

Office of Research on Women's Health



Science Series
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Chronic Fatigue Syndrome

Efforts by the National Institutes of Health to Understand CFS and Plan for Future Research
JUNE 2003 NIH Scientific Workshop Focuses the Discussion

What is CFS?

Chronic Fatigue Syndrome (CFS) is characterized by incapacitating fatigue (experienced as profound exhaustion and extremely poor stamina) and problems with concentration and short-term memory. It is accompanied by flu-like symptoms such as pain in the joints and muscles, unrefreshing sleep, tender lymph nodes, sore throat, and headache. Distinctive characteristics of the illness is post-exertional malaise—a worsening of symptoms following physical or mental exertion occurring within 12 to 48 hours of the exertion and requiring an extended recovery period.

The symptoms of CFS are highly variable and fluctuate in severity, which complicates treatment and the person's ability to cope with the illness. Most symptoms are not obviously visible, making it difficult for others to understand the vast array of debilitating symptoms with which CFS sufferers must cope.

Why is CFS a Problem?

It is estimated that as many as 800,000 people nationwide suffer from this illness, and 90 percent of these individuals have not been diagnosed and therefore are not receiving proper medical care for their illness. CFS strikes people of all age, racial, ethnic, and socioeconomic groups, and research has shown that CFS occurs about three times as often in women as in men.

What Is NIH Doing

About CFS?

As part of National Institutes of Health (NIH) program to combat this syndrome through increased research, the NIH Office of Research on Women's Health (ORWH) and the Trans-NIH Working Group for Research on Chronic Fatigue Syndrome cosponsored a scientific workshop, Neuroimmune Mechanisms and Chronic Fatigue Syndrome: Will Understanding Central Mechanisms Enhance the Search for the Causes, Consequences and Treatment of CFS, in June 2003. Although research to date has identified neither a cause nor a cure for CFS, evidence suggests that CFS alters the immune and neurological systems. With that evidence in mind, distinguished experts from outside the NIH community joined in this workshop with intramural NIH scientists to explore the mechanisms by which hormones and proteins that regulate the immune system act as intermediaries between the brain and other body systems.

Because fatigue can be understood in terms of central nervous system (CNS) functioning, the scientific experts at this workshop theorized that studying CFS and related disorders should focus on the CNS. Significant CFS symptoms such as pain, sleep disturbance, and impaired cognitive functioning are also best understood in terms of CNS function.

Research on What Causes CFS

Research during the past 15 years was stimulated first by the observation that about 70 percent of people with CFS reported that their illness started with a viral or bacterial infection, particularly an upper respiratory or influenza-like illness, and that they never recovered from that infection. As a result, early studies focused on viral agents, particularly viruses that had the ability to persist or be dormant, such as herpes viruses. Many viral and other microbial agents have been studied and then discarded as being the primary cause of CFS.

The second wave of research focused on immune-related findings, triggered by CFS patients' reports of more frequent and severe illnesses and longer recovery times. Two other areas of investigation have been the autonomic nervous system and objective measures of sleep. Recently, researchers focusing on a fifth topic of investigation have asked whether a genetic predisposition exists for fatigue in general, and more specifically for CFS. A theory that has permeated the literature since CFS was first described attributes the illness to some form of atypical depression or other psychiatric disorder that has yet to be well defined.

Models for Future Research

Any model of CFS must take into account a wide variety of published observations and findings. For instance, some experts believe that CFS is part of a family of disorders and thus is not a unique, identifiable disorder. Previous studies have detected a variety of biological abnormalities that are not specific for CFS and that are not consistently associated with severity or type of symptoms. The many meanings of "fatigue" also need to be addressed by investigators when designing studies that clarify a model for CFS; "fatigue" is a broad term that needs clearer definition and specification.

Many researchers believe that changes in physical and mental functioning at the core of CFS are not well understood, but that most symptoms and findings can be explained by problems related to hormones that influence the activities of nerves. Researchers will need to design their studies to focus on models that can link mechanism and causation.

Some areas ripe for investigation include whether neuroendocrine dysfunction is the cause or the result of physical inactivity, why significantly more women than men get CFS, what are the biological underpinnings of perception, and how perception is altered in individuals with CFS.

Methodological and Other Issues to be Resolved

A variety of issues that are as yet unresolved include:

- CFS studies must be conducted in multiple locations with adequate numbers of participants to ensure statistical power, and they must be long enough to account for cycles of remittance and relapse that are commonly seen in people with CFS.
- Procedures such as sampling time, specimen shipping conditions, processing methods, and preservation must be standardized.
- Useful characterizations for CFS symptoms must be developed so those symptoms can be measured accurately.
- An animal model for CFS needs to be developed.

- Researchers should take advantage of the newest scientific methods and techniques in order to provide immediate insights into CFS symptoms. Use of these approaches will ensure that studies undertaken are interdisciplinary in nature.
- Unexplained variability in signs and symptoms of CFS underscore the vital importance of medical histories as a key element to explain this chronic disease.

To address these issues, NIH released a Request for Applications in July 2005, Neuroimmune Mechanisms and Chronic Fatigue Syndrome (RFA-OD-06-002), to solicit research grant applications that explore topics raised at the scientific workshop. NIH also supports ongoing investigator-initiated research through its Program Announcement, Chronic Fatigue Syndrome: Pathophysiology and Treatment (PA-05-034).

For More Information . . .

...on NIH CFS research, the Institutes that support CFS research, and this workshop, please contact the NIH Office of Research on Women's Health, Bethesda, MD, at

<http://orwh.od.nih.gov/cfs.html>
or by telephone at 301-402-1770.