US Department of Health and Human Services

Chronic Fatigue Syndrome Advisory Committee (CFSAC)

Inaugural Meeting

At

National Institutes of Health
Building 31C, Conference Room 10
Bethesda, Maryland

September 29th, 2003

10:00 AM to 5:00 PM

MEETING SUMMARY

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Members in Attendance

Committee Members

- Dr. David S. Bell — *Chair*
- Nancy C. Butler
- Jane C. Fitzpatrick
- Dr. Kenneth J. Friedman
- Dr. Nelson Gantz
- Dr. Nahid Mohagheghpour
- Dr. Roberto Patarca
- Staci R. Stevens

Acting Executive Secretary

- Dr. Larry E. Fields

Ex Officio Members

- Bill Anderson, Office of Medical Policy, Social Security Administration (SSA)
- Dr. Marc Cavaillé-Coll, Division of Special Pathogen and Immunologic Drug Products (DSPIDP), Food and Drug Administration (FDA)
- Dr. Eleanor Hanna, Office of Research on Women's Health, National Institutes of Health (NIH)
- Dr. William Reeves, Viral Exanthems & Herpesvirus Branch, Centers for Disease Control and Prevention (CDC)
- Dr. William Robinson, Center of Quality, Health Resources and Services Administration (HRSA)

Invited Speakers

- Jill McLaughlin, National CFIDS (Chronic Fatigue Immune Dysfunction) Foundation (NCF)
- K. Kimberley Kenney, CFIDS Association of America (CFIDSAA)

Committee Members Absent

- Dr. Anthony L. Komaroff
- Dr. Charles W. Lapp
- Lyle D. Lieberman

Call to Order

Dr. Larry E. Fields called the meeting to order. He thanked Chronic Fatigue Syndrome Advisory Committee (CFSAC) members and requested the roll call. Dr. Debra Nichols completed the roll call and thanked the committee.

Advisory Committee Meeting

Greetings

Dr. Fields then acknowledged greetings from Dr. Arthur Lawrence, Deputy Assistant Secretary for Health-Operations and Acting Principal Deputy Assistant Secretary for Health in the Office of Public Health and Science, who was unable to attend the meeting. Dr. Fields noted that CFSAC will be making recommendations to the Office of Public Health and Science and to Dr. Cristina Beato, Acting Assistant Secretary for Health, who also could not attend the meeting due to a prior commitment.

Dr. Fields then shared remarks on behalf of Dr. Beato and Dr. Lawrence. Dr. Beato sent her warmest wishes to the committee and expressed her commitment to working with CFSAC on action-oriented recommendations.

There are three core charges for CFSAC:

- Maintain a central focus on patients with CFS.
- Commit to work collaboratively.

- Focus on an evidence- and science-based approach.

Dr. Fields then expressed Dr. Beato and Dr. Lawrence's gratitude to everyone in attendance and to those who have worked hard to ensure that important issues were not lost in this transition period. They recognize that there are many issues to consider, ranging from definitions and terminology to effectively caring for individuals suffering from CFS.

Introductions

Dr. David Bell, CFSAC Chair, thanked Dr. Fields and then asked members and invited guests to introduce themselves.

- **Dr. David Bell** is a pediatrician practicing in Lyndonville, New York. In 1985, he saw approximately 200 patients who subsequently were diagnosed as having CFS. He continues to see CFS patients today.

- **Nancy Butler** is an elementary school teacher and a technology specialist who became interested in CFS as a patient; she likely has had CFS since she was 17 years old.

- **Dr. Marc Cavaillé-Coll** is a Medical Officer Team Leader, FDA. His division is charged with reviewing products to treat CFS, and he has been involved with these products since 1996.

- **Dr. Larry Fields** is Senior Advisor to the Assistant Secretary of Health and felt privileged to be working with CFSAC.

- **Dr. Ken Friedman** is Associate Professor of Physiology at New Jersey Medical School in Newark. His daughter contracted CFS, and he became involved in writing the New Jersey Chronic Fatigue Manual funded by the New Jersey legislature, entitled *Diagnosis and Treatment of Chronic Fatigue Syndrome*. He has been very active in writing research protocols and examining ways of improving the treatment of CFS.

- **Dr. Nelson Gantz** is Chief of Infectious Diseases at Boulder Community Hospital in Boulder, Colorado and has been involved in writing the case definition for CFS and is currently involved in caring for CFS patients.

- **Dr. Eleanor Hanna** is Associate Director for Special Projects and Centers in the Office of Research on Women's Health, NIH.

- **K. Kimberly Kenney** is President and CEO of CFIDSAA. She has been with the organization for over 12 years and has been engaged in a range of areas such as education and public policy.

- **Jane Fitzpatrick** is experienced in healthcare administration and physical therapy. She became interested in CFS since her son was diagnosed with the illness. She is also interested in what has and can be done with physical therapy to address CFS. She has also worked with several national organizations that deal with CFS.

- **Jill McLaughlin** is Executive Director of NCF. She has two daughters with CFS and has worked with several CFS support groups.

- **Dr. Nahid Mohagheghpour** has worked in immunology and infectious diseases, including HIV. She has done research at University of California at Berkeley and the California Pacific Medical Center. She has served on the scientific board of the CFIDSAA.

- **Dr. Roberto Patarca** is based in Miami, Florida. He is a scientist who has worked in academia and has conducted AIDS research. He has worked on CFS issues since 1990, including the development of therapeutic protocols. He was editor of the *Journal of Chronic Fatigue Syndrome*.

- **Dr. William Reeves** is a Branch Chief at CDC and has been responsible for CDC's CFS program since 1992. He is excited to work with CFSAC. CDC is committed to CFS. Dr. Drue Barrett, National Center for Environmental Health, who is responsible for CDC's Gulf War activities, is an alternate.

- **Dr. William Robinson** is Director, Center of Quality and Chief Medical Officer, HRSA. He worked with the Chronic Fatigue Syndrome Coordinating Committee (CFSCC), the predecessor to CFSAC, for several years.

- **Staci R. Stevens** is Chair of the Workwell Foundation and Workwell Physiology Services. She is involved with CFS patients, rehabilitation, disability evaluation, and other areas.

Organizational Matters

Dr. Bell then asked Dr. Fields to discuss organizational matters.

Listserv opportunity

The first issue Dr. Fields discussed was the opportunity to create a listserv for the committee to support timely release of public information.

Website

Creating a website is also a budgeted option for the committee. This website could provide CFSAC information and linkages.

Other issues

Dr. Fields expressed appreciation for the attendance of Dr. Donna Dean, who has worked hard to establish progress in this area.

Dr. Bell thanked Dr. Fields and said the listserv and website were good ideas. Dr. Fields noted that these help to ensure communications with patients, patient advocacy groups, and public and professional organizations. Dr. Bell proposed creating the listserv and website and asked for any objections or strong feelings from other members.

Ms. Fitzpatrick asked if the listserv and website would be hosted and developed in Dr. Fields' office under CFSAC's direction. Dr. Bell responded affirmatively. Dr. Friedman then motioned to establish the listserv. The motion was seconded and all members voted in favor of the motion.

Dr. Bell asked for any discussion on the website, noting that it will be an informational, not interactive, website. After no comments were provided, Dr. Friedman motioned to establish the website; it was seconded, and all members voted in favor of the motion.

Background Presentation

Dr. Bell then introduced the ex officio members, asking them to take as much time as necessary. He remarked that he is very interested in hearing what participatory departments have done in the past in terms of a brief history and more importantly, what projects they are working on in this area now and will be in the future.

Dr. Fields stated that the presentations would start with a historical perspective from Dr. Donna Dean.

Donna Dean, PhD, CFSCC Co-Chair (1999 to 2001)

She welcomed the committee to NIH campus and apologized for barriers that members encountered coming to NIH as a result of post-9/11 security measures.

Dr. Dean was involved in the previous CFSCC from 1999 to 2001 and provided a brief history of the CFSCC, which began as a dialogue between researchers and community. The CFSCC was established and chartered while Dr. Phil Lee was Secretary of Health.

This committee was managed out of the Office of the Assistant Secretary of Health and had both federal and non-federal members. The original plan was that the administrative support for the coordinating committee would rotate between CDC and NIH; at that time, the National Institute of Allergy and Infectious Diseases (NIAID) was taking the lead for NIH, since at that time it was believed that a single infectious agent might be identified as a cause for CFS.

There was also a time when the General Accounting Office (GAO) was invited to come in because community groups were concerned that government agencies were not being prudent with the use of the funds for CFS. A GAO investigation in itself, however, was not unusual. There are 10 to 20 GAO studies being completed at NIH and CDC.

In late 1998 and early 1999, HHS decided to move the committee support to NIH, since NIH had the infrastructure to support advisory committees, and it was time for NIH to assume its 2-year administration handling of the coordinating committee. The Director of NIAID and Surgeon General David Satcher served as co-chairs of the CFSCC.

The same summer as the GAO report was being completed, Dr. Anthony Fauci, NIAID Director, met with the Dr. Harold Varmus, Director of NIH, and concluded that CFS was more complex and activities should be relocated from a single NIH institute. At that time, Dr. Dean was special advisor on science and policy to Dr. Varmus and to his deputy, Dr. Ruth Kirschstein. Dr. Varmus asked Dr. Dean to take over coordination of CFS activities and be the liaison to work with the department. She also worked with Dr. Varmus and Dr. Drue Barrett at CDC on Gulf War illnesses, so she was pleased to see Dr. Barrett involved with CFSAC.

During her time as Acting Co-chair with Dr. Satcher, Dr. Dean noted that she wore an "NIH" hat (now worn by Dr. Hanna) and an "HHS hat" (now worn by Dr. Fields and others in HHS) at the same time.

Between 1999 and 2000, there were several ups and downs for the CFSCC as they worked through the GAO report. CFSCC worked on the first "survey of the science" meeting put together by NAID staff and a larger fall 2000 research conference in Virginia. There were several congressional meetings that Dr. Dean and Acting NIH Director, Dr. Ruth Kirschstein, had with many interested congressional members.

Dr. Dean's involvement with CFSCC ended in January 2001 with a meeting in conjunction with the biannual meeting of the CFS Society scientific meeting in Seattle.

Dr. Dean and her administrative assistant planned for an orderly transition into its new structure in December 2000 to January 2001. An outcome of the GAO report was to bring the CFSCC in line with other HHS committees, where federal members would be ex officio non-voting members.

Dr. Dean described CFSCC's accomplishments while she was Co-Chair:

1. A scientific meeting and research planning conference.

2. Creation of a listserv for the committee, which acted as a conduit for accurate and up-to-date communication of official information from the CFSCC.

3. Scientific evidence that CFS is a complex, multi-factorial, multi-symptom condition that involves neurological, immunological, endocrine, and other systems.

Dr. Dean noted that all of her NIH-related files on the CFSCC were given to Dr. Hanna and the department-related files are with HHS. She continues to be a resource on the historical memory of CFSCC.

Q & A

Dr. Fields and Dr. Bell thanked Dr. Dean for her presentation. Dr. Bell also noted that Dr. Dean did a good job and that the GAO period required tremendous leadership. The listserv, for example, was a wonderful point of communication.

Ms. McLaughlin commented the real reason for the GAO review was that the Inspector General found that CDC misspent several million dollars. Though she does not want to keep rehashing these issues, she reminded CFSAC of the importance of remembering the past so as not to repeat it.

Dr. Bell asked if this was appropriate time to discuss this issue or if someone else was going to speak to it.

Dr. Dean said that speaking with her "NIH hat," they were very concerned to know that NIH had spent CFS funds appropriately. As they disclosed data to GAO, they did discover some inaccuracies in the data NIH reported; this was fully disclosed and discussed at the July 2000 CFSCC meeting. NIH got a very accurate picture and they have moved on.

Dr. Bell asked Dr. Dean if she was aware of any ongoing, unresolved issues when she left. Dr. Dean thought there may had been issues regarding what the agencies were going to propose to do in the future, what was to become of the CFSCC as it transitioned into the advisory committee, and how soon this transition would happen.

Dr. Fields noted that the discussion made a good segue for the other presentations.

Dr. Reeves said he was intimately involved in this issue and wanted to make a comment from the CDC perspective. He acknowledged that errors happened in the past for a variety of reasons and agreed that one should study the past so as not to repeat it. He perceived the agency to be very concerned about this issue and believed the necessary actions were taken to rectify the situation. CDC has an independent auditor that reviews all expenses in detail each year for the CFS program. He noted that CFSAC should move forward with the important scientific and public health issues that need to be addressed.

Dr. Bell asked if the committee is comfortable leaving this matter behind or if they wanted to reopen the issue. He said that he felt comfortable moving forward as long as there are strong provisions to prevent this issue from occurring again. Dr. Fields noted that all CFSAC members nodded affirmatively.

Ex Officio Member Presentations

Dr. Fields then introduced Dr. Eleanor Hanna.

Eleanor Hanna, PhD, Office of Research on Women's Health, NIH

Dr. Hanna explained that prior to October 1999, the responsibility for NIH CFS activities was held by NIAID. From October 1999 to March 2001, Dr. Dean simultaneously served as Co-Chair of the CFSCC for the Office of the NIH Director and Chair of the Trans-NIH Working Group.

Dr. Hanna was pleased that CFSAC has been convened since during the interim period, there were expectations that the Trans-NIH Working Group would be responsible for issues that fell under the CFSCC.

In February 2000, NIAID held a State of Science Consultation, which resulted in commissioning the *Defining And Managing Chronic Fatigue Syndrome* report that was subsequently released in October 2001 (AHRQ report number 42). This report essentially found that it was difficult to find treatments to recommend for CFS other than behavioral therapy or exercise treatments.

In June 2000, the last meeting of the CFSCC meeting was held, and the GAO report and future activities were discussed. In October 2000, a State of the Science Symposium was held, and in December 2000, the NIH working group was charged with writing a program announcement that incorporated the findings from this symposium.

Dr. Hanna explained that in April 2001, the responsibility for NIH CFS research was transferred to the Office of Research on Women's Health, OD, NIH. The Trans-NIH Working Group for Research on CFS was re-constituted.

In December 2001, program announcement PA-02-34 was published. This PA reflected the results of the State of Science Symposium; it encouraged multidisciplinary studies that look for connections between different body systems and creatively thinking "outside of the box."

After the publication of the PA, the number of grants reviewed increased from five in January 2002 to 15 for January 2004. Dr. Hanna noted that when she took over this group, one of the problems was that researchers were not submitting grant applications. In October 2002, the first council round of review took place in which applications acknowledging PA-02-34 were received. Since that time, 15 out of 67 applications have been assigned for review through January 2004.

CFS research funding was $7.2 million for FY 2002, $7.5 million for FY 2003, and $7.7 million for FY 2004. These figures are an increase from the two lowest funding levels since 1994, which were $5.9 million in 1999 and $5.8 million in 2000. NIH funds 24

individual studies in addition to three Cooperative Research Centers. In addition, the National Center for Research Resources makes their facilities available.

Dr. Hanna noted that there are immunological studies, circulatory studies, neurological studies, epidemiological studies, Career Development Awards for research in psychiatric co-morbidities of CFS, brain studies that examine serotonin receptors and neurons, behavioral intervention studies, and complex research centers across the nation that supported 19 different studies for CFS researchers. A research grant funded in September 2003 is particularly critical to what the advocacy community was looking for and ranked in the top 5 percentile of applications in its second review. This study (1-RO1-HD-43301-1A1) examines CFS in adolescents at the University of Illinois, Chicago and is co-funded by ORWH and NICHD for a 5-year period.

Dr. Hanna noted that the NIH review process requires a testable hypothesis and researchers must explain how they will accomplish the study. Research proposals must rank in a respectable percentile to be funded. CFS research at NIH will only grow if more grant applications are submitted, accepted, and funded.

Dr. Hanna then reviewed more immediate activities at NIH. In June 2003, a scientific workshop, *Neuro-immune Mechanisms and Chronic Fatigue Syndrome: Will Understanding Central Mechanisms Enhance the Search for the Causes, Consequences and Treatment of CFS?*, was held. They took a whole-body approach. In October 2003, the Trans-NIH Working Group will begin drafting an RFA based on this workshop. She anticipates that based on the amount of time it takes to release a PA, it may be a year before this proposal is released.

NIH and CDC have been trying to work more closely together in the last few years and are exploring the possibility of putting out joint RFAs in areas where their interests intersect.

About 100 people attended the June 2003 workshop, and the 30 active participants were scientists and clinical researchers from around the country. Three questions were posed at the workshop:

- Can CFS be understood as a disorder of CNS physiology and maintained by alterations in areas of the brain involved in learning?
- What are the methodologies available to investigate this question?
- Are there therapeutic approaches that target the CNS that could be helpful in treating CFS?

The overall outcome was a better understanding of how the brain fits into the schema for understanding CFS; however, it will be exceedingly difficult and expensive to study.

Dr. Hanna discussed the mind-body relationship and how stress impacts on the entire system. She then discussed Dr. David Goldstein's work as an example of intramural involvement. Dr. Goldstein, NIH scientist in neurocardiology, is starting to include CFS in his research. Dr. Hanna said she would like to get Dr. Goldstein more involved since he was excited about the issues. She noted that CFS themes were consistent with other diseases we do not understand very well.

Some specific recommendations came out of the workshop:

- Fatigue is difficult to measure and a useful phenotype should be defined.
- Small sample-sized experiments repeating immunologic findings about which there is already sufficient evidence should no longer be considered. Dr. Nancy Klimas gave a review of all immunologic findings, emphasizing that the studies were done in ways that do not allow meaningful comparisons. She suggested networking and developing a database that does allow comparisons.
- Large hypothesis driven, longitudinal and multi-site studies with standardized measurements, markers, and testing procedures should be encouraged.
- Circadian rhythms of studied systems must be accounted for in this research
- Changing hormonal status of women must be factored in.
- Must understand the basis for the female predominance.

Dr. Hanna asked CFSAC to review their website and to provide feedback on how to improve it: www4.od.nih.gov/orwh/cfs-newhome.html. She noted that some individuals were still going to the original CFSCC website and did not realize that the PA was released. She noted that the workshop summary will be posted on the website soon. There was a lot of interchange between the scientists and the audience, and the meeting was very well received. She said she would provide a hard copy of the workshop brochure to attendees.

In closing, Dr. Hanna shared the list of working group members who represent the 16 NIH institutes and centers.

Q & A

Dr. Bell asked Dr. Hanna to clarify the relationship between ORWH and OPHS. Dr. Hanna explained that ORWH is part of the Office of the Director, NIH. OPHS is in the Office of the Secretary, so they do very different work. ORWH is research-focused; this is why she is pleased that CFSAC was created since they were being asked to deal with broader issues as well. ORWH's role is to examine how to best help the people who have CFS and those who take care of them, and it is an appropriate office to address this issue.

Dr. Bell then asked about the status of the centers. Dr. Hanna explained that the NIAIDS Advisory Council recommended that the centers not be re-bid because they are located in Section 39, which was disbanded. Current centers will be funded until they close out their critical activities; they have been encouraged to submit RO1's.

Dr. Bell said he thought the purpose of the centers was to conduct a variety of related studies on the same group of people and asked if they will this be able to extend this research. Dr. Hanna said they should be able to, and if they take Dr. Klimas' guidance, they should be able to form a network to do studies. Currently, however, the centers cannot compare research. She said they are hoping that people will look for innovative ways to address these questions.

Dr. Friedman pointed to Dr. Hanna's second bullet on the *Focus for the Immediate Future* slide, which refers to the Trans-NIH Working Group deciding on and drafting an RFA. He asked how big the NIH working group is. Dr. Hanna explained that there are 16 representatives, and their names, institutes, and contact information are listed on the website.

Dr. Mohagheghpour asked if the RFA is going to ask for multi-center studies. Dr. Hanna answered affirmatively and suggested that CFSAC review the PA on their website.

Dr. Patarca asked if there had been discussions about creating repositories or databases. He explained more than multi-site research, the challenge is dealing with a heterogeneous population and a disease that has a variable remission period. Though the centers tried to address these issues, there is a more basic problem underneath this research. He asked Dr. Hanna about funding based on the working group recommendations. Dr. Hanna explained that the funding has to be discussed by the working group.

Dr. Patarca said that the private and pharmaceutical sectors are facing some similar challenges and are trying to tap into a higher source of thought. He asked if something is in the works. Dr. Hanna said that if there is enough interest and it is brought up, it may be possible to do something like this in the future.

Dr. Mohagheghpour asked if they have allowed a budget for establishing a sample bank (e.g., blood bank) for future studies based on the results of previous studies. Dr. Hanna said they would try to. She also mentioned possible submission of such proposals under the NIH Roadmap Initiative, a link to which is on their web site.

Ms. Kenny asked if it will be possible to get a list of Principal Investigators, institutions, and dollar figures for these grants. Dr. Hanna said most of this information is available to the public through CRISP; however, the exact funding information is sent to Office of Budget and is not published. Ms. Kenny suggested that CFSAC review this list annually.

Dr. Friedman asked if there is an Executive Summary of the workshop. Dr. Hanna responded affirmatively.

William Reeves, MD, DVRD, NCID, CDC

Dr. Reeves reviewed what has been happening at CDC.

He began by explaining that CDC is responsible for disease control and prevention, so the objective of the CFS program is to control and prevent CFS. Basic science is in the purview of NIH, while FDA and HRSA deal with other aspects.

Specific aims of CDC's CFS program are to:

- Estimate the magnitude of the problem
- Determine if CFS is a single disease
- Define clinical parameters and natural history
- Identify risk factors and diagnostic markers
- Provide technical information

Estimate the Magnitude of the Problem

Dr. Reeves explained that CFS is a complex, multidisciplinary problem that requires a complex, multidisciplinary effort. Within CDC, they have expertise in the areas of epidemiology and clinical epidemiology (doctoral level staff), pathology, molecular biology (genomics, proteomics, and bioinformatics), and more recently public health economics. They also have a close collaboration with Emory University and their departments of Department of Psychiatry (neurosciences), Department of Endocrinology, and Division of Neurology. Substantial funding has gone for provider education, survey research, bioinformatics, and post-infectious fatigue searching for novel or uncharacterized pathogens. This is the in-house, supportive collaborative network, including CFIDSAA.

They have also convened and support the International CFS Study Group annually. This group is composed primarily of investigators from major centers around the world, and their most recent focus has been on aspects of case definition.

Dr. Reeves reviewed the different gains they have made with CFS, beginning with the magnitude of the problem. CFS is vast, and many patients describe it as falling into a dark pit with no bottom. It is, however, a "pit" that can be explored with a controlled approach. In estimating the magnitude of the problem, they must examine the burden that CFS places on populations in the US, not patient practices. There have only been three population-based studies on specific communities:

- A CDC pilot study estimated the risk of CFS on the population in San Francisco to be 230 people per 100,000 people.

- Leonard Jason, PhD at DePaul University in Chicago estimated that the estimated risk is 422 cases per 100,000 people.

- Based on the previous two studies, the most recent CDC study estimated that the risk in Wichita, Kansas is 235 people per 100,000 people.

Dr. Reeves then summarized a study in which telephone interviews were conducted with 90,000 people. Based on telephone interviews in Wichita, approximately 2.5% of the women meet the case definition of CFS, which is a much higher rate than men (373 per 100,000 women and 82 per 100,000 for men). White women in Wichita had a risk of 352 per 100,000, while Black women in Wichita and Hispanic women in Chicago had higher rates. Limitations on the study design, however, do not allow the separation of race and ethnicity as a variable, but this area needs to be examined further.

Based on these studies, CFS and CFS-like symptoms pose different risks to different age groups. The peak is at 42 to 59 years. It does occur in children, particularly among adolescents, but the risk of illness for adults appears to be much higher. The impact on children may be greater in terms of the phases they experience through their lifetime.

Based on Dr. Jason's study and the Wichita study, CDC planned a nationwide study on CFS. The pilot study was conducted with 2,728 households (1,040 urban and 1,670 rural) and 7,317 residents. The events of September 11, 2001 occurred during the study, and CDC decided it was not feasible to proceed with the full study at that time.

The urban data were based on interviews in Oakland, Baton Rouge, Chicago, and Buffalo, and surprisingly, over 1% of the urban populations surveyed had a CFS-like illness, compared to almost 2% of the rural populations. CDC would likely not have proceeded with a full national study, since conducting clinical evaluations was not practical on a large geographic base, though they are critical to CFS. He stated, however, that there are important issues to follow up on and examine.

First, the study revealed no regional differences in the occurrence of any of the illnesses, but the risk in rural areas appears to be higher. People with lower SES have a significantly higher risk.

Based on the CDC studies, Dr. Buckwald's Seattle study, and Dr. Jason's Chicago study, there are an estimated minimum of 800,000 adults with CFS cases nationally. The average duration of the illness is 5 years. Twenty-five percent of these individuals are unemployed or receiving disability, and fewer than 20% have been diagnosed and treated by a physician.

The Wichita study also provided enough data to conduct an economic analysis of the impact of CFS. These data are not published and are still being analyzed. The unanswered questions regarding CFS are the:

- Importance of race and ethnicity

- Importance of socioeconomic status
- Importance of access to health care and utilization
- Importance of urban and rural differences
- True economic impact of CFS in terms of both direct and indirect costs

The next CDC study will be the *Surveillance of CFS in Georgia*. Georgia is geographically diverse with mountainous, foothill, and plain regions. They are in the process of submitting the study for OMB and IRB clearance and aim to identify the many factors associated with CFS in metropolitan, urban, and rural populations in Georgia. They will determine the economic impact on these areas of the state, derive an empirical case definition based on data, and identify of subjects for detailed in-patient clinical research centers similar to those at NIH. Unlike the studies at NIH, however, the subjects will be representative of the general CFS population and not derived from clinical practices. Dr. Reeves reviewed some elements of the planned study.

CDC anticipates that this study to be ongoing, prospectively to examine the clinical course and change in the clinical characteristics of subjects. They are also developing detailed 3- to 4-day in-patient clinical research center studies at the various universities.

Is CFS a Single Disease?

Dr. Reeves noted that CFS has been studied for more than a decade, and there are approximately 3,000 articles in the MEDLINE database reporting on CFS. These studies have not found a consistent risk factor associated with CFS for three reasons:

- Studies have been clinic-based.
- Different case definitions have been applied.
- Case definitions are based on self-reported symptoms and are generally not uniformly assessed.

Dr. Reeves then reviewed the 1994 CFS case definition, which defines "fatigue" as persistent and relapsing for more than 6 months, not alleviated by rest, resulting in a substantial reduction in activities, and having no explanatory medical or psychiatric causes. Accompanying symptoms include impaired memory or concentration, post exertional fatigue, unrefreshing sleep, headaches, muscle pain, multi-joint pain, sore throat, and tender lymph nodes.

The core question regarding the CFS case definition is whether CFS is a single disease. A published empirical case definition was developed based on the Wichita data and the International CFS Study Group is working primarily on this issue. CDC will also develop an empirical definition based on the Georgia data.

Define Clinical Parameters and Natural History

Dr. Reeves noted that CFS as a population-based illness in a public health setting. CDC CFS clinical studies have been designed to characterize clinical parameters for a case definition and are necessary to identify treatment strategies and understand the pathophysiology. There are manuscripts currently in press based on the longitudinal studies in Wichita; these studies followed individuals over 4 years to examine clinical attributes, utilization of health services, treatment, and other factors.

They have also sponsored several modeling studies that examine interferon-α, post-infectious disease (University of New South Wales), allergy and exercise challenge (Dr. Jones at the National Jewish Medical Center), and tissue cytokines. As previously discussed, there are also the in-patient clinical center studies in Wichita and Georgia.

The Wichita clinical study objectives were to characterize the physiologic and mental status of CFS. During a 2-day hospital stay, they conducted detailed clinical measurements that included neuroendocrine and immune function, sleep, neurocognitive function, psychiatric function and stress, gene expression profiles, and neurotransmitter/immune regulatory gene polymorphisms. The measurements were then correlated with illness characteristics with the hope of identifying biological markers and environmental, psychosocial, and genetic risk factors.

The hypotheses for the study were:

- Cortisol would be lower.
- Inflammatory cytokines would be higher.
- Primary sleep pathology would be more common.
- Neurocognitive deficits that can be characterized would be present.
- There would be different stress responses.
- Different gene expression profiles would be discerned.

All of the people classified with CFS over a 4-year period in Wichita were invited to participate in a 2-day in-patient study, and approximately 55 and 70 people enrolled. CDC brought in another group who had: 1) CFS along with major depressive disorder, 2) insufficient symptoms but fatigued (ISF), and 3) insufficient symptoms found with major depressive disorder. ISF individuals are chronically fatigued but do not meet the case definition. An equal number of non-fatigued members of the population were matched with CFS cases for sex, race and ethnicity, and age.

During the 2-day in-patient study, the following were conducted:

- Medical and psychiatric evaluation
- Symptom evaluation
- Sleep lab study
- Tilt table
- Endocrine/immune function review
- Psychometrics
- Life experiences evaluation
- Genetic polymorphisms, gene expression, and proteomics

Identify Risk Factors and Diagnostic Markers

The CFS Molecular Epidemiology program has four areas: pathogen discovery, genomics, proteomics, and bioinformatics. CDC has been involved with pathogen discovery since 1992, including classic serum epidemiologic and agent recovery isolation efforts that found evidence that there is no single agent, known or unknown, that is associated with CFS in most cases.

Dr. Reeves then discussed genomics, proteomics, and bioinformatics, explaining that bioinformatics ties all of these factors together. A major challenge with CFS is that there is no identified lesion or pathophysiology, which raises questions about what sample is representative of CFS. He described an exploratory and descriptive approach that CDC is taking, which draws from a very basic molecular epidemiological perspective. Humans are coded by DNA, and our DNA are expressed through our messenger RNA, which codes the body's proteins. CDC is not heavily involved in genomics, except to look for polymorphisms.

He began by discussing transcriptomics and their attempt to measure messenger RNA expression profiles. Gene expression profiling is an attempt to measure the activity — not the presence — of all genes in a cell, correlate expression levels with disease phenotype, and correlate expression patterns with disease phenotype.

He then described the microarray technology that they use. With the Genome Project, they can study 30,000 genes at a time on microscope slides. CDC is working closely with the National Cancer Institute on this project, and an article based on this study is also currently under review.

Most CFS cases are similar in terms of gene expression and can be separated from controls. These distinctions, however, are not very clean. The analysis is very complex and involves 30,000 observations per person. They identified genes that are over or

under expressed in CFS patients. Most genes are involved in transcription; a smaller number are involved in signal transduction, and the smallest number are involved in immune response.

In proteomics, mass spectrometry of serum proteins is used to identify biomarkers of disease. The technique they use is called SELDI-TOF. Proteins are placed on a slide, and the amount present is determined. An article using this technique with the Denver modeling study is currently under review.

Dr. Reeves explained that his presentation shows the breadth of CDC's clinical activities. If they can measure the various groups of individuals with CFS, with other illnesses, and those who are well in the general population, they could potentially:

- Determine if CFS is a single disease.
- Define natural history and clinical parameters.
- Identify risk factors and diagnostic markers
- Ultimately, devise control and prevention strategies.

He emphasized that this is a very complex process, and it requires different approaches in the 21st century.

Provide Technical Information

CDC also provides technical information through the following:

- Consultation with government agencies, hospitals, and foreign governments
- Technical assistance on many of their techniques and strategies
- Publications in the peer review mainstream literature that let investigators know about CFS and its importance
- Meetings, such as cutting-edge scientific meetings, the International Working Group's meetings, special symposia, and committee meetings
- A CFS web page
- Provider education projects, such as a cutting-edge, grassroots program that Dr. Robinson will discuss and that includes a train-the-trainer program and CME components through print, film, and web

Q & A

Ms. McLaughlin asked Dr. Reeves if the large population-based Georgia study will include children. She also asked about a paper that Dr. Reeves published which addressed abnormal expression of the Huntington's disease gene and possible similarities to CFS.

Dr. Reeves explained that in the Georgia study they will not be evaluating children mainly due to human subject protection issues. They have not gotten permission to interview children over the phone, and they have had tremendous problems using surrogate interviews in past studies. In addition, although they know that children have CFS and are greatly affected by it, they are currently evaluating the population with the greatest risk in these initial studies. They are extremely interested in the childhood history of patients, however, and a complete family history will be done. They may go back to research the children later.

Dr. Reeves said Ms. McLaughlin's second question is more difficult to answer. He explained that there are a lot of misconceptions about genes. When a gene has been unambiguously identified, it is typically similar to a gene that has been unambiguously identified in another animal (usually rats), or it has a sequence from which they can infer function. CDC gets excited when they see a gene that is similar to the Huntington's gene because it provides an area to explore. They are working with Dr. Steinberg at the National Institute of Mental Health. The particular study that Ms. McLaughlin referred to was a proof of concept study that must be elaborated on in much more detail; they plan to do this with the rest of the program.

Ms. Stevens asked if Dr. Reeves' presentation could be made available to the committee. Dr. Reeves said he could, but noted that some of the material is under peer review for publication. All of their briefings, however, are posted on the CDC CFS website, so they will prepare a briefing of this presentation.

Ms. Kenny asked what CDC spending on CFS is. Dr. Reeves responded that he could not answer this question in detail and stated that CDC is spending approximately $12 million to $13 million annually on CFS, including overhead costs, and that this budget is audited regularly. Approximately 80% of this budget goes to extramural programs and the remainder is for intramural activities.

Dr. Fields thanked Dr. Reeves.

Marc Cavaillé-Coll, PhD, MD, DSPIDP, CDER, FDA

Background

Dr. Cavaillé-Coll described the activities of the Division of Special Pathogen and Immunologic Drug Products (DSPIDP) in FDA's Center for Drug Evaluation and Research (CDER). They review drugs for a wide range of illnesses, including

tuberculosis, malaria, organ transplantation, and CFS-related conditions. Part of the FDA mission is to review drugs for safety and efficacy. Investigational new drug (IND) applications for CFS are reviewed by a multidisciplinary team that includes physicians, pharmacologists (toxicologists and clinical pharmacologists), chemists, microbiologists, mathematical statisticians, and consumer safety officers who help manage all of their projects.

FDA works closely with sponsors of therapeutic agents throughout the drug development process but cannot comment on the status of specific drug applications prior to approval. Dr. Cavaillé-Coll explained that he would provide an overview of the typical DSPIDP drug review process but cautioned that this process can vary based on the nature of the investigational agent, the sponsor, and the FDA reviewing division.

Drug sponsors are responsible for conducting clinical trials. During pre-clinical drug development and prior to human testing, sponsors are encouraged to discuss their plans with a "pre-IND" team of FDA scientists. The Pre-IND Consultation Program is open to all sponsors and was developed to facilitate safe and timely drug development, particularly in areas that are innovative and/or deal with serious and life-threatening illnesses.

Once an IND has been filed, FDA scientists work closely with drug sponsors to insure that proposed clinical trials are safe for patients and are designed appropriately to meet their stated objectives.

As studies are completed, FDA scientists review results and provide feedback to sponsors on any remaining requirements prior to submission of a New Drug Application (NDA). Upon receipt of a NDA, the multidisciplinary scientific team at FDA reviews all of the data to ascertain whether the new product is safe and effective for its intended use. Once a drug is approved, FDA remains actively involved in post-marketing surveillance of drug safety through ongoing review of spontaneous adverse event reports and pharmacoepidemiologic studies.

Accomplishments

Dr. Cavaillé-Coll then reviewed some highlights of their accomplishments. In May 1997, FDA allowed to proceed an open label study of Ampligen in patients with seriously debilitating CFS, and authorized the manufacturer to charge human subjects for the investigational drug under 21CFR312.7. Since FY 1998, additional patients have been authorized to enroll in this open label uncontrolled study.

In order for an investigational agent to be eligible for cost recovery, in addition to other requirements, its sponsor must provide objective evidence to FDA that they are actively pursuing marketing approval with due diligence. At a minimum, this must include an active controlled clinical investigation that could ultimately support approval. Authorization by FDA to charge for human subjects for the investigational drug should not be equated with having demonstrated safety and efficacy, nor does it imply that FDA

has any expectation that a product will or will not be demonstrated to be safe and effective.

Permission for cost recovery for Ampligen in CFS patients was granted because its sponsor, Hemispherx Biopharma, agreed to perform a Phase III clinical trial to assess whether the product is safe and effective for that indication. In FY 1998, as announced by the manufacturer of Ampligen on April 14, 1998, FDA allowed to proceed a randomized, double-blind, placebo-controlled clinical study of Ampligen in the treatment of CFS. The study will enroll over 200 patients at approximately 8 to 10 clinical sites and was initiated in October 1998.

Other investigational products continue to be evaluated in the treatment of CFS and are in various stages of development under INDs in DSPIDP. FDA does not publicly comment on the status of any sponsor's drug development program. However, under the FD&C Act, substantial evidence of safety and efficacy from adequate well-controlled trials is required for marketing approval and such evidence should be available as part of any New Drug Application. The Pre-IND Consultation Program in the Office of Drug Evaluation IV in CDER, in collaboration with DSPIDP, has also provided guidance to assist investigators and sponsors over the years in submitting successful IND applications to evaluate investigational drugs in the treatment of CFS.

In addition to ongoing involvement in various stages of CFS drug development, FDA has been proactive in drug development in the following ways:

- Ongoing involvement with CFSAC and its predecessor, CFSCC, and participation in all activities.
- Maintenance of an active role in education about its function in drug development through publications and public speaking.
- Through the Office of Special Health Issues, FDA works closely with DSPIDP and facilitates appropriate liaisons for individuals with CFS and their advocates. This office also provides the public with information on the drug approval process and access to investigational drug products.

Action Plan

Dr. Cavaillé-Coll then reviewed their FY 2004 action plan. He stated that FDA is committed to providing timely review of IND study protocols and study reports for CFS drug therapies. They will continue to work closely with sponsors of CFS drug therapy at all stages of drug development.

As the need arises, they will update the Antiviral Drugs Advisory Committee (ADAC) on progress in the field of CFS drug development. ADAC discussions of CFS-related issues will include representation by an expert in the field of CFS and a CFS patient advocate.

In addition, FDA will also continue to do the following:

- Participate in activities with CFSAC.
- Actively participate in CFS meetings and workshops in order to develop and delineate requirements for clinical trials.
- Promote development of CFS clinical trial endpoints, through work with sponsors and researchers.

Q & A

Ms. McLaughlin asked is he could share what drugs are under study. Dr. Cavaillé-Coll apologized that he cannot disclose this information under confidentiality rules. She then asked if he could tell them approximately how many drugs are under review. He responded that there are probably less than 20 products in his division.

Ms. Kenney said she knew that there was an FDA advisory committee meeting to discuss fibromyalgia. She asked Dr. Cavaillé-Coll what this meeting was about and if there were any outcomes that may impact CFS. Dr. Cavaillé-Coll responded that this work is a part of a completely different program. Ms. Kenney asked if it would be possible to get more information, Dr. Cavaillé-Coll explained all FDA advisory committee information is posted on their website and includes executive summaries, transcripts from meetings, and information presented at the meeting. He also noted that the Office of the Commissioner, Office of Special Health Issues may be able to provide them with additional information.

Dr. Bell asked if there were consistent protocols for looking at the end points because one of the problems clinicians experience is that they use different inputs. Dr. Cavaillé-Coll explained that when they work with investigators from companies, they do try to address the issue of clinical endpoints. They try to examine other studies to see what may or may not work.

Ms. Fitzpatrick asked how to access the CFS information on the FDA website. Dr. Cavaillé-Coll clarified that there is not a specific CFS section, but among the most valuable information on their website is the advisory committee meeting materials.

<u>William Robinson, MD, Center of Quality, HRSA</u>

Dr. Robinson explained that the written material he distributed provides a lot of information that CFSAC members need to know about HRSA, but he would not be reviewing all of it during his presentation. He planned to focus on providing background on HRSA for those who have not worked with them before. HRSA is agency with several programs that deal with many Americans' lives, reaching into the corners of the entire country and providing a solid safety net for health services in this country. President Bush and Secretary Thompson made it a clear priority to assure a safety net,

especially for those who need services. HRSA has a $7 billion budget that is used for a variety of activities.

The President's initiative is to expand HRSA's community health centers. There are currently 3,500 of these centers that serve more than 11 million people around the country. These centers reach urban and rural underserved areas as well as small towns. This program and the Health Service Corps provide preventative and primary health care to low-income, unemployed, and underserved families. They have programs such as the Ryan White CARE Act, which has a budget of $2 billion dollars and ensures that those with HIV/AIDS receive medications and services.

Dr. Robinson said he would not discuss CFS specifically; HRSA has no programs or budget specifically earmarked for CFS. Their focus is on providing comprehensive systems of care, primary care, and training to public health and primary care providers, which are all important to people with CFS.

HRSA works with states to ensure that mothers and children have access to care. The Maternal and Child Health Bureau provides most of its funding to states to ensure comprehensive systems of care. They also have programs that address specific children's health care needs, such as reducing infant mortality through the Healthy Start program and Poison Control Centers.

Under Title 7 and Title 8 of the Public Health Service Act, HRSA also trains health professionals; Title 8 specifically addresses nursing in communities, and Title 7 addresses all other health professions. The goal is to increase the number and distribution of primary care providers around the country. There are several programs funded under this act, and Dr. Robinson referred specifically to the Health Education Centers, noting that this is an area that supports some of the activities CFSAC is trying to accomplish.

Rural health care has also been a significant problem in the US. There are many remote areas where services are difficult to obtain. HRSA has worked to address this problem through State Offices of Rural Health, and people have started a variety of programs to provide health care in these settings.

Also part of HRSA's approximately 40 programs are its national Organ Transplantation program and the National Vaccine Injury Compensation Program for children who have been injured by vaccines. Dr. Robinson said CFSAC members can read more about these programs in the material he provided.

Some time ago with the CFSCC, several questions were raised regarding health profession training institutions. HRSA funds training in general medicine, pediatrics, family medicine, and other general areas. Members of the CFS community were asking why there were so many patients having a hard time getting physicians to take this CFS seriously.

HRSA was initially approached by the Office of Women's Health, since women experience a disproportionate impact. Dr. Robinson's group was asked to become a part of the CFSCC because CFS had implications beyond women's health.

During these meetings they tried to determine how existing resources could be utilized to address CFS issues through collaborations. They were fortunate to develop collaborations with Dr. Reeves and CDC and Ms. Kenney and the CFIDSAA. They worked together to determine how to use their resources and HRSA's contacts. They held a national video teleconference in conjunction with CDC in order to reach out to practitioners at 73 sites in 20 states. Too many clinicians and others they were trying to reach were unavailable. Feedback suggested that they needed to collect more information on what would constitute a good CME mechanism to reach people.

They then began planning another joint project with CDC, CFIDSAA, and others. They worked with Richard Wansley and his staff at the University of Illinois to identify other activities they could engage in. The Director of Bureau of Primary Health Care sent a dear colleague letter to hundreds of community health care center sites around the country, and at a minimum, they ensured that the resource materials developed by NIH and CDC were being distributed. They then began to design a curriculum to train people in primary care on CFS, working with experts who would ensure an appropriate design. The curriculum has been expanded into a train-the-trainer program since practitioners tend to learn better from their colleagues. Practitioners who are already knowledgeable about the disease would train their colleagues, who would then go on to train additional people, achieving a cascading effect. Most of this work happened up to 2001. Dr. Robinson noted that he would identify which components he could begin working on again.

In closing, Dr. Robinson said that a part of their work was to examine how they can engage other parts of HRSA. The Maternal and Child Health Bureau, for example, likely has a greater role they can play in addressing issues related to CFS patients under the age of 21. He also would like to engage their Office of Rural Health and their Office of Telehealth and Telemedicine, which may have mechanisms and technologies to disseminate information.

Activities related to CFS also slowed down due to issues related to 9/11 and the anthrax attack, and Dr. Robinson expressed his commitment to enhance attention in this area. He asked CFSAC members for recommendations for priorities and collaboration, such as their partnership with CDC and NIH. He emphasized that HRSA does not have the funding resources but can provide the technical expertise.

He suggested that CFSAC members visit their website for more information about their programs; he can also be reached through Dr. Fields if they have any questions.

Q & A

Dr. Bell said that for children who have this illness, the education component has been a major issue. He asked if there was a liaison in the Maternal and Child Health Bureau who works with schools. Dr. Robinson responded that the challenge with education is that the school systems are so decentralized. The Maternal and Child Health Bureau attempts to work at the macro level with the states. He suggested that CFSAC may want to consider recommending getting the Department of Education involved as a federal partner.

Ms. McLaughlin added that schools have no idea what is happening with CFS. They had gone to states and their response was that it is a federal issue. Dr. Robinson noted that this may be an opportunity for a partnership between HHS and the Department of Education.

Ms. Fitzpatrick said that her experience in successfully interacting with health professions (mainly nurses, physical therapists, and occupational therapists) in the school system is to have someone present on a topic at their national meetings. As a result, the presentations get published in their national journals and disseminated to the appropriate individuals. Educational opportunities may be an issue that CFSAC can address.

Dr. Robinson commented that one of the problems is that there have not been enough nurses to provide the services that Ms. Fitzpatrick is referring to. The train-the-trainer program is not specific to physicians and part of what they are trying to do is to use health education centers as a model. This training should be provided to anyone who provides primary care — whether they are nurses, physician assistants, or in family medicine.

Dr. Fields thanked Dr. Robinson for his presentation.

Bill Anderson, Office of Medical Policy, SSA

Mr. Anderson explained that there are eight physicians, psychologists, and speech pathologists and a staff of 14 professional staff in the Office of Medical Policy. They develop the rules and regulations for evaluating medical impairments and publish the Listing of Impairments. If individuals meet the criteria for an impairment, can apply for disability, and are not working, they can automatically be classified as having a disability and receive benefits. In contrast, the complete working definition of disability is the inability to perform substantial gainful activity (SGA). He explained that evaluation of medical impairments cannot be done without understanding the listings.

Dr. Laurence Desi, an occupational medicine specialist who has extensive experience dealing with people with impairments in the working population, will be primary the SSA representative to CFSAC.

Their office worked closely with the CFSCC. Many people turn to their office for help with solving problems. He stated that people need to know about SSA and disability benefits. SSA must work with the medical profession so that providers know what SSA needs to decide disability.

SSA published a report on CFS with the help of several people who are on CFSAC and present at today's meeting. Since that time, they have seen a difference in the number of people who are identified with CFS in their system. Mr. Anderson said SSA tries to impress upon their staff the importance of this information.

In the short term, SSA cannot determine how many people approach SSA and allege having CFS. They can only provide the number of people who filed or the number who were identified by adjudicators. Unless CFS is identified as the primary or secondary problem, however, it is not recorded.

Mr. Anderson noted that prior to publishing the SSA ruling on CFS, 755 people filed and were identified at the initial level as having CFS in FY 2000, 215 of which were allowed while 550 were denied. After publication of the CFS ruling, 2,286 were classified as being either disabled or not, 712 of which were found to be disabled. These numbers more than tripled, most likely as a result of educating their staff about CFS. In FY 2002, 2,767 cases were adjudicated, and 636 were allowances while 2,131 were denied. Preliminary numbers for FY 2003 are 2,465 identified, 471 allowed, and 1,694 denials. He noted that it is time to conducted training on CFS again.

There is a process for individuals who receive an initial denial, but as Ms. Kenney and others who help CFS patients through the process know, this can be a very complex and difficult process to get through. The people who end up going through reconsideration usually have more extreme cases. Adjudicators receive approximately 2 million initial applications or adjudications each year, and they face the same challenge as many agencies that must process large volumes with a set budget.

Last Thursday, Commissioner Barnhart announced major changes in processes to identify people who are severely impaired earlier in the process, and the new processes would be in effect by mid-2005. For those in the spectrum of having an impairment or those with impairments needing medical attention or help returning to work, there are many things built into the process to detect these cases sooner. In the last 10 to 12 years, SSA has dealt with a lot of return to work issues. They found that SSA needs to reach people with impairments early — before they get too far out of the workforce.

Mr. Anderson said it is unlikely that the number of people coming to SSA with CFS has fluctuated and acknowledged the need to train their staff again on CFS. He said part of the problem is with the medical community and getting sufficient evidence to prove or disprove a disability. SSA provides consultative examinations that take 35 to 45 minutes and are performed by practitioners in the community for individuals who do not get regular medical care. There is a need to train consumers and doctors to recognize CFS and provide the medical evidence.

He noted that SSA also does outreach. They have an exhibit at national conventions for major medical organizations, including nurses, speech pathologists, and others. Mr. Anderson summarized and asked CFSAC for input and guidance.

Q & A

Ms. McLaughlin asked if they could get an impairment code for CFS. Mr. Anderson responded that they already have a code for CFS, but Ms. Laughlin's question is probably referring to creating a listing for CFS. The listing is an administrative efficiency for SSA and is set up to more quickly identify people who are disabled even if they can do basic work. CFS is highly variable, which makes it difficult to develop an agreed upon listing criteria. He committed to ensuring that those making decisions about disability are aware of CFS, and he said they almost always have to do an individual assessment on people with CFS because the impact is so variable from person to person.

Dr. Fields asked for further comment about the listings. Mr. Anderson said he doubted that it would help SSA adjudicators or patients filing for disability to develop a listing without doing a full individual assessment. Mr. Anderson also recommended that CFSAC look at the SSA website to review the criteria.

Ms. McLaughlin asked if there was a listing for fibromyalgia, and Mr. Anderson responded that there is not. He explained that they do not even have an SSR for it, but it was included by association in the CFS SSR. He was not sure if there is an impairment code for fibromyalgia.

Ms. Fitzpatrick asked if it is reasonable to assume that if someone needs to be examined by an SSA evaluating physician, that these doctors will have been trained in the specific disability. Mr. Anderson said this was a good question, but a better approach would probably be to develop a list of what to look for in CFS patients and to provide this information to the physicians when they conduct the exam. When they send someone to an orthopedic surgeon, for example, the examining physician is given a two to three page list of symptoms to look for. He said he was concerned about focusing on specialists, since neither the medical community nor the patient community agree on what the appropriate specialty for CFS is.

Fields asked a clarifying question about SSA going to primary care providers. Mr. Anderson explained that they will examine this approach to see if it is reasonable.

Dr. Bell said he agreed with Mr. Anderson's concern about specialists. He went on to ask if it is possible with SSA outreach efforts to teach primary care providers how to document the impairment. Mr. Anderson said he agreed with Dr. Bell and acknowledged that this is a reasonable approach to examine.

Dr. Gantz commented that clearly disability is a functional definition, since CFS lacks a diagnostic marker, which makes it very difficult. He noted that the diagnostic criteria

SSA uses for CFS seem outdated and that the functional capacity evaluation to determine what a patient can do is expensive.

To address the first issue, Mr. Anderson explained that SSA does not set criteria for medical impairments; they follow the medical community's standard for diagnostic criteria. If an illness is considered a medical impairment, it must be according to "current community standards." They struggled in writing the SSR for CFS because there is still disagreement about what is specifically required to identify CFS. He agreed with Dr. Gantz about access to medical care. SSA has discussed conducting pilots in which people who apply for disability are provided access to care to allow the collection of longitudinal data on their treatment. This will take some time to develop, however.

SSA relies on others to define the medical standards and then develops criteria from there. What they encounter with CFS is similar to when HIV/AIDS, Epstein-Bar, and other illnesses were first discovered; there was disagreement about what the illness was and how to diagnose it.

For this reason, Mr. Anderson noted, SSA does use a very functional definition of disability. Since the listings of impairments are not always functional criteria, people perceive that getting a listing is the way for people to receive benefits. It is difficult to argue against this perception, however, when 55% to 60% of their initial allowances are paid based on the listings, and the other 40% are based on whether they can do their past or current work. The listings were created not by statute but by regulation to quickly identify individuals that people can agree have an impairment without taking them through the full functional process. Over the years, some of their listings have become more functional in nature. Mr. Anderson said he did not think a functional definition is the ultimate solution for CFS.

Dr. Gantz asked how the people who are denied differ from those who are selected because they have similar symptoms. Mr. Anderson agreed this is true and stated the difference is based on how an individual functions. Many have medically terminal impairments that can have a wide range of functional impacts. It is the job of the adjudicator to deal with assessment of the functional impact.

Dr. Reeves commented that it may be worthwhile to discuss what emerged as an issue in both Dr. Robinson's and Mr. Anderson's presentation: the lack of optimal CFS education for health care providers. SSA cannot make things happen; health care providers have to properly diagnose and document these illnesses. This includes school nurses who determine what services people need. Dr. Reeves suggested that this is a major area for the committee to consider and that this is important to look at early because it crosses other issues, including CDC's issues with the case definition. There is a need to measures all of the symptoms that impact a person's disability, impairment, or functional ability, and both CDC and NIH have a research interest in developing these measures. He noted that in terms of provider education, it is an ongoing project and an area in which many of the agencies have expertise.

Dr. Friedman expressed another view, that of the legal profession representing CFS patients to obtain social security benefits. He said that it would be interesting to look at the correlation between the number of attorneys representing CFS patients and the number of people receiving benefits.

Dr. Friedman noted that these discussions seem to fault the documentation that is coming to SSA as the reason why more CFS patients are not receiving benefits. He said that his wife fell ill with CFS following an auto accident 2 years ago and was careful to select a physician whose sole practice was to treat CFS. They submitted the documentation to SSA, and she was denied benefits. She is now being represented by an attorney whose sole practice is to represent CFS patients. It has been a year, and she is still fighting for benefits. In the meantime, she lost her job and does little else than try to maintain her health and her health regimen. He stated that patients who are denied benefits may fall out of the system because all of their energy is going to maintaining themselves rather than pursuit of benefits.

Mr. Anderson stated that very few patients have attorney representation at this level because these are strictly people who have filed initial consideration claims. He agreed that there are people who do not file again or push forward with their appeal rights. He said he tells everyone that they need to do what is best for them. On Dr. Friedman's second point, he said that he thinks they are doing a better job — not great job — of getting SSA staff to recognize and deal with CFS. What he shared is that one of their major obstacles is getting documentation from treating sources. Once they get the documentation, Dr. Friedman is correct. He acknowledged that there are people who are frustrated and believe they deserve benefits. This is the reason why the Commissioner had to testify before Congress.

Mr. Anderson said he did not intend to imply that documentation is the only issue. He said most would agree that the SSR that they published is a major improvement from the past, and his job is to ensure that the SSR is applied appropriately.

Dr. Bell adjourned the meeting for lunch at 1:30 pm and asked CFSAC members to return at 2:15 pm.

Presentations by Invited Guests

Dr. Bell noted that invited guests would be speaking, and asked that discussions be limited to 10 minutes. He asked Dr. Fields if there were other issues he wanted to discuss before the presentations began, Dr. Fields said not at this time.

Dr. Fields introduced Ms. Kenney.

K. Kimberley Kenney, CFIDSAA

She thanked Dr. Fields and Dr. Bell. She expressed her for gratitude Dr. Fields' commitment to meet in FY 2003 and for the opportunity to participate in the CFSAC meeting. She also thanked the other CFSAC members.

CFIDSAA has been around since 1987 and has worked hard to ensure that a committee like CFSAC exists at the HHS level. They believe it is vital. CFSAC is an important forum for discussion and debate, research, and public policy that CFS patients need. It is also a symbol to the community that they are being heard, represented, and recognized within HHS and the public health paradigm.

CFIDSAA has had much collaboration with many of the people participating in this meeting, and they look forward to engaging with the new CFSAC members. In addition to their work with federal health agencies, they have also been active with Congress through the appropriation process and oversight activities. They have had 12 lobby days over time when they bring patient advocates, family members, and friends to meet with Congress and discuss their illness. Their 12th lobby day was held two weeks ago during Hurricane Isabel.

She explained that CFIDSAA work deals with education, patients, the public, the media, health care providers, and researchers. They conduct public policy efforts with health agencies and Congress and have directly funded approximately $4 million in medical research over time. They have been active in hosting, co-hosting, and working with federal agencies on research meetings, including three symposia that were held a couple of years ago to look more deeply into CFS issues.

As CFSAC begins its work, Ms. Kenney said it is important that they work hard together to regain the momentum they lost over the past 2.5 years. While individual agencies are engaged in CFS efforts, they have not had a forum to share information, so it was helpful to hear updates on what agencies are doing and how they are improving their efforts. When a committee engages two to three times per year, they can act as a catalyst for what happens during the other 363 days of the year. Bringing people together sparks interaction, dialogue, and information sharing, allowing efforts to be strengthened through communication. She was pleased to hear that the website will be started, since communication is important.

She noted that CFSAC has opportunities to engage on critical issues, and they can help deepen the knowledge of CFS both in terms of the science and the personal experiences of the patients and the caregivers who suffer with them. She said CFSAC could also bring tremendous credibility to the illness through its mere existence. As Dr. Dean noted, there is a growing appreciation of the complexity and multi-systemic nature of CFS. They can engage people in different program areas to work on these issues together.

She further stated that there is a need to reflect and provide guidance on difficult issues such as study methodology, improving the rigor of the science, definition issues, bringing

researchers to the field, and an issue of immediate importance and interest to the community, the name change. The breadth of expertise, diversity of experience, and continuity of commitment is essential. CFSAC will be the focus of what people see as progress in the area of CFS.

Ms. Kenney again thanked CFSAC for the invitation to this meeting and offered to be available to the committee as a whole or to individual members. She has been involved with CFS for 12.5 years, and her work has become a passion. Like Dr. Dean, she also offers an institutional memory that she is willing to share.

She stated that Dr. Reeves and others have demonstrated the magnitude of this illness in terms of its complexity and incredible human suffering, which warrants responsive public health policy and genuine public concern. There is a tendency to think of CFS has sporadic, but there have been outbreaks in workplaces and communities.

Ms. Kenney noted that there have also been other emerging populations that will be important to CFSAC as they do their work. With military conflicts with Afghanistan and Iraq, there are hundreds of thousands of troops that will be coming home. The Department of Defense and the Department of Veterans Affairs are already beginning to prepare for Gulf War Syndrome II, when people return and begin to experience CFS-like symptoms. People who do not die from SARS and West Nile Virus seem to have a hard time recovering from these illnesses. These populations may serve as good study models. In addition, in the aftermath of 9/11, Environmental Protection Agency concerns regarding environmental and experiential exposures have been noted. There may be illnesses following the communities that experienced the greater impact of the terrorist attacks.

Ms. Kenney concluded by expressing her appreciation for the individuals who have agreed to serve on CFSAC.

Dr. Bell thanked Ms. Kenney and asked if she would she be available for questions and to provide guidance to CFSAC, since she served as a member of the CFSCC. Ms. Kenney said she would be delighted to assist CFSAC.

Dr. Bell then asked for her thoughts on the name change issue. Ms. Kenney said Carol Lavrich, who was the Chair of the Name Change Workgroup, would be discussing this issue with her. Dr. Bell then introduced Carol Lavrich and suggested that questions for Ms. Kenney be held until after Ms. Lavrich completes her presentation.

Carol Lavrich, Chair, Name Change Workgroup, CFSCC

Ms. Lavrich began by introducing herself as Director of Patents and Licensing for American Red Cross and the stepmother of a child with CFS, who is now an adult doing well. She expressed a commitment to making sure that CFS is examined globally across many different spheres and referred back to Dr. Reeves' discussion about getting the community together again. One of the issues she would like to see addressed is education

about CFS. She stated that despite having four physicians in her family, when her stepson became ill, none of them knew anything about this illness.

She stated that a CFSCC name change workgroup was formed in 2000 to examine this important issue. Members from a variety of backgrounds participated in this group:

- John Herd, a patient advocate
- Leonard Jason, PhD, DePaul University
- Daniel Kahn, MD, VA Medical Center, Iowa
- K. Kimberley Kenney, CFIDSAA
- Nancy Klimas, MD, University of Miami, VA Medical Center
- Charles Lapp, MD, Hunter-Hopkins Medical Center, Charlotte, North Carolina
- Carol Lavrich
- Susan Levine, MD, a physician in New York who treats CFS patients
- Arthur Lawrence, PhD, HHS

Ms. Lavrich noted that the workgroup has met mostly through conference calls and at other meetings. After having numerous dialogues with the community, leaders, researchers, and federal officials and surveying the patient community to get feedback from variety of sources on their recommendations, they developed a working draft of a recommendation that can be built upon. The Name Change Workgroup would like to ask CFSAC to move forward and complete their work.

Dr. Bell asked if the draft recommendations have been presented to the HHS Office of Public Health and Science. Ms. Lavrich responded that it was never formally presented to anyone. She noted that the goal was to draft a recommendation and submit it to the CFSCC.

Dr. Bell asked if the recommendation is to look at the issue from the beginning, and Ms. Lavrich responded affirmatively. Dr. Fields noted that despite discontinuation of the CFSCC, this workgroup decided to continue working although it has been an external activity because the CFSAC charter is new. He said that a lot of people are very committed to this issue.

Ms. Kenney said whatever term is used should represent a broader construct than what is defined by the case definition to accommodate borderline cases where patients do not meet the full case definition but experience many of the same disabilities, illnesses, and lack of access to care and providers who understand CFS. She also noted the overwhelming degree to which people feel CFS is an inadequate term, stating that there is universal agreement on this point, but the breakdown occurs in deciding what to call it.

Dr. Bell suggested they continue the name change discussion at the end of the meeting in order to complete the presentations by the invited guests.

Dr. Fields then introduced Ms. McLaughlin.

Jill McLaughlin, NCF

Ms. McLaughlin began by expressing her appreciation for the opportunity to address CFSAC and to share suggestions and recommendations. Based on the discussions they have heard so far, she said they would all likely agree that there are several problems related to CFS, but the main overall problem is that it has not been a priority. She alleged that the majority of physicians do not take this illness seriously.

She noted that more resources need to be devoted to chronic diseases and that it will likely be cost effective to do so. She then asked to make two issues immediate priorities: name change and children. She said that an accurate name, diagnosis, and classification are essential for further progress to be made.

Ms. McLaughlin noted that ambiguity of the case definition has caused widespread discrepancies in epidemiological studies and that issues including diagnosis, treatment, research, and disability hinge on the case definition. She noted that CFS is comprised of heterogeneous conditions and that there are marked differences in the types and severity of symptoms, immunological abnormalities, prognosis, and response to treatments.

She stated that NCF endorses the Name Change Workgroup's recommendations. She noted that myalgic encephalomyelitis (ME) is a more specific and appropriate diagnosis than Chronic Fatigue Syndrome. She asked that the Name Change Workgroup be supported to continue their work and that CFSAC hold a name change session.

She then read a quote from the testimony of Sara Bass to the CFSCC in 1998 about pediatric CFIDS and noted that although this was presented in 1998, she can say the same thing 5 years later: that little is being done for children with CFS and that few epidemiological studies have been done. She noted that the first step is to develop a pediatric case definition and that Dr. Reeves had noted earlier that children have a lower risk of CFS. She then wondered about the number of undetected cases of childhood CFS.

She then focused on causes of death in persons with CFS, stating that a recent study by Dr. Jason found that approximately 60% of deaths were caused by heart failure, cancer, and suicide and that those who died of cancer and suicide were considerably younger than those who die from these conditions in the general population. Ms. McLaughlin noted that several circulatory and immunological abnormalities in CFS patients have been discovered that might increase occurrence of other conditions or decrease life expectancy, warranting further investigation.

Ms. McLaughlin noted that there are still patients who are falling through the cracks. She noted that CFSAC cannot solve all of the issues but that it has an opportunity to provide direction and leadership.

She thanked CFSAC.

Q & A

Dr. Bell asked if there were any questions, and no one responded. Dr. Fields thanked the invited special guests.

Discussions

Dr. Bell opened the discussion of carry-over issues.

Carry-over Issues

Name Change

Dr. Bell asked if CFSAC were to advise changing the CFS name to neuroendocrine dysfunction syndrome, what would be the implications for CDC activities and case definition?

Dr. Reeves then offered some technical comments relating to name change and case definition. He explained that CDC worked with the complex case definition issue since 1988 and that CDC has assembled a large and distinguished international group to develop the case definition. The group has met over the last 3 years.

He noted that the primary problem with case definitions is that they are primarily based on anecdotal clinical experience rather than scientific evidence. Secondly, case definitions cannot be quantified. A case definition should be based on standardized, validated information on the characteristics of the fatigue, as well as on symptoms of other disorders they experience. He noted that these are complex, multi-faceted constructs that require a very serious effort to address. As a result, they are working with a collaborative group that includes NIH, CDC, and Canadians. He then noted that this group agrees with the need to develop a case definition that addresses all of the issues that have been discussed, including pediatric issues, but it must be based on scientific data.

Dr. Reeves then made some technical comments regarding name change, stating that they are echoed by the majority of international experts that CDC works with. They all agree that CFS is an inadequate name and that there is currently no alternative and valid term for this illness, but he noted that the reality is that CFS is recognized and is gaining increased credibility. He said that changing the name will likely put back much of the educational and scientific publication accomplishments and that it may set a precedent for an HHS-chartered committee to recommend changing the name of an illness.

Dr. Reeves noted that patient concerns should not be discounted in discussions of name change. He went on to note that changing the name of a condition typically sets back medical research, for example, as experienced with the six name changes that Hepatitis B went through. The experience with HIV/AIDS was also similar, even though

terminology was changed for scientific reasons. He noted that typically, each name change cycle negatively affects the proper indexing and understanding of the past research.

Dr. Reeves suggested that a higher priority should be establishment of an appropriate case definition because this problem would remain even after a science-based name change. He noted that illnesses are typically renamed by those doing scientific investigations on the illness in question.

Ms. McLaughlin acknowledged that changing the name is not perfect, but is a step for consideration.

Dr. Friedman commented that his participation on CFSAC is as both a research scientist and a parent, so he probably understands the situation confronting committee better than many. Based on what he heard in the general discussions, the movement to change the name is mainly patient based, which is one perspective. The other perspective, eloquently stated by Dr. Reeves, is the researchers' perspective. Dr. Friedman stated that he agrees with the researchers' perspective, even though they could fall out of favor with some patient representatives. He, like Dr. Reeves, believes that changing the name alone now, without a new set of criteria or a new case definition, will impart more harm than good.

Dr. Friedman proposed a process whereby patients and patient representatives can have a better understanding of the consequences of a name change on the patients and their main goal of getting a better understanding and treatment for themselves. He estimates that it would set the field back by 5 to 10 years in terms of confusion, treatment, and advancement of knowledge. He said he was speaking from his own experience, sharing that his daughter's symptoms are more like fibromyalgia.

Dr. Friedman stated that the fibromyalgia case definition was changed in 1991 and that when he wrote a review of fibromyalgia, many things that were written before the change had to be thrown out because data no longer applied to the new case definition. He indicated that changing the name at this time is not likely to be constructive and that a mass educational campaign would better serve patients and patient representatives.

Dr. Reeves offered to give a more detailed presentation on where they are with revision of the case definition at the next meeting. He said that an article is under review. CDC is also funding a multinational meta-analysis. Dr. Bell agreed that a presentation was a good idea.

Ms. Fitzpatrick recommended that they accept the information that has been submitted to them on the name change. She added that she has also been involved with name changes with two national organizations. Both organizations spent a great amount of time putting together recommendations, and both recommended not changing the name, mainly because history has shown that changing the name does not work. She discussed hippotherapy, which was a term known in many other countries, and was brought into the

US. They dealt with several problems in using this term, but it is finally getting recognized. She also mentioned Crohns disease is another example of an unappealing name.

Ms. McLaughlin mentioned that even though the CMO national report came out in the UK, it still said CFS is a motorneuron disease, MS, or severe neurological disease. She noted that if there were a decent case definition, the name would take care of itself.

Ms. Kenney explained that in January 2001 the CFSCC recommended bringing different people to the table to better understand the impact on medical reimbursement, ICD codes, and indexing. They have not had the opportunity to have this discussion, which is important to carefully analyze the advantages and disadvantages of a name change. This discussion was put off. She added that as both a member of the workgroup and the CFSCC, she thought this was an important recommendation to consider.

Dr. Reeves added that there is a need to review evidence on true perceptions of a scientifically representative population with CFS. Ms. McLaughlin noted that they have such surveys, and Ms. Kenney stated that she could make these data available.

Dr. Bell suggested that they not make any decisions about this issue today without further discussion; it is not a decision to be made lightly. Dr. Bell then asked CFSAC members if they should set a time aside to discuss this issue.

Ms. Fitzpatrick responded that she would like to consider other issues on the table before addressing the name change. She felt that they had already taken a considerable amount of time on the issue.

Ms. McLaughlin noted that the CFSCC had planned to have a separate day devoted to this issue before it was dissolved. Dr. Bell then asked CFSAC if this would be a practical approach, including different agencies and patient organizations.

Dr. Reeves cautioned that with all of the CFS issues that CDC is currently addressing — identifying risk factors, markers, treatments for CFS — a discussion about the case definition and other strategies would be of higher priority. Dr. Reeves noted that his necessary priorities include thinking technically, epidemiologically, and public health wise about CFS. He added that having a full day with agencies would likely dilute what they are trying to accomplish.

Dr. Gantz, indicating agreement with Dr. Reeves, said that it would be premature to change the name. He noted that a sexier name may better characterize the more severe symptoms, but that it would put understanding of the illness back further. He noted that a better definition is needed first.

Dr. Bell proposed tabling this discussion for the remainder of the meeting.

Ms. McLaughlin asked Ms. Kenney what she thought about this issue as a former member of the Name Change Workgroup and the CFSCC. Dr. Fields apologized for interrupting and noted a desire to stay within protocol.

Dr. Fields then asked Dr. Bell if he had made a motion, and Dr. Bell said that he did. The motion was seconded by multiple CFSAC members, and all voted in favor.

Dr. Bell said they should consider developing a summary similar to what the Name Change Workgroup was working on and asked Ms. Kenney if she could be involved. Ms. Kenney responded affirmatively and noted that she would provide reports that contain data on how positions changed over time and other information collected through surveys. Dr. Bell said that would be beneficial, and they could present a concise summary of thoughts that develop over the next few months.

Ms. McLaughlin then asked if she could briefly ask another question, and Dr. Bell answered affirmatively. She then asked Ms. Kenney if she had a position on name change. Ms. Kenney noted that a personal opinion was not relevant here.

Dr. Fields suggested that in view of the personal nature of this discussion that it was a discussion that could take place but in another forum.

New Issues

Dr. Bell then returned to new matters.

Dr. Reeves suggested that education be a major priority for CFSAC, focusing on professionals who do not believe that CFS exists. He said that there are three major educational foci:

- Health care providers, such as doctors, nurses, and physician assistants
- Third party providers, such as health plans and others who may economically benefit from a change in perception
- The general population

Dr. Reeves noted that the satellite education effort was less technically successful than they had hoped, but that it was the first unified effort to get a group of government, private, and academic people together for a multimedia conference. He also noted that they have been having discussions with Ms. Kenney about the educational campaign that CDC funded through HRSA to identify different venues that might be more effective. He stated that they learned a lot since they had never attempted it for this illness before.

Dr. Robinson agreed with Dr. Reeves' comments regarding the teleconference. Dr. Bell asked that they continue discussing provider education and asked Dr. Robinson how he

thought they could make an impact. Dr. Robinson suggested that there may be a way to use some of the teaching materials that HRSA is developing for the people at SSA.

Dr. Reeves suggested that CFSAC may want to spend more time on SSA at the next session. He added that CFIDSAA is the first patient advocacy group that came forward with education as a priority and a concept for how to provide it. Dr. Reeves said that CDC worked with them on that concept, and HRSA also worked with them using CDC funding. He noted that at a future meeting, there could be an update on the name change, a more detailed presentation on the CFIDS educational program, and presentations by SSA and private care providers.

Dr. Patarca shared that his expectation for this first meeting was to gain exposure to what each agency has been dealing with and to define topics for future, including education and types of basic and clinical research. With all of their collective experience, they do not want to duplicate efforts. He said it would be very helpful to avoid duplication of effort and to look at the whole field to map out what their priorities are going to be and where they can do the most good. He added that once priorities are defined, then CFSAC could determine who should come to speak on CFS-related issues. Otherwise, they may spend too much time on individual issues and not accomplish what will move the field forward.

Dr. Bell agreed and turned attention to defining CSFAC priorities, stating that education is a critical issue since it is also related to the credibility issue. Dr. Patarca agreed that education is important, but noted the necessity for a global strategy that will influence how and who they educate.

Dr. Hanna agreed with Dr. Patarca and noted that the government agencies should present on the activities that they are engaged in, and then, CFSAC would advise the agencies on how they can improve these activities, a role that advisory committees typically play. Dr. Bell said that this is an excellent point.

Dr. Bell suggested wrapping up the education issue before they move on.

Dr. Reeves commented that he did agree with Dr. Patarca and Dr. Hanna. The way the committee functioned in the past is that the federal agencies presented their programs. The committee would examine the programs together to see if there were any gaps or other issues; they would then make suggestions. Dr. Reeves then noted that one of the strategic holes is education about CFS and that it is important to have agency updates to ensure that they are acting appropriately, but they have to be placed within the global strategy.

Dr. Fields added that some of the elements that Dr. Patarca referred to could be contained in a mission statement, asking what would committee members say in a few sentences? He suggested that this links to Dr. Patarca's statement about strategies. If CFSAC had a simple overarching statement, then specific issues like education and the case definition would be linked and discussed within the context of this statement.

Dr. Bell asked for a volunteer to draft the CFSAC mission statement. Ms. Fitzpatrick said that CFSAC has a defined purpose, which is a good place to begin. Dr. Bell said he would like someone to begin drafting a statement that integrates the topics they want to concentrate on; he then asked Ms. Fitzpatrick if she would volunteer, and she agreed.

Ms. Fitzpatrick also suggested that CFSAC members be provided a copy of the curriculum that Dr. Robinson has developed for review. Dr. Robinson agreed and noted that he would work with Ms. Kenney and Dr. Reeves to get the curriculum to CFSAC members.

Dr. Robinson then shared comments on how he perceives CFSAC's role, inviting CFSAC to not only to look for gaps in programs but also for ways to make the whole greater than the sum of its parts by working more collaboratively.

Dr. Reeves noted that the education effort originated from the CFIDSAA who approached HRSA. He added that CDC then became involved because of funding and case definition expertise. This is an example of a cross-agency and private sector collaboration that worked.

Ms. Kenney added that CDC's finding in a pilot national survey that rural areas have higher rates of CFS could impact HRSA in terms of their community health centers and rural health concerns. She offered this as a type of information that bridges across programs and agencies.

Dr. Patarca congratulated HHS for putting together such a diverse group that would allow them to share ideas. He suggested that CFSAC create a wish list of activities and topics that are priorities to be accomplished, and then they could decide how best to make things happen. He expressed a concern about how they would accomplish anything by only meeting twice a year. He said maybe they could have subcommittees to focus on specific areas, and then they could recruit the people they need externally. He said that they will need a lot of information from the agencies and other sources. First, however, they need to know their agenda, how they will go about it, and how to make it work. Dr. Bell agreed.

Dr. Reeves noted that the committee may need to decide how often they want to meet. He added that in his experience with other committees, it is sometimes necessary to meet more frequently in the beginning.

Dr. Bell then asked CFSAC members how many meetings they should have in a year and suggested four. He asked Dr. Fields if that would be financially possible, since he has mentioned two or three meetings earlier in the day.

Dr. Fields responded that they are there to support the committee's work, so they would consider what CFSAC would like to do. Strategically, he noted that FY 2004 starts on October 1. Dr. Fields suggested that the next meeting be early and that a draft mission and list of priorities (starting in October for FY 2004) be brought for discussion.

Ms. Fitzpatrick suggested that before they finish today's meeting that they capture their thoughts on what everyone sees CFSAC doing and all the things they want to accomplish. If they write them down on a newsprint sheet, they will at least have them written down even if they do not get to prioritize them. Dr. Fields then began scribing the list on an easel.

Dr. Bell then asked the committee what other topics they would like to see included, offering science funding as a topic.

Ms. Butler said that she would like to see other health care professionals educated such as occupational therapists. She has been using an NIH program for arthritis patients for years, which has been very effective with CFS. CDC and NIH may have other programs to possibly adopt.

Dr. Bell suggested putting this idea under education. He then asked Dr. Patarca if he would begin looking at the education issue and where opportunities may exist with HRSA and other organizations.

Dr. Mohagheghpour added case definition and biological makers for diagnosis. She said it would be helpful to get a listing of ongoing grant proposals to get a sense of where the science community is going. She added that prior to CFSAC meetings, they can communicate and refine their ideas, so that so much time is not spent on these issues during their meetings.

Dr. Patarca suggested that they could try to define what is needed by any researcher or clinician in any location to deal with CFS — what basic or core resources need to be there and how federal agencies can help provide these resources. Dr. Reeves then suggested that all of the federal agencies may be able to create a resource list that could be available.

Dr. Patarca said he was also referring to other types of resources. Should they, for example, recommend the creation of repositories, epidemiological studies that will help them access certain populations, or research on children or other areas that are not being studied adequately?

Dr. Bell asked if there are any opportunities for seed grants.

Dr. Friedman noted that the NIH grant process can be daunting for a disease like CFS. He added that in the area of patient treatment where there are a number of modalities that have not been explored, an attempt to map a full NIH RO1 study dedicated to CFS would require a preliminary study to be funded before it would get the nod of the review committee. Therefore, he noted, if they want more short-term therapeutic modalities available for CFS patients, then they would probably want to have smaller, less formal grants; if the smaller studies work, then they could go for the full RO1. He went on to say that without some kind of seed money to allow for these kinds of studies, people like him will be approaching clinical departments or schools and universities.

Dr. Bell said Dr. Hanna has likely dealt with seed grants for many years and asked her if she thinks this is a problem of concern that they need to discuss.

Dr. Hanna responded that NIH has a program call Just-in-Time Grants where an investigator can be funded for $25,000 at a time. She added that if a study is not working, one would know early on. This program, however, requires breaking the proposals up into sections, and investigators still have to go through the review process.

Dr. Reeves agreed with Dr. Hanna's remarks, and then, he referred back to the discussion on making CDC resources available. He added that CDC recommendations on subclassifying CFS could be made more widely available on the website or through other means for those who would like to apply for grants, as well as the recommendations that come out of CDC and NIH workshops.

Dr. Patarca said he would like to a see mechanism that places CFS under a specific disease category for funding — whether it is autoimmune, infectious, or neurological. He said that they need to find a way to bring together FDA's and CDC's efforts to determine the causes of CFS. He emphasized the need to look at what they have, what they need, and then, strategies to move forward. He said that people can say that the community is disjointed and that there are many schools of thought; the only way they can address this is to make a recommendation that objectively captures what needs to be done. He stated that he would rather look at CFS from this high level, which is where they have the authority to function (rather than getting into the nitty gritty of what is happening in a laboratory or clinic).

Dr. Hanna commented that NIH is looking at the big picture as reflected in the recent workshop. Dr. Patarca asked Dr. Hanna what they need from CFSAC, and Dr. Hanna responded that there is a gap in the resources area. She said the only way to get more funding though is for more researchers to apply for grants.

Ms. Fitzpatrick asked if she thought that they needed to stimulate more activity in the research grant area. Dr. Hanna explained that that is what they are trying to do but that it has been slow; they had five applications last January and 15 by this spring. A question Dr. Hanna posed for CFSAC was, what can they do to stimulate university research?

Dr. Bell questioned whether this discussion was practical and in line with CFSAC goals.

Dr. Reeves commented that this was tricky area. He said the system works well, and there is a need to understand the system. He recommended that CFSAC understand how NIH and CDC are working and said it would be extremely helpful if the committee advised them on how they can improve what they are doing. What can the committee suggest that the agencies have not thought of?

Dr. Mohagheghpour agreed and said she was trying to explain that they have access to published literature, but if they know where the grants are going, they know where the research is going.

Dr. Bell responded that he did not think that this would be helpful right now. Researchers will develop proposals based on what they want to study over the next few years. He was not sure if any recommendations they make would influence that process.

Dr. Friedman suggested that some reviewers might reject an application that is too close to their own research because they see the area as their domain. He recognized that CDC and NIH have a long-term perspective, which is fine, but there is an immediate need for patient care.

Ms. Kenney said she saw an opportunity with NIH's interest in funding an RFA, which is to tell the research community that they are interested in CFS and have set funding aside for it. She suggested using this opportunity to elevate and enhance the credibility of the illness and explain why it is more attractive for researchers to submit an application to NIH than it was 5 years ago.

When they organized their symposia series, Ms. Kenney noted that they had several senior scientists who would not take the time to put together an RO1 application, but they had a great deal of intellectual engagement and interest in CFS. They had many ideas on what needed to happen, where the gaps were, and what other fields could contribute in terms of sleep disorders. She said that they need to find a way to tap into this and convince these people to enter the field, and the RFA provides this opportunity.

Dr. Mohagheghpour asked Dr. Hanna if an RFA could be issued if CFSAC were to come up with new areas of research or reinforce new areas that NIH has identified. Dr. Hanna responded that they have issued a PA and that after they review the summary of their workshop, they will see what the RFA will focus on. She pointed out that applications went up from five to 15 as a result of releasing the PA, the State of Science symposium, going to meetings, and doing other outreach. She noted that CFS is at least on the map.

Dr. Fields asked if someone like Laura Hillenbrand working with the national Ad Council could help to increase the applicant pool size. Dr. Bell then asked if there was consensus that Laura Hillenbrand's work has benefited the community and should be recognized.

Dr. Cavaillé-Coll stated that 6 years ago, the last CFSCC discussed appealing to people who have great ideas but have not had a chance to apply their work to CFS. Part of their recommendation was to urge the Secretary to increase funding in order to increase the number of applications; getting the word out would help, and they saw this with the symposia. Part of the success with AIDS research, for example, resulted from making additional funding available to people who had a background in tuberculosis and used different techniques. AIDS was not seen as a retrovirus until people with microvirus experience began paying attention to the illness.

Ms. Fitzpatrick said she would like to discuss recognizing Laura Hillenbrand but as part of a larger CFSAC strategy. For example, should others be recognized in the future? Ms. McLaughlin then suggested that HHS do a public service announcement (PSA) instead. She noted that HHS developed one, but they never saw it.

Dr. Fields explained that PSAs are typically played at suboptimal times. He noted that if there is an annual recognition or celebration that fits within the CFSAC agenda, the recognition could be in the research area one year and another area the next.

Dr. Bell asked if there were other topics to add to their list, such as the pediatric case definition. Ms. Fitzpatrick said that they should encourage CDC to pursue it. Dr. Reeves said he would discuss the complex issues around case definitions at another meeting.

Dr. Cavaillé-Coll noted that FDA approves drugs for all populations including children. If a drug is submitted for approval for CFS, whether it is applicable to children or not will be an issue. They also have different ways of encouraging drug development that require information on whether the drug is safe for use with children; therefore, a case definition for children is an important step to develop drugs. In addition, Dr. Cavaillé-Coll said he would like to know what types of information CFSAC wants to know about FDA and their programs. He said he can propose links to include on the CFSAC website to make it easier to access FDA information.

Dr. Bell commented that they had developed a good outline of six topics with which to start.

Ms. McLaughlin then asked about lack of HRSA funding for CFS.

Dr. Hanna explained that they had two center programs that she saw as ideal for CFS if they can be adopted and transferred. The first program trains researchers in the field of women's health. The second program she discussed was specialized Centers on Sex and Gender Research, which is more translational in nature for people who treat women. This is a broader concept in which CFS was included, but no applications were received in the area. She said it would be helpful if the committee could recommend one thing that would cut across all areas.

Dr. Bell asked Dr. Hanna if she would provide a summary of what she was describing. Dr. Hanna responded that she would send the actual proposals for both programs and for the centers.

Dr. Bell asked if there were additional comments before they moved to the public comment period.

Ms. Butler asked Dr. Cavaillé-Coll if he was involved with the primary outcome measures for the drug trials for Ampligen and if there is a mechanism to look at similar drugs in the same class. Dr. Cavaillé-Coll responded that he thinks they will learn a lot from the clinical studies, but he could not comment on anything that was in the application process. He emphasized, however, that they do not initiate studies; they receive them.

Public Comments

Dr. Bell then opened the meeting for public comments and asked that each person limit their comments to 5 minutes.

Dr. Fields said they received two sets of comments by the requested deadline in the Federal Register notice. Since then, he received a couple of other comments and recommended that they be appended to the record. Dr. Fields then asked Dr. Mary Sweitzer to share her comments.

Mary Sweitzer, PhD

Dr. Sweitzer began by saying that she was pleased to hear a lot of the discussion today and how people want to do more than what she has heard in a while. She noted that the word "fatigue" is an absolute anathema for CFS patients because people laugh at them and doctors will not treat them. She alleged that there is only one doctor in her home state of Delaware who will treat CFS patients. She noted that her comments were going to deviate from her written statement.

She provided two comments on the research. She began by noting that there are researchers in England already writing about "CFS," and they are using a different definition than CDC. She said that if they use Sharp's definition of CFS, CDC will need to multiply its estimate by 20 and say that there are 20 million Americans with CFS. She noted that Simon Wesley in England sees CFS as a psychological disease.

She stated that CFS research is already confused. Dr. Sharp says that cognitive behavior therapy helps people with CFS, but only 5% of the people he sees would meet the CDC definition. Dr. Wesley is treating a whole other group of people who are probably depressed. She said that the reality is that CFS does not have a single meaning in the research. If CDC does use their definition, then they should label each definition because a lot of different ones are being used.

She then noted that poverty is biggest problem. She said she got two phone calls from people who were being evicted from their houses. She noted that she was able to attend the CFSAC meeting today because her husband's work allows them to afford Ampligen treatments. When she was sick, she had to be taken care of and could not be let out of the house by herself. People who have never experienced this have no idea what it is like. She said she is writing a book entitled *Living Death* because that is what it is like to live with CFS. She said if Ampligen were taken away, she would be living death again.

Pat Fero, Executive Director, Wisconsin CFS Association

Dr. Fields then read Ms. Fero's written statement to CFSAC.

The statement began by thanking CFSAC members and attendees for continuing this journey. She said she hoped that CFSAC will research the issues, choose one thing to do,

and do it well. She said that CFS patients in Wisconsin also needed restored confidence that public health agencies will not exclude them.

If CFSAC members fall into the "Grand Canyon" of CFS issues, nothing will be accomplished, and many of them will want to leave the table. To understand the importance of their work, CFSAC members need to start by looking at the trenches. They understand that research is slow and that CFS research is under funded in proportion to the number of people suffering from this illness.

The problem is that the CFS pathology endangers their well being and sometimes their lives. Her statement shared the stories of two cases. One of our members received a letter from her assisted living agency. In 2001, the agency took this case as a traumatic brain injury case. It was clear that the patient was a danger to herself: she would black out several times and wake up on the floor. One time she woke up to find her glass coffee table shattered on the living room carpet.

This member called Ms. Fero and told her that she had scratches on her forehead and only remembered was falling and hitting her head. She was unable to put two words together to make a sentence. After another fall, she had further examinations, and her primary physician was overwhelmed with the case and said she was so ill that she required more than the services of a single person. Ms. Fero said the response from the agency was that it was "not the agency's or the staff's fault that the funding system does not recognize CFS as a disability."

The agency is attempting to move her again and cut off services. Ms. Fero observed this case from the start and believed that the agency totally misjudged the data, despite the information that she had provided and a videotaped lecture that Ms. Fero made at their offices at their request. They say they cannot support her, as the doctors say among themselves that she is clearly a drug addict, has severe psychological problems, and/or effectively hides information that can be used to help her. This woman, however, does not have cognitive ability to strategize anything.

Another woman has skin cancer on her face and sought help for lesions on her face and body for 3 years. She was originally diagnosed with shingles and invested in alternative therapies, investing thousands of dollars to remove the lesions. Last winter, her doctor decided it was a fungus and that she must not have been taking her prescriptions because it had not cleared up by June. He sent her to a dermatologist who removed the lesions and started chemotherapy the same week. As one would expect, the cancer spread after 3 years.

Situations like these are complex and all too common. As they seek treatment for symptoms, CFS patients haul the CFS mythology with them. No one looks for life-threatening conditions in a head-to-toe symptom complex. Ms. Fero wrote that it had happened to her, and she was lucky to resolve her situation through surgery.

They are caught in belief system and have nowhere to turn. Part of the problem is the need to redesign the health care delivery system for chronic illness, but that goes beyond the scope of CFSAC.

Life in the trenches is dispiriting. Ms. Fero acknowledged that sometimes the buck stops at her feet, and she does what she can and moves on. People are dying in the trenches, and a 15-year old person who participated in CFS research studies was told that if she had come to them a year earlier, more could have done more for her. She died last year. One of the leaders in Ms. Fero's group died from liver failure.

Those who step up are overwhelmed and become the subject of ridicule. They retreat with, "Patient expectations are too high." Others continue to work with CFS patients and slowly lose credibility with their institutions. Sanctions from CFS mythology must be lifted with clinicians and researchers. Across the country, people with CFS are striving to increase public awareness in medical education. They do this sporadically because sometimes they are alone at home while they are ill and cannot speak publicly and institutions refuse to acknowledge their situation. Over the years, hospital, clinic and medical school administrators have told Ms. Fero the same thing: CFS patients need a champion in the system, and they cannot help them.

Ms. Fero again recognized that they have a "Grand Canyon" and asked CFSAC to do research, choose one thing to do, and do it well.

Additional comments

Dr. Fields noted that comments from Dr. Marianne Spurgeon were submitted after the Federal Register requested date.

Wrap Up

Next Meeting

Dr. Bell then asked CFSAC if they could set a date for the next meeting. Dr. Mohagheghpour suggested that they meet in 2 months to give them time to prepare for the next meeting. Dr. Bell agreed and suggested the beginning of December and said that they would send out an email to get agreement on the date.

Action Steps

Dr. Bell summarized what CFSAC members are to complete for the next meeting:

- Submit agenda items for the next meeting.
- Dr. Bell will summarize the discussion regarding the pros and cons of a name change.

- Ms. Fitzpatrick will draft the CFSAC mission statement and send it out for other members' review.

- Dr. Patarca will explore issues regarding education.

- Dr. Mohagheghpour will contact Dr. Hanna and explore the issue of increasing CFS grants for the research community.

- Dr. Fields will obtain the PSA from its makers and make it available for review at the next meeting, and Ms. Kenney also offered to share the history of PSA. It will be discussed at the next meeting.

Dr. Bell asked if they should invite a representative from the American Medical Association or the American Academy of Pediatrics or if it was premature. Dr. Patarca thought it was premature to pursue this opportunity.

Fields asked for feedback about today's meeting:

- Ms. Fitzpatrick commented that she would like to see CFS in the press and would be happy to work to gain exposure. Dr. Fields replied that this would be great.

- Ms. Kenney commended Dr. Bell on how he chaired the CFSAC meeting.

- Dr. Cavaillé-Coll said he was glad to see CFSAC's momentum and would like more time to make travel arrangements and schedule the meetings.

- Dr. Bell asked how much time CFSAC wanted to reserve for a public comment period for the next meeting. He suggested 1 to 1.5 hours.

Dr. Nichols reminded CFSAC members to complete their forms and to return them to Olga Nelson before they leave.

Adjournment

Dr. Bell adjourned the meeting and thanked everyone for attending.