Dr. Komaroff's Progress Report on Chronic Fatigue Syndrome Research - Sept. 2008

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by Anthony L. Komaroff, M.D., September 2008

It has been several years since we sent you a Progress Report. I'm pleased to report that there has been a lot of progress in research and in public recognition of the problem of chronic fatigue syndrome (CFS).

International Research Conferences/National Meetings

October 2004: Madison, Wisconsin. An international research conference organized by the International Association for Chronic Fatigue Syndrome (AACFS) attracted over 500 attendees, and over 100 research presentations were made.

April 2006: Barcelona, Spain. Sponsored by the Human Herpesvirus-6 Foundation, this international research conference involved over 100 research presentations, from scientists all over the world. The conference focused on one virus, human herpesvirus-6 (HHV-6), that our research group first linked to CFS. Since then, the virus has been linked to several other diseases, as well.

November 2006: National Press Club, Washington DC. Organized by the CFIDS Association, this event was standing room only for the media. Recent research about CFS from the U.S. Centers for Disease Control & Prevention (CDC) and other research teams was summarized. Dr. Julie Gerberding (Director of the CDC), Dr. William Reeves (head of the CDC's CFS research program), Dr. Nancy Klimas (a noted immunologist) and I updated the national media about CFS research.

May 2008: United States Senate, Washington DC. Organized by the CFIDS Association, this well-attended event was held to acquaint members of Congress with the latest research on CFS.

June 2008, Baltimore, Maryland. The HHV-6 Foundation organized another international research conference on HHV-6, and a second conference on Viruses in CFS, which I co-hosted. Hundreds of scientists from all over the world attended (including two winners of the Lasker Prize for Medicine, regarded as second in prestige only to the Nobel Prize), and over 100 research presentations were made.

Studies of the Impact of CFS

Dismissed by some when it was first defined 20 years ago, studies from the CDC (and our research group and others) have determined that CFS may affect 1-4 million adults in the U.S. The CDC estimates that CFS causes over $9 billion/year in lost productivity—and billions more in medical costs.

Studies of the Immune System

In the 1980's and 1990's, our group and others studied circulating immune system cells and chemicals, and found evidence that in many patients with CFS the immune system is in a state of chronic activation—as if it is waging a war against some intruder, like an infectious agent. In the past 5 years, it has become possible to study which genes are turned on in immune system cells. Studies from the CDC and other laboratories around the world find that the genes that activate immune system cells are indeed turned on more often in people with CFS than in healthy people. In addition, immune system chemicals called pro-inflammatory cytokines are found at higher levels in the blood, and these cytokines are known to be capable of producing some of the symptoms of CFS.

Studies of Infectious Agents

As you may recall from past reports, 16 years ago we reported that the virus called HHV-6 was "active" (making copies of itself, and infecting new cells) more often in patients with CFS. We also had noted that some of our patients who met the CDC criteria for CFS had both symptoms and laboratory test findings that suggested seizure disorders and multiple sclerosis (MS). But in the past

two years, considerable evidence has been published linking HHV-6 to temporal lobe seizures and to MS. (Another virus linked to CFS, Epstein-Barr virus, also increasingly is being linked to multiple sclerosis). It is not proven that there is a connection between CFS and MS, or CFS and temporal lobe seizures, and it is not proven that HHV-6 is a cause of CFS, seizures or MS. However, the evidence that the virus may be triggering these illnesses in some patients is considerably stronger than it was five years ago.

Neurological and Brain Hormone Studies

Brain hormone studies—Since the last progress report, many more published studies have found abnormalities in certain brain hormones in patients with CFS. The hormones studied most often are corticotropin-releasing hormone (CRH), growth hormone, prolactin and serotonin. In particular, evidence is emerging that various molecules that involve the body's "stress axis" and the communication between the stress axis and the brain's serotonin system are different in patients with CFS. Variations in genes for some of these molecules have been identified, and unusual patterns of gene expression (whether a gene is turned on or off) have been identified.

Collectively, all of these studies demonstrate that something is subtly interfering with the function of the hypothalamus, which is part of the limbic system of the brain. What that "something" is remains unclear: you can't just reach into the middle of the living human brain and study it, and so one tries to get clues by indirect techniques.

Autonomic nervous system (ANS) studies—The ANS begins in the brain, and sends nerves to all parts of the body. These specialized nerves control vital functions such as blood pressure, body temperature, and digestion. As described in past Progress Reports, many research groups including our own have found abnormalities in the autonomic nervous system. What is not yet clear is whether any particular treatments work to correct these abnormalities.

Other studies of the brain—The majority of studies using various techniques for taking pictures of the brain—CT scans, MRI scans, PET scans—continue to report abnormalities in patients with CFS. In addition, a recent study identified a group of proteins in the spinal fluid (which bathes the brain) of patients with CFS that were not present in the spinal fluid of healthy people. The proteins indicated a low-grade inflammation in the brain. We are currently analyzing electroencephalograms (brain waves) from patients with CFS, patients with depression and healthy people to see if there are clear differences: preliminary analysis indicates that there are.

Energy Studies in CFS

Every cell in our bodies requires energy to function. The tiny "power packs" inside a cell are called mitochondria, and they liberate energy from oxygen (a process called oxidation). There is growing evidence that the process of producing energy in cells is impaired. There are differences in the levels of several molecules important in energy metabolism, considerable biochemical and genetic evidence of "oxidative stress", and some evidence that the mitochondria are physically damaged. It seems simplistic, but it may be true: the lack of energy felt by a person may indicate that the person's cells are having trouble generating energy.

Diagnostic Tests for CFS

In the last Progress Report I mentioned that several studies had found a defect in an anti-viral enzyme system called the 2-5A system. This defect is found much more often in patients with CFS than in healthy subjects, and could reflect an underlying viral infection. In these preliminary studies, the test seemed to differentiate patients with CFS from patients with other fatiguing illnesses and from healthy people. Since then, other types of tests also have been rep reported that seem to be very accurate in diagnosing CFS. However, all of these tests currently work only in research laboratories. More work is needed to simplify them and further test them before they can be considered diagnostic tests.

Treatments

There still are no treatments for CFS that have been proven in large, randomized clinical trials to be effective. One study conducted by the manufacturer found that a drug called Ampligen® improved the level of function. The drug must be given intravenously (it is not a pill) and is still experimental: it is not available for use.

A small non-randomized study conducted at Stamford University, and published late in 2006, suggested that treatment with an anti-viral drug called valganciclovir (Valcyte®) helped patients with CFS and evidence of reactivated infection with human herpesvirus-6 and/or Epstein-Barr virus. A small randomized trial is now underway, and has not yet been published. Valcyte is a pill, and is

already on the market. I am waiting to see results of the randomized trial before considering prescribing it.

Conclusion

There continues to be progress in understanding CFS, and a growing number of scientists around the world who are studying it. This should be heartening for all of us who study CFS, and for those who suffer from it.

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