a thing.

"It was emotionally devastating when it didn't cure me," she recalls. She has also tried acupuncture, herbs, homeopathy, vitamins, anti-depressants, sleeping pills, diet changes, mineral treatments, anti-viral medications and antibiotics. Nothing worked.

All CFS suffers say the syndrome has taken a devastating toll on their lives. Woodside stopped working in 1991 and has resigned herself to being "productive" only about two hours a day. Both "Chris" and Patterson say their girlfriends broke up with them because of the illness. Patterson moved to Florida last year to be close to a doctor he thinks can help him with his gastrointestinal and cognitive problems. Meanwhile, his memory and reading comprehension are so unreliable he has given up practicing law unless he has an associate to fall back on.

For some patients, the most painful aspect is encountering doctors who don't take the disease seriously and treat their problems as psychologically induced rather than biological. "We hear heartbreaking stories of people struggling to find someone who will listen to them," says Woodside, president of the California Capital CFIDS Association, a patients' group in Sacramento.

Now that's changing. "More often, now, people will get the diagnosis, but the doctors don't know what to do for them," Woodside says.

try at London's Institute of Psychiatry. His studies of CBT have found positive results for chronic fatigue patients in their functioning and fatigue. "However, that also does not prove this is a psychological disorder," he adds. <sup>16</sup>

But DePaul's Jason points out that CBT is not a cure for CFS. Although in clinical trials it helps about 70 percent of patients feel better, it has not produced total recovery. <sup>17</sup>

While acknowledging that CBT helps some patients cope with their illness, K. Kimberly Kenney, president and CEO of the Chronic Fatigue and Immune Dysfunction Syndrome Association of America (CFIDS), says, "Behavioral therapies are no more a cure for CFS than they are for cancer." <sup>18</sup>

Patient groups have developed hostility toward CBT because some of the earliest British researchers tried to convince patients that their illness had no organic cause and made no secret of their belief that patients had become phobic about exercise, says Jason, who is studying CBT for CFS patients in the United States. Kenney notes that of the 44 studies rated for the British report, CBT studies had the highest dropout rate and did not include patients too disabled to make it to the clinic.

Moreover, Jason and Kenney charge, medical personnel who have heard about CBT sometimes try to practice it in a crude form without any training. "Here's a patient who can barely walk for five minutes, and they're being told to walk half an hour three times a week," Jason says. It just makes the patient feel more "neglected and misunderstood," he adds.

Some patient advocates fear that CBT could be employed to make patients over-exert themselves and get sicker. Kenney warns that CBT "has the po-

tential to cause severe relapses, especially when not administered by skilled professionals." <sup>19</sup> Kenney says most U.S. practitioners are not educated about CFS, and managed-care companies often won't pay for the number of CBT sessions needed to be successful.

Meyer's reaction to the British recommendation favoring CBT is typical of other patients. "[Those] who think it's psychological have never been there," she says. CFS sufferers "would do anything" to get well. "I don't see how CBT would fix it."

The British committee's recommendation on graduated exercise was equally contentious. Several patient representatives resigned from the panel rather than support urging more exercise. <sup>20</sup> Most patients say carefully monitoring and limiting activities that exacerbate symptoms, like exercise, is the only way to avoid entering a vicious cycle

of overactivity and then crashing with fatigue. For instance, Meyer says she can work out on a treadmill for up to 30 minutes, but any more will land her in bed for four days.

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Meyer's approach, known as "pacing," is based on the "envelope" or "glass-ceiling" theory: that energy is finite and living within this envelope is the best way to manage the illness. <sup>21</sup>

However, no research supports pacing, and some clinicians say it perpetuates the illness, the British report noted. Even so, the panel supported pacing as a third treatment alternative because it is popular with patients — a decision that prompted four panel members to resign, claiming it played down the psychological and social aspects of CFS. <sup>22</sup>

Some CFS experts in the U.S. also condemned the pacing recommendation, including Stephen E. Straus, former chief of the clinical investigation lab at the National Institute of Allergy and Infectious Diseases and one of the first National Institutes of Health (NIH) researchers reported to suggest a possible psychological basis for the disease. He said the British group's conclusions "appear more shaped by anecdote than by evidence." By encouraging patients to avoid increased activity, pacing "may condemn [CFS patients] to stay ill longer," he said. <sup>23</sup>

## BACKGROUND

## Victorian Precursor

In his 1998 book, *Chronic Fatigue* and its *Syndromes*, psychiatrist Wessely argues that "neurasthenia" or nervous exhaustion — a favorite upperclass disease in Victorian England and America — was the precursor of modern CFS. <sup>24</sup>

Much like the modern syndrome, the 19th-century disease featured excessive fatigue; difficulties with thinking, speech and memory; and neuromuscular weakness. Doctors blamed the condition on exhausted muscles and nerves. The recommended cure was total rest, and fashionable spas were crowded with sufferers.

By the end of the century, however, the condition fell out of favor as the disorder came to be viewed as psychological. The upper classes did not want the stigma of having a psychological disease, Wessely writes.

By 1906, the disease was being described as a condition mainly of the working classes. By the late 1920s, medical journals were questioning the organic nature of the condition, and by 1960 neurasthenia was dropped as an official psychiatric classification in the United States and England

Neurasthenia "provided a haven for those . . . who either insisted on its solely organic basis or saw it as a refuge for the mentally infirm," writes Wessely. Both arguments have resurfaced in connection with modern CFS, he writes. In both the old and new illness, he argues, the issue of legitimacy — "namely what constitutes an acceptable disease" — is at stake.

# The First Epidemic?

In the United States, chronic fatigue symptoms reappeared in 1984, when patients started complaining of extreme tiredness and flulike symptoms in Incline Village. Physicians Paul Cheney and Dan Peterson asked the CDC to investigate. A year later, a similar outbreak occurred among Bell's patients in Lyndonville.

However, the CDC's report on the Lake Tahoe outbreak, published on May 30, 1986, questioned whether the disease existed and suggested the two doctors had misdiagnosed the condi-

tion. In her book *Osler's Web*, journalist Hillary Johnson writes that CDC investigator Jon Kaplan suggested the doctors had colluded with their patients to identify as a single disease a syndrome that varied wildly in the symptoms and length of tiredness. <sup>25</sup>

"CDC investigators . . . could not document any more cases in Incline Village than appear normally in the population," says the CDC's Reeves. "There's no good evidence that anything unusual was going on there." The practitioners specialized in chronic fatigue and were sought out by such patients, he noted, which could explain the large number of patients with similar symptoms.

Because of its similarity to mononucleosis, the illness was dubbed "chronic Epstein-Barr virus" (CEBV) or "chronic mononucleosis." That name fell out of favor after it became clear that most healthy adults were exposed to Epstein-Barr sometime during their lives.

In 1988, the CDC published its first official definition of "chronic fatigue syndrome" in the *Annals of Internal Medicine*. That same year a patients' organization known as the Charlotte CEBV Association began to meet. It later became the CFIDS Association of America, based on the hypothesis that a flawed immune system causes the condition.

Media interest in the new syndrome grew in the 1980s, and the Lake Tahoe practice was inundated with calls from people around the country reporting similar symptoms. The condition acquired the label "yuppie flu," because of the many young urban professionals and Hollywood personalities who were struck by the illness. The preoccupation with AIDS, and the search for a causative virus in both diseases, also contributed to media interest. <sup>26</sup>

In 1988 a television show, "The Golden Girls," featured episodes dramatizing a character's CFS diagnosis. That same year the CFIDS Association was flooded with more than 10,000 requests for information, and a quarter of the calls to the communications office of

# Chronology

the National Institute of Allergy and Infectious Diseases were about CFS. <sup>27</sup>

#### CDC Restores Misspent Funds

In 1990, Congress authorized the NIH to fund several CFS research centers around the country. In 1994, the CDC loosened its 1988 definition of chronic fatigue syndrome. In addition to at least six months of fatigue, patients now only have to suffer from four symptoms — not eight — to meet the diagnosis.

In 1996, journalist Johnson — who suffered from chronic fatigue — published her book portraying NIH and CDC officials as hostile to the idea that CFS was a medical disease. The book renewed the concerns of patient advocates that the government was not aggressively investigating the condition.

Two years later, Reeves accused CDC Administrator Brian Mahy of diverting CFS research funds to other areas. In 1999, the CDC inspector general confirmed that between 1995 and 1998 some 57 percent of CFS funds were actually spent on other programs. The agency agreed to restore the misspent funds over the next four years. <sup>28</sup>

Reeves now says the CDC has restored the \$13 million and reinvigorated the CFS program. The agency is focusing on possible problems in brain or immune-system functioning.

## CURRENT SITUATION

## New Prevalence Rates

N ew studies are finding that CFS is actually more common in the general population than once thought and, surprisingly, most common among ethnic minorities and blue-collar workers, rather than "yuppies."

## 1900s-1920s

Neurasthenia, or nervous exhaustion, falls out of favor among the upper classes when doctors begin viewing it as a psychological disease.

### 1906

Neurasthenia is described as a disease of the working classes.

ISOS Reported CFS outbreaks attract media interest and investigation by the federal government. The mysterious syndrome is dubbed "chronic Epstein-Barr virus."

### 1984

About 200 cases of CFS are reported in Incline Village, Nev.

#### 1985

Dozens of patients in Lyndonville, N.Y., report severe flulike symptoms.

#### 1986

Centers for Disease Control (CDC) finds no evidence of an epidemic at Incline Village and questions whether CFS exists.

#### 1987

CFS is called "chronic Epstein-Barr virus" in the United States, based on preliminary studies by the National Institutes of Health (NIH). But it soon becomes clear most people are exposed to Epstein-Barr.

#### 1988

The CDC coins the term "chronic fatigue syndrome."

1990\$ Congress authorizes CFS research, but the CDC resists. The syndrome is found among Persian Gulf War veterans.

#### 1990

Congress orders NIH to establish CFS research centers.

#### 1994

The CDC redefines CFS, reducing from eight to four the number of symptoms besides fatigue needed for a diagnosis.

### 1997

A CDC study says Gulf War veterans have higher rates of CFS than their military counterparts who did not participate in the war.

### May 1999

The CDC's inspector general finds that the agency diverted funds Congress intended for chronic fatigue research. Agency agrees to restore funds.

### Oct. 11, 1999

Chicago study finds CFS is most common among ethnic minorities and blue-collar workers.

2000\$ Controversy continues over whether CFS is biologically, psychologically or socially induced.

#### Jan. 11, 2002

In a compromise between patients and medical skeptics, a British government panel recommends both behavioral therapies and a carefully limited lifestyle. It is attacked by both sides.

In a 1999 study of more than 18,000 Chicago adults, DePaul's Jason projected that as many as 800,000 people nationwide suffer from CFS — 422 out of every 100,000 Americans — nearly twice the rate previously reported by the CDC. <sup>29</sup> Latinos and blacks had the highest prevalence rates. The researchers speculate that the higher rates among Latinos and blacks may result from generally poor health due to stress, poor nutrition, inadequate health care and more hazardous jobs.

The CDC's most recent population study — conducted in Wichita, Kan., but as-yet unpublished — found an even higher rate among African-Americans, the highest prevalence of any racial ethnic group, Reeves says.

Reeves suggests that some of the differences between the Chicago and Wichita studies may reflect the different racial and ethnic makeup of the two cities. A CDC study in San Francisco also found that CFS-like disease was most common among blacks and those with household incomes under \$40,000. 30

Jason speculates that the perception of CFS as a mainly white, professional illness may have stemmed from the focus of most previous studies on patients referred to private doctors. Such surveys could have missed minorities and lower-income workers, who rely more on public health clinics or emergency rooms. By contrast, the Chicago study used a random sample of adults. It found that more than 90 percent of adults who met the criteria for CFS had never been diagnosed, and most were receiving no treatment, according to Jason.

CFS is rarely diagnosed, he says, because its most salient symptom — fatigue — is also a common sign of many other disorders, notably depression. "Making the distinction between CFS and depression is absolutely critical," he says. "Yet lots of regular physicians [without] psychiatric training can't differentiate anxiety disorders and depression from chronic fatigue syndrome."

## How Psychological?

P hysicians who doubt that CFS is a genuine disease tend to view data like Jason's as further evidence that most people manage to cope with tiredness and aches until told they have a specific disease. UNC's Hadler is among those skeptics who believe it's actually harmful to tell patients they have a disease when there's still no medical evidence of what causes it.

But Jason contends that people who are unaware that their suffering has a name are not coping that well. Compared to healthy people, participants in the Chicago study who had CFS symptoms were more likely to be unemployed, receiving disability pay or working part time. Most met the criteria for a psychiatric problem, the study found, but about 20 percent had never experienced a psychiatric illness. Jason says his data suggest that most CFS sufferers become depressed as a result of their illness rather than before.

"Once these people get sick, they can't work anymore," he says. "You have the family questioning you, your social relationships start dropping off and then you have medical personnel saying, 'This is all in your mind, and you could easily reverse it if you wanted to.' It's not hard to understand why those people would get depressed."

Like past researchers, both the recent CDC and Chicago investigators found that CFS is more common among women than men. Some CFS skeptics argue that the gender difference provides additional evidence that CFS is psychologically rooted, because U.S. women often carry the double stress of work and family. But other experts think it may reflect the fact that women are more likely to seek medical care.

Moreover, several other diseases — especially those involving the immune system — affect far more women than

men, including lupus, multiple sclerosis and rheumatoid arthritis. "It's a plausible hypothesis that hormonal differences make immune-mediated diseases more common in women than men," says Harvard's Komaroff.

## Gulf War Illness

A ccording to the CDC, there is no evidence that CFS is contagious. <sup>31</sup> Since the so-called outbreak in Nevada, the agency has investigated reported outbreaks in other states, but found no evidence of an epidemic — with one exception.

The agency says the so-called Gulf War Syndrome, suffered by soldiers who served in the Persian Gulf War in 1990-1991, was the first documented cluster of CFS. A 1997 CDC-funded study found a significantly higher rate of both medical and psychiatric conditions among Gulf War veterans than among their military counterparts who did not serve in the war. <sup>32</sup>

As of 1999, the Department of Veterans Affairs found that a quarter of those who served in the war were disabled with service-related medical conditions. Most who were severely ill also met the definition for CFS, according to the CDC's Reeves. To date, no single substance has been identified as the cause of Gulf War illness, which has symptoms such as multiple chemical sensitivity and depression. <sup>33</sup>

A team of researchers led by Wessely has suggested that the soldiers' pre-war inoculations, combined with the stress of deployment, may be linked to their health problems. <sup>34</sup>

"Calling Gulf War illness chronic fatigue syndrome makes a big jump policy-wise that cannot be completely backed up by the data," Reeves cautions, noting that the government has been reluctant to make that conclusion because of the liability implications.

Continued on p. 300

# At Issue:

## Is chronic fatigue syndrome a "real" disease?

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ften, when people hear that there is no known test or cause for CFS, they misinterpret that to mean the illness is not real. But over the past 15 years, scientists have identified numerous biological abnormalities that provide evidence for the reality and seriousness of CFS.

However, because there are no diagnostic tests yet for CFS and none of the biological abnormalities clearly distinguishes CFS patients from other individuals, testing primarily is used to rule out other illnesses that also can cause chronic fatigue.

The leading model of CFS pathogenesis is rooted in scientifically identified abnormalities in the brain and endocrine and immune systems, which each influence and after the function of the others in a reciprocal cycle. Low levels of cortisol, identified in several CFS studies, can increase immune activation, theoretically resulting in brain dysfunction. When the immune system is activated, it makes chemical messages. Brain and immune-system cells can receive these messages, possibly leading to fatigue, cognitive dysfunction, enhanced sense of pain, hormonal dysregulation and other features of CFS.

Several immune-system abnormalities seen more often in CFS patients mimic the immune pattern of a body fighting a virus, even though no virus has been identified as the cause of CFS.

The most intriguing recent immunological finding in CFS is the discovery of a novel, low-molecular-weight protein called RNase-L, which is found in white blood cells and is part of a chemical process that gets turned on when white cells are needed to fight viral infections. This protein is found more often in CFS patients than in healthy people or in people with two other fatigue-producing conditions: depression or fibromyalgia.

Considerable evidence also indicates that the brain and central nervous system are involved in CFS. "Soft" evidence includes patient-reported symptoms such as cognitive dysfunction; sensitivities to stimuli such as bright lights; numbness in the extremities; and disordered sleep. "Hard" evidence includes hyperintense signals on MRI scans and reduction in cerebral blood flow on SPECT scans — an abnormality that changes over time and is not an indication of brain damage.

Altogether, these and other findings provide important evidence that CFS is not an imagined illness. While there still is no CFS test, scientists are moving closer to developing tools to assist clinicians in diagnosing it. In the interim, scientists have provided clues to the biology of CFS and have given clinicians, scientists and patients critical data showing that CFS is a real and serious illness.

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arious viral infections and malignant tumors, or leukemias, produce overwhelming chronic fatigue, as do a variety of neuromuscular diseases. These usually can be diagnosed. The unfortunate term chronic fatigue syndrome was coined to identify conditions for which tiredness is a prominent symptom. However, the extreme fatigue that characterizes organic diseases is absent, and a feeling of lassitude is misconstrued as fatigue.

The diagnostic criteria advanced by believers include persistent or recurrent symptoms over at least six months without identifiable causes. The rest of the symptoms resemble those for fibromyalgia, chronic irritable bowel, temporomandibular joint syndrome and so-called chronic Tyme disease. All of these self-reported disorders have symptoms that cannot be scientifically verified, and all are said to be complicated by "cognitive dysfunction" — self-reported memory impairment.

Chronic fatigue is called a "syndrome" because there is no consistent definition of symptoms, nor is there objective proof of a link to an organic disease.

It is an example of social pathology, in which patients react to environmental factors by social mimicry: Once someone complains of the symptoms, they are copied, not necessarily volitionally, by others. The media contribute to these epidemics via talk shows, wide-eyed reports on local news and myriad newspaper features that discuss them as if they were real.

Chronic fatigue is an urban and suburban contagion of learned behavior, rarely diagnosed in rural areas where it would not be tolerated. While nearly everyone experiences these symptoms at some time, only a proportion give in to them. Without the secondary gain — in sympathy, compensation and toleration — the symptoms would ultimately disappear.

Unfortunately, activist advocacy groups encourage giving in to the symptoms, as do trial lawyers and well-meaning but misguided doctors and compensation systems that have bought into these erroneous concepts. By giving these symptoms names, we are driving the complainants into the hands of those who would profit from their discomforts, where they will be told that they are disabled and have little chance of getting well, and that someone or something (such as an accident) is responsible for their syndrome.

We are not saying these patients are malingering or imagining their symptoms. But we do believe psychological factors, fed by erroneous terminology, make their experienced symptoms worse and prolong them. Continued from p. 298

Komaroff, who served on two National Academy of Sciences panels investigating Gulf War illness, says the veterans' syndrome has been studied even less than CFS or fibromyalgia. "I would put Gulf War illness in the category of one of those illnesses that overlaps with chronic fatigue syndrome," he says. "But whether it's really the same will remain unknowable until we figure out the causes."

## **OUTLOOK**

## **Funds Sought**

P atient advocacy groups cite the latest estimates of the number of CFS sufferers as cause for increasing federal funding for CFS research. NIH funding has been about \$6 million annually for seven years, even though national estimates of the number of CFS sufferers have increased from the CDC's earliest estimate in the 1990s of about 10,000 to the most recent estimate of 800,000.

DePaul's Jason cites his own study to argue for increased government funds to help CFS sufferers with everything from housing to financial assistance. At the current budget, Jason estimates, federal funding for CFS research amounts to less than the government devotes to less-prevalent illnesses. 35

Meanwhile, experts increasingly view all disease as an interplay of biological, psychological and social forces, even in such clearly biological conditions as cancer and heart disease. Most agree that all these factors are probably involved in chronic fatigue syndrome, but they disagree over their relative importance.

Acknowledging that psychological factors play some role, Komaroff, says,

"It's a question of whether this explains the phenomenon or only a few people with the phenomenon."

If researchers eventually find some organic cause, patients will be proven right in their conviction that CFS is a biological disease. If the diagnosis fades away, much like neurasthenia did early in the 20th century, skeptics will be proven right in their belief that it is just a fad masking psychosocial distress.

## **Notes**

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- <sup>14</sup> Chief Medical Officer, Department of Health, Report of the CFS/ME Working Group, Jan. 11, 2002, at http://www.doh.gov.uk/cmo/cfsmereport/index.htm.
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- <sup>17</sup> For a summary of the research on which the British report was based, See Penny Whiting *et al.*, "Interventions for the Treatment and Management of Chronic Fatigue Syndrome," *JAMA*, Sept. 19, 2001, pp. 1360-1368.

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- <sup>24</sup> Information in this section drawn in part from Simon Wessely *et al.*, *Chronic Fatigue and Its Syndromes* (1998), pp. 96-116.
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## FOR MORE INFORMATION

American Association for Chronic Fatigue Syndrome, 515 Minor Ave., Suite 18, Seattle, WA 98104; (206) 781-3544; www.aacfs.org.

Centers for Disease Control and Prevention, National Center for Infectious Diseases, Mailstop C-14, 1600 Clifton Rd., Atlanta, GA 30333; (404) 639-7394; www.cdc.go/ncidod/diseases/cfs.

CFIDS Association of America, P.O. Box 220398, Charlotte, NC 28222; (704) 365-2343; www.cfids.org.

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# The Next Step:

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## CITING THE CQ RESEARCHER

Sample formats for citing these reports in a bibliography include the ones listed below. Preferred styles and formats vary, so please check with your instructor or professor.

## MLA STYLE

Koch, Kathy. "Truck Safety." <u>CQ Researcher</u> 12 March 1999. CQ Electronic Library. Richland Coll. Lib., Dallas. 25 Jan. 2002 <a href="http://library.cqpress.com">http://library.cqpress.com</a>>.

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