

The Invisible

WILHELMINA JENKINS WAS WORKING AS A GOVERNMENT PHYSICIST and a teacher at Howard University when she suddenly fell ill with a disease absolutely no one was able to diagnose. Jenkins, then 33, had many symptoms, including profound exhaustion. But the most troubling was a rapid loss of mental clarity.

For five years, Jenkins tried to work around the problem by taking a less pressured teaching job and then quitting regular work altogether to do independent research, but her decline continued. Finally, in 1988, a psychiatrist sent her to an internist, who determined that she suffered from what had recently been named chronic-fatigue syndrome (CFS), a neurological, metabolic and immunological disease that can disable victims for years (see box, page 71). Early on, sufferers typically experience a range of symptoms—from an ongoing, low-grade fever and lymph-node pain to night sweats and temporary amnesia—but the persistent hallmarks are a near-paralytic weakness and what patients often describe as a constant mental fog.

For Jenkins, as for many patients, the emotional toll has been nearly as great as the physical debilitation. "I felt I had been robbed," she says. "The things that I had been told could never be taken away from me—my education, my intelligence—had been taken away. Now there are days when I cannot get through a comic strip. The emphasis on fatigue in this disease is over-

played—the cognitive problems are what break you."

Before 1984, few doctors had ever encountered such an illness; by the end of the decade, the phenomenon was common. Precise measurements of the epidemic's breadth have yet to be made, but some estimates suggest that a million or more people are sick, to varying degrees, with this incur-

Epidemic

able malady. Women are diagnosed with CFS at least twice and perhaps three times as often as men. Among the rich and famous who were open about their struggle with CFS were Cher and Gilda Radner, who suffered from the disease during the year preceding her ovarian-cancer diagnosis (preliminary research suggests that CFS may lead to cancer in some sufferers). A number of other public figures are known by insiders to suffer from CFS but are unwilling to reveal their condition.

Although one wag has called the disease "girl AIDS," CFS afflicts men and children as well as women; three and a half years ago, Jenkins's daughter, Kamilah Neal, then 14, was diagnosed with it. (Several CFS researchers have observed that, not infrequently, the disease spreads within families.) Nevertheless, measured by years of productivity lost rather

Chronic-fatigue syndrome is a debilitating disease diagnosed far more often in women. Why is it being ignored? BY HILLARY JOHNSON

than by mortality, CFS may well pose the most serious health threat to women in their prime.

During the late '80s, TV and print journalists were on familiar terms with the disease, usually calling it the "yuppie flu" because it seemed to strike mostly upper-middle-class whites. By 1990, as a result of some intriguing scientific findings, the disease had become a popular news topic. Yet today CFS has fallen into a kind of Bermuda Triangle of misplaced epidemics. Powerful forces have conspired to render it invisible—namely, doctors confounded by the disease and federal health officials who, burdened with projects they deemed more important, hoped the brouhaha would simply blow over. Indeed, that a public-health issue of this magnitude has been overlooked—in effect, "disappeared"—is one of the most remarkable chapters in 20th-century medicine.

The Data Shortage

Key to understanding any new disease is assessing its breadth. Yet close to 10 years after a highly publicized outbreak in Incline Village, Nev., no one is certain how many people in the U.S. have CFS or how it is spread. Responsibility for this crucial task rests with the Atlanta-based Centers for Disease Control and Prevention (CDC). The agency's first brush with the disease was its perfunctory and unrevealing investigation of the 1985 Nevada outbreak. A few influential scientists and doctors soon advanced the notion that CFS was a psychiatric disorder. How else to explain why healthy, productive members of society would suddenly drop out, claiming an array of dramatic-sounding symptoms?

Congress harbors a distaste for interfering in the scientific activities of federal health agencies like the CDC, on the reasonable grounds that science can't be legislated. Bowing to pressure from patients, though, it shed its neutral role in the late 1980s, much as it had done with AIDS, and began demanding more and better CFS research. Each year for the last seven, Congress has asked the Atlanta agency to perform national surveillance,

appropriating ever-larger sums of money—from \$400,000 in '88 to \$4.7 million this year. The cash-starved agency has funneled the money into its various labs and scientific branches in the name of CFS research, but its epidemiologists have yet to perform reliable national surveillance.

Assuming that the disease was extremely rare, if it existed at all, the agency's epidemiologists launched a limited "passive-surveillance" program in Atlanta, Reno, Wichita, Kans., and Grand Rapids, Mich., in September 1989, using one of the least trustworthy methods: a doctor-based referral system. Doctors, it's been noted, are notoriously unreliable reporters of disease; imagine the problems that might arise when the disease is one that few doctors understand well enough to diagnose and that many have been led to believe exists only in the minds

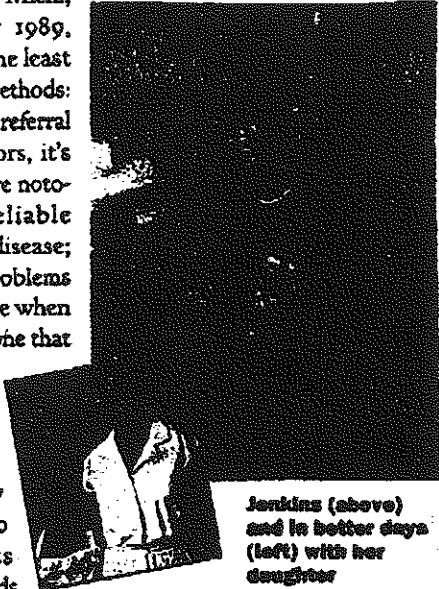
of malingerers, bored housewives and excitable members of the press. In addition, reported victims had to be subjected to hours of psychological evaluation and have their cases approved by a panel of researchers—several of whom had little practical experience with CFS—using the CDC's definition of the disease, which has been extensively criticized, even within the agency. (A revised version, which elevates neurocognitive symptoms from a minor to a defining characteristic of the disease, is expected to be published in the *Annals of Internal Medicine* next month.) Walter Gunn, the CDC's principal CFS investigator until his retirement in 1991, frequently attended CFS support-group meetings in Atlanta. "There were inevitably 100 to 200 people there," Gunn says. "I always asked how many were enrolled

in our surveillance program. Usually, just a few raised their hands."

A year ago, a CDC report stated that there were 3,000 to 10,000 people in the U.S. with chronic-fatigue syndrome, or an average of 4.5 victims for every 100,000 adults (the agency recently changed the figure to four to 10 cases per 100,000). The low assessment stunned students of the disease, including Dr. Paul Cheney, an internal-medicine specialist in Charlotte, N.C., who, with his then-partner, Dr.

Daniel Peterson, had brought the Nevada outbreak to the CDC's attention. Cheney, who now sees CFS patients exclusively, notes that "at four per 100,000, there should be 40 cases in the Charlotte area. But I have 300 patients from Charlotte alone. . . . I would say [the CDC] is off 10- to 100-fold."

In several independent studies, epidemiologists have found vastly higher rates of disease by surveying populations, a more accurate means of measuring disease prevalence. Researchers at Harvard Medical School and the University of Washington in Seattle, studying the incidence of CFS among members of a Seattle HMO, recently arrived at an estimate of 98 to 267 cases per 100,000 people, up to 90 times the CDC's initial estimate for the general population. Such a rate suggests that CFS is more prevalent than a well-known disease like multiple sclerosis. Investigators who have looked at populations in which CFS rates were thought to be even higher have had their suspicions confirmed. Epidemiologist Sandra Daugherty of the University of Nevada surveyed the populations of Incline Village and neighboring Crystal Bay and found



Jenkins (above) and in better days (left) with her daughter

that more than four of every 100 people had fallen ill with CFS in the previous seven years—a vastly higher number than the government's. An ongoing study of Chicago nurses being done by DePaul University clinical sociologist Leonard Jason offers a second model. "The rates that we are coming up with are approximately 680 per 100,000 nurses," says Jason.

The big numbers in the Nevada prevalence study suggest "time-space clustering," a signal that the disease may be transmissible, as patient activists and some CFS experts have long believed. The Chicago study supports another theory, held by Gunn and others, that there is an unusually high degree of CFS among medical professionals. Many experts believe their vulnerability may result from exposure to sick people, some of whom are CFS sufferers yet to be diagnosed.

According to Dr. Keiji Fukuda, who is assigned to the disease at the CDC, agency staffers are lately admitting that their passive-surveillance system "undercounted" patients. Now, says Fukuda, "we're going to do it better" by using an active system to look for cases that involves dialing telephone numbers at random in selected cities.

Institutionalized Indifference
In 1988, the CDC officially began to identify the malady as chronic-fatigue syndrome. Besides making the disease sound harmless, the name has had the subtle effect of inspiring hostility toward the victim. Gunn, a psychologist with cross-training in epidemiology, is well versed in standardized systems of evaluating the psychological import of words.

"Chronic-fatigue syndrome has a real negative impact," he says. "The word *chronic* is associated with chronic complainers, chronic whiners. And *fatigue* is even worse." No wonder CFS has frequently been viewed in professional and lay circles alike as a "volitional" disability.

To some degree, all chronic maladies generate indifference: "It's a cultural ethos," explains University of Illinois psychiatrist and CFS researcher Judith Richman. "Americans are freaked out about death, but disability is invisible. If you're half dead, no one cares."

As a result of their low status within the medical establishment, CFS patients have almost no safety net. As with other chronic illnesses, the disease has been considered a preexisting condition that usually precludes health-insurance coverage. But unlike other chronically ill people, most CFS sufferers have had tremendous difficulty winning disability support from the Social Security Administration, which only recently established a code for the disease. Because they lack the medical and social supports usually accorded to the seriously ill, CFS sufferers often end up going to court to settle cases involving bankruptcy, divorce, child custody, employers' refusal to pay disability and even involuntary confinement in psychiatric hospitals.

Not surprisingly, many CFS sufferers are angry. "The government's just not taking it seriously," says Wilhelmina Jenkins. "There has been no effort, for example, to reach out to the public and explain how very serious this disease is. The loss to this country of people whose skills could be helpful is simply not understood."

Closing the Credibility Gap

If epidemiologists in Atlanta have shortchanged the public on documenting this pressing matter, the scientists at the nation's premier medical-research agency, the National Institutes of Health (NIH) in Bethesda, Md., have hardly done better in investigating the origins of the disease. Since 1987, the NIH's National Institute of Allergy and Infectious Diseases (NIAID) has made a few grants, but in amounts many researchers consider so small as to be mere tokens. In 1991, for instance, the institute funded three CFS research centers at universities. Typically, such centers are awarded multi-million-dollar grants; the CFS centers averaged \$450,000 apiece. "You would have to ascend from Atlantis to be able to do the level of work that they thought you could do for that kind of money," says immunologist Nancy Klimas, an AIDS and CFS specialist at the University of Miami.

An "intramural," or in-house, program exists to study the disease at NIAID. For a decade its agenda has been dominated by Dr. Stephen Straus, chief of the Laboratory of Clinical Investigation and an influential architect of the "psychoneurotic" theory. In 1988, he wrote in the *Journal of Allergy and Clinical Immunology* that an appraisal of CFS patients "often uncovers histories of unachievable ambition, poor coping skills and somatic complaints." (One sufferer quipped in response, "I'd like to be in the room when you tell that to Cher.") Straus included no supporting data for his comments. In a 1989 article, he suggested, on the basis of his evaluation of 28 people, that CFS sufferers were psychologically different long before they ever fell ill. Straus's CFS research has cost taxpayers an average of \$800,000 for each of the past five years. (He declined to comment for this article.) These days, NIAID administrators say they believe that the physiology of the disease also merits investigation. Says Dr. John La Montagne, who directs the division of microbiology and infectious diseases at NIAID, "This is not a trivial disease—cer-

Money can
do many
things, but
it cannot
expunge
scientific
bias

DO YOU HAVE CHRONIC-FATIGUE SYNDROME?

In spite of its name, fatigue alone will not justify a diagnosis of chronic-fatigue syndrome. In fact, the disease can't be cured by sleep. Most often, CFS begins suddenly. Patients and inexperienced doctors alike often confuse early symptoms with those of the flu or mononucleosis. Prodromal exhaustion is accompanied by flu-like symptoms such as a sore throat, headaches and muscle and joint pain. In time, patients develop neurological problems like short-term memory loss, difficulty finding words, confusion and balance disturbances. CFS expert Dr. Paul Cheney estimates that for those who are ill longer than four years, the recovery rate is anywhere from 5% to 20%. For more information, contact the CFIDS Association at 800-442-3437.

tainly not in the minds of patients."

In the fall of 1990, an immunologist from Philadelphia's Wistar Institute, the nation's oldest independent scientific research center, unhinged Straus's psychoneurotic theory at a neurology conference in Kyoto. Elaine DeFreitas described her discovery of viral gene fragments in CFS patients, the first time anyone had linked a potentially new virus specifically with the disease. American reporters were galvanized. Formerly a subject of hilarity, the disease now had an enormous horror quotient: It might be "catching." Major papers reported the story; the malady's baptism by media was complete when a CBS reporter pronounced CFS a real disease capable of turning "an active person into a virtual invalid overnight." *Newsweek's* editors put the story on the November 12 cover, calling CFS a "gray plague," which could be read as a play on either the politically incorrect term "gay plague" or the Black Death. Indeed, "gray plague" seemed an apt synonym for a disease that, unlike the 14th-century scourge, cast its victims into unending illness without killing them. The magazine estimated that there were two to five million Americans suffering from CFS. That issue of *Newsweek* was the hottest-selling of the year.

For a while it seemed that CFS might come to be viewed as the public-health catastrophe its victims and their advocates in medicine believed it was. University of California at San Francisco microbiologist Jay A. Levy, one of the discoverers of HIV, announced that he had created a test to help diagnose CFS based on an immune-system irregularity. The scientist's stature ensured wide coverage of his finding. Unfortunately, Levy's test proved to be less than universal in its ability to identify sufferers, a fate that has haunted many of the discoveries surrounding CFS. In 1993, virologists at the CDC revealed that they had been unable to replicate DeFreitas's work. The embattled scientist, now a professor at the University of Miami Medical School, and her clinician-collaborators, Charlotte's Paul Cheney

and Harvard pediatric-CFS expert David Bell, insist that the government failed to employ DeFreitas's more costly and time-consuming protocols; government scientists counter that their own methods were sufficient.

Despite the inconclusiveness of DeFreitas's work, it was one of a series of events that heated up the research climate. The NIH's Straus, for one, has appeared to be engaged in a game of scientific catch-up. Earlier this year, Straus's research group reported finding immunological aberrations in CFS patients. The NIH issued a press release as if this were a breakthrough, but, in fact, many CFS investigators had for years been documenting abnormalities,

such as aberrant levels of several kinds of white blood cells.

In the absence of further high-profile discoveries, awareness of the disease has receded, even if the disease itself hasn't. Although Cheney reports that he continues to see "a lot" of new cases, which he defines as people who have been ill for less than a year, 1987 is the year most frequently named as the one in which CFS sufferers fell ill. It may be that the epidemic peaked in the late 1980s, but, according to Cheney, if it took 10 years to reach a peak, it could take three times that long to level off. (Cases have now been identified dating back to the late '70s, and some theorize that CFS has occurred in isolated outbreaks for decades.) "The exponential growth has lessened," says Cheney, "but the number of people getting sick is still growing."

The Misery Index

Despite the government's stance and the disease's name, CFS has one of the highest morbidity rates (degrees of suffering) of any illness, rivaling the physical misery of advanced cardiac disease and cancer. Dr. Phillip Peterson, head of the infectious-diseases department at Minneapolis's county medical center, opened a CFS research clinic there in 1988. The average age of the clinic's

patients then was 38, and 80% were women. "Roughly half the patients could walk only three blocks or less," Peterson says. He and his collaborators explored the "functional severity," or degree of disability CFS imposes, using the Medical Outcome Study, in which a score of 100 is "best health." They compared their patients' scores with those of healthy people and people who had suffered a heart attack or who had rheumatoid arthritis. Healthy people scored an average of 75, heart-attack patients in the mid-40s and victims of

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rheumatoid arthritis slightly higher. Clinic patients scored, on average, 16.5, a level never before measured on the Medical Outcome scale. University of Minnesota medical professor Nicole Lurie had to redraw the scale to fit the clinic patients onto a diagram Peterson used for a formal paper on the subject. A 1991 study, published in the *Journal of Clinical Psychiatry*, compared the severity of CFS with that of multiple sclerosis, lupus and Lyme disease and found CFS to involve significantly more debilitating fatigue.

A Grassroots Struggle

The "disappearing" of CFS as a public-health issue can be blamed on a phenomenon even more profound than an antipathy to chronic illness or the impoverishment of science at government agencies. If ever there was a disease that required listening to patients and carefully observing them, this is it. Yet an increasing dependence on medical technology has served to erode and devalue the methods that served physicians for centuries. The art of cognitive medicine lost ground when blood tests, MRI scans and sonograms arrived to provide the diagnosis. In an age of high-tech medicine, the voices of doctors who recognize the singularity of this (Continued on page 74)

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(Continued from page 72) disease by observing their patients have been overpowered. Today, the NIH scientist or the influential university department head carries all the authority. In such a climate, a disease has no reality unless a diagnostic test exists, a pathogen is clearly linked to its transmission—or the patient dies.

In the meantime, the struggle for recognition endures at the grassroots level: patients appealing to legislators whose subcommittees appropriate money to the CDC and the NIH. For each of the last three years, Congress has increased CFS spending by nominal amounts, ranging from \$1.1 million to \$2.2 million. But money is no longer the only issue, notes health lobbyist Tom Sheridan, who was engaged in 1992 by the Charlotte-based CFIDS Association, the largest patient organization in the country (the acronym represents the name that patient-activists prefer: chronic-fatigue immune-dysfunction syndrome). Money can do many things, but it cannot expunge scientific bias.

"This situation is unique," notes Sheridan, who also represents a number of AIDS-patient organizations. "I have told my [CFS] clients, I can go to Congress and get more money for the NIH and the CDC. But before we ask, let's get an infrastructure in government that is helpful to you rather than hurtful."

In order to advance the discovery process, both the CDC and the NIH need to fold into their ranks scientists who come to the issue with open minds and fresh ideas, and to include more patients and patient advocates in their decision-making bodies, as they do with other major diseases. NIH committees reviewing outside scientists' grant proposals need to be composed of true peers—doctors and scientists who either have hands-on experience with CFS or are well-educated in its clinical and laboratory hallmarks. Above all, health officials need to start listening to patients and to those rare observant doctors who have been listening for years. ■

Hillary Johnson is the author of the forthcoming Osler's Web: Inside the Labyrinth of the Chronic Fatigue Syndrome Epidemic.