A note from the Editors about the use of initials/acronyms in this article:

Most of the slides prepared by Dr. Kenneth Friedman, the guest speaker for the second part of this forum, displayed "ME/CFS" in reference to the illness. However, during their verbal co-presentations, Dr. Friedman and Dr. Gurwitt often used "CFS", which still designates the name most used in the medical research community, i.e. Chronic Fatigue Syndrome. Therefore, this summary will show both acronyms, relatively in sync with their use throughout this program. Elsewhere on this website the illness may be called CFS/CFIDS/ME, for Chronic Fatigue Syndrome/Chronic Fatigue and Immune Dysfunction Syndrome /Myalgic Encephalopathy. Similarly, MassCFIDS, a shorter, long-standing form of the Association's name, is frequently used in longer articles for clarity and brevity.

Article index

The Massachusetts CFIDS/ME & FM Association (MassCFIDS) held its Fall 2011 educational forum, co-sponsored by the Massachusetts Department of Health, on November 5, 2011, at the UMass-Hinton State Laboratory Institute Auditorium in Jamaica Plain, MA. The second segment of this forum focused on developments and discussions from the September 2011 International Association for Chronic Fatigue Syndrome /Myalgic Encephalomyelitis (IACFS/ME) Conference held in Ottawa, Canada, which could have considerable impact on ME/CFS patients. The guest speaker, Dr. Kenneth Friedman, and Dr. Alan Gurwitt, president of MassCFIDS, shared the presentation and spoke about these topics with insight, conviction and optimism.

Dr. Friedman, a recently retired Professor of Pharmacology and Physiology from the University of Medicine and Dentistry of New Jersey, is a fervent and outspoken advocate for CFS, a working member of the IACFS/ME, scientific advisor to several ME/CFS patient groups, and a longstanding friend of MassCFIDS. Dr. Friedman briefly described how he became involved

with CFS and the Association many years ago. While his daughter was attending Tufts University, during the early 1990s, she came down with infectious mononucleosis and eventually went on to develop CFS. He spoke appreciatively about the information and support that he and his daughter received from the Association during that difficult time.

Dr. Friedman singled out developments and studies from the Ottawa conference which he considered to be important to ME/CFS patients, not only from a research standpoint, but also their impact on patient care. The key points in Dr. Friedman's lecture (taken from the slides that he had prepared for this forum) are as follows:

- Is it time to get beyond ME/CFS case definitions?
- Should we use exercise testing in lieu of a biomarker?
- Investigating the efficacy of anti-viral and antibiotic therapy
- Stepping up to the plate by the Private Sector

Is it time to get beyond ME/CFS case definitions?

Dr. Friedman started by drawing attention to the uncertainty and debate which now surrounds the three most popular case definitions for CFS, ME or ME/CFS. As chairperson for the session on "Case Definitions for Research and Practice" at the Ottawa conference, Dr. Friedman noticed some researchers/clinicians were unsure about the case definitions or not in agreement with each other, while others sought ways to get beyond these case definitions. He thought some researchers were positively influenced by the approach being taken by Dr. Leonard Jason at DePaul University in Chicago, IL. In order to arrive at the most suitable definition for the illness, Dr. Jason focused on identifying the most appropriate features in the illness and identifying the most appropriate case definition and criteria for CFS. (At the Ottawa conference, Dr. Jason's study described a statistical technique, data mining, which was used to help determine which questions and items would provide the most effective data).

The use of Electronic Medical Records (EMR's) affords a practical way to record and characterize patients' symptoms along with other relevant information. Patients' medical data could be compared to case definitions or other data along an infinite array of parameters. Dr. Friedman stated that the technology exists and it continues to become increasingly more accessible. So, it would be possible to assess patients in this manner and determine if they met at least one the case definitions. Furthermore, he thought that if the patient would meet "one or any" of the illness criteria, that would suffice. What Dr. Friedman described was the relationship

of case definitions, EMR's and patient registries that could lead to a system with many possibilities for ME/CFS research.

Another approach that could help facilitate diagnosis of ME/CFS and selection of treatments, would be the switch from the "single definition/single cause" model to one that supports subsets. Dr. Friedman made the analogy of ME/CFS to breast cancer, to the extent that breast cancer is described not as a disease but a category of disease in which there can be multiple types of breast cancer (or subsets). In this approach, treatments will often depend on the specific type of cancer that the individual patient has. Dr. Friedman mentioned how this model for breast cancer was recently reviewed on the *Doctor's Radio*, a satellite radio station, which led him to see this as a viable and appropriate strategy for ME/CFS. There already exists considerable evidence to support multiple causes and subsets in ME/CFS, and the benefits that patients would gain from more individualized treatments is obvious.

Back to top

Should exercise testing be used in lieu of a biomarker?

There is also debate over the expressed need for a biomarker-that is, in order to confirm the illness in patients, a biomarker must be found. Dr. Friedman proposed the consideration of exercise challenge tests for their proven ability to measure and identify distinctive features of ME/CFS. More specifically, exercise testing like the Stevens Protocol (i.e., the method developed by Staci Stevens at the University of the Pacific, Stockton, CA) has effectively detected multiple abnormalities unique to ME/CFS and objectively measured the reduced ability of ME/CFS patients to perform exercise and certain activities (i.e., those needed for sedentary work or activities of daily living). Exercise testing can induce postexertional malaise (PEM)-now being recognized as the hallmark symptom of ME/CFS, and then it can quantify the effects of PEM on the patients' functional capacity.

As a result, this method is able to confirm the presence of this illness in patients. Having a tool available that could confirm or document ME/CFS could also facilitate the disability review process, and possibly accelerate the approval of the applicants and the release of their benefits. Dr. Friedman empathized with patients in how this is often a long and difficult process. Furthermore, this type of tool could help to demonstrate efficacy of potential treatments, especially those which require FDA approval (i.e., Ampligen was mentioned as one treatment that needs to be pushed through). Therefore, Dr. Friedman has recommended the acceptance

and utilization of exercise tests as a valid protocol in lieu of a biomarker.

Back to top

Investigating the efficacy of antiviral and antibiotic therapy

Going beyond anecdotal evidence for use of antiviral or antibiotic treatments, several research papers at the Ottawa conference reviewed positive responses to antiviral therapy and antibiotic therapy in CFS-in particular, for those patients who had high antibodies to enteroviruses or in CFS precipitated by the Epstein Barr Virus (EBV). Dr. Jose Montoya (at the Stanford School of Medicine, Palo Alto, CA) has been studying an antiviral regimen which he has developed for treatment of ME/CFS, but the actual protocol has had limited circulation. Dr. Montoya has agreed to prepare a paragraph for inclusion in the IACFS/ME *Physician's Primer* which suggests that an approach and rationale could (and perhaps, should) be developed for the use of particular agents for ME/CFS patients who demonstrate particular viral loads. The efficacy of treatments with antivirals or antibiotics needs to be further investigated. It also needs to be determined what would prompt a well-planned, carefully executed clinical trial.

A study showing positive response to antibiotic treatment in ME/CFS was presented by Dr. Sam Shor, from the Washington, D.C. area. Dr. Shor placed his ME/CFS patients on the same treatment regimen-a combination of multiple, long-term antibiotics-which he used for his chronic Lyme Disease patients. Patients with ME/CFS met the international case definition and were negative for Lyme Disease (LD). Improvement of symptoms was found in 66% of ME/CFS patients even though they were seronegative for LD. Several possible interpretations of these results, according to Dr. Friedman, would be: 1) the possibility of these CFS patients having LD, 2) viewing the improvements as potentially due to the immunomodulatory effects of the antibiotics, or 3) an infection that could be at the root of their CFS was responding to the treatment. Similarly, a Norwegian study discovered that a cancer agent, rituximab, had reduced symptoms of CFS, raising the same questions with regard to that drug's immunomodulatory effects. Dr. Friedman explained these agents work on the same system (the immune system) and felt that research of drugs with these particular properties would be worthwhile for ME/CFS.

Back to top

Stepping up to the plate by the Private Sector

Dr. Friedman wrapped up his presentation with very encouraging news about several new private initiatives which are being set up for CFS research. He reported there were now three non-federal funded sources for ME/CFS research: the Whittemore Peterson Institute (WPI) which is well recognized by the ME/CFS community; the Chronic Fatigue Initiative, Inc. (CFI), an organization funded by a $10 million donation from a private family (the donation will be used on multiple CFS studies, after investigators determine "critical" questions and areas in ME/CFS research); and the Simmaron Research Foundation, an organization of friends and patients of Dr. Daniel Peterson that will donate an as-yet-to-be-determined amount of money to support Dr. Peterson's research done in collaboration with other research groups.

Back to top

Developments in pediatric ME/CFS

Dr. Alan Gurwitt was particularly interested in news and developments in pediatric ME/CFS and had attended a workshop on the same, chaired by Dr. Miike from Hyogo, Japan. Dr. Gurwitt was pleased to see that the workshop was very well attended by researchers and clinicians from literally all corners of the world. He found this most encouraging, given the shortcomings in pediatric diagnosis and treatment during earlier years.

Evaluating children with CFS has been a challenge for quite some time, especially since the 1994 U.S. Fukuda criteria was developed for adults and adult manifestations of the illness. It was really not adequate for use in children and adolescents, explained Dr. Gurwitt. Approximately 6 years ago, an international group of ME/CFS researchers and clinicians was formed and they co-authored criteria specifically intended for children called, *Pediatric Case Definition for Myalgic Encephalomyelitis and Chronic Fatigue Syndrome*
(Dr. Leonard Jason,
et al
). He stated there are differences in the characteristics of CFS between children and adults. In particular, children tend to have more abdominal pain and rashes. Part of the pediatric criteria includes references that could be used by school personnel. However, Dr. Gurwitt finds that schools still show limited knowledge and understanding about CFS in children and their tendency is to suspect "school phobia" in children ill with ME/CFS. At the workshop, he discovered the situation was not much better for children with ME/CFS in many other countries.

Another terrible situation faced by some families has been the faulty accusation of Munchausen syndrome by proxy (i.e., the child's illness is assumed to be fictitious and to be caused by the parent or parents). Dr. Gurwitt is very disturbed by such occurrences of pure ignorance and undue hardships to families, and urged action by ME/CFS organizations to find ways to educate physicians and school personnel in how to distinguish phobias from legitimate illness such as ME/CFS.

The pediatric workshop reported a variety of news, such as how infectious mononucleosis was found to be a fairly common pre-illness event in children and youth who developed CFS (i.e., in about half of the cases); in some cases, immunizations were thought to be the precipitators of CFS-like conditions (i.e., no particular vaccines were identified but Dr. Nancy Klimas is working to clarify this); mold exposure was reported by some families as another CFS trigger; and Japanese researchers identified chronic sleep deprivation in children and teenagers as a major precipitator of CFS. Children as well as adults in Japan appear to be at a higher risk for sleep deprivation. Melatonin was the sleep agent most used in children. Though Ritalin was used fairly often, many researchers/clinicians are quite concerned about its use in children with CFS. The Japanese research group described an intense treatment regimen they created for children/youth with CFS, which usually included hospitalization and intensive sleep-wake circadian rhythm treatment to help restore their circadian rhythms-good results were reported on improvements made with their sleep disturbance, but not of all their CFS-related symptoms.

Dr. Katherine (Kathy) Rowe was recognized for the program that she had helped to develop and implement at the Royal Children's Hospital in Melbourne, Australia. Dr. Gurwitt described the Australian program as being "sophisticated and methodical" and unlike anything that other countries are doing. This program has followed close to 800 children (pediatric patients) for over 15 years, which has allowed them to create a history of the illness. The extensive information collected at scheduled intervals throughout this period of time included duration, recovery, education, work, treatments/diets, and other events and changes in these patients' lives. Although the average duration of illness was 5 years, this level of follow-up and ongoing support continued for many years.

The Australian program requires that new patients undergo a very careful evaluation for ME and the evaluation process include the parents-both parents, with a special emphasis about not leaving fathers out. Once a diagnosis has been made and appropriate treatments started (i.e., standard medications or therapies), other interventions also include family counseling, maintaining close contact with schools, and helping with necessary adaptations for the patient's/student's educational needs.

Back to top

A brief, informal overview of the Physician Primer

Both Drs. Friedman and Gurwitt informed the audience that the *IACFS/ME Physician Primer* was nearing completion and its release is expected during early 2012. A few things which they could share about the Primer, at this time, was why it was created, who it is intended for, what is its purpose, and its content (in a very general sense), as follows:

- it is a practice manual, written by a group of physicians, specifically for primary care physicians so they would have the necessary information to be able to diagnose ME/CFS

- it offers specific treatment recommendations, informs a physician of his/her responsibilities to the patient, and makes recommendations when it is appropriate to refer the patient to specialists
- it is geared for adult patients and does not include any information for pediatric care, but future plans are to compile a pediatric version
- it will be recommending the Canadian Case Definition for ME/CFS and it will not be using the 2011 International Consensus Criteria for ME because it is new and not clear how it will compare or do clinically (referring to what Dr. Friedman mentioned earlier in his presentation)

Drs. Friedman and Gurwitt reiterated the Physician Primer is a concise, very dense and highly technical handbook-for physicians and not intended for patient use.

When the IACFS/ME is ready to release the *Physician Primer*, MassCFIDS will send out an announcement via our E-newsletter and post the news on the website.

Back to top

Advocacy-its importance and its impact

What is MassCFIDS? was the title of a report prepared and presented for members and guests in attendance by Ms. Charmian Proskauer. Since MassCFIDS was founded and registered as non-profit charity 501(c)3 organization more than a quarter of a century ago, many newer members and guests have asked to learn more about its past, current work, and future goals.

MassCFIDS is the short name for the Massachusetts CFIDS/ME & FM Association. Fibromyalgia (FM) was added to the Association's mission (and name) during the 1990's. The history of the Association is available on the website, under the topic " About Us ."

MassCFIDS has an all-volunteer Board (currently of 14 members) which holds bi-monthly meetings. Officers are elected from within the Board. All the work of the Association is done by volunteers.

Ms. Proskauer shared with the audience how she had been initially recruited several years ago to help create a new website for Association. Eventually, she was elected to the Board and now oversees several committees. She also spoke about her desire to become an advocate for the illness; she is a family member of someone who has CFS. Finding herself with a little extra time, she wanted to work with others towards something that would make a difference-the Association fulfilled this need.

MassCFIDS is the oldest patient-run CFS organization in the country and its mission has remained the same, although the organization has evolved over time. Our members and volunteers continue to work and advocate for patients and their families in many ways: conveying information through the website and an E-newsletter; responding to questions by emails or phone calls; providing community outreach/patient services; speaking out (or writing) on issues which may negatively impact patients; and sponsoring educational events. A note about the patient and/or patient's family contacts we receive-70% of these are requests for services and 2/3 are for physician referrals. To be able to provide patient outreach and programs, it is important that we continue to build up our membership; but there is also strength in numbers which really matters when it comes to advocacy.

Dr. Gurwitt and Ms. Proskauer echoed the same message-the impact of advocacy may not be immediately realized, but it can have a far-reaching effect and pay off in many ways. Statistics collected on the Association's website traffic reveal the extent of its global reach-during the past 12 months there were 20,000 unique visitors from 151 different countries. The video of Dr. Anthony Komaroff's April 2010 lecture has been viewed from around the world and translated

into 4 languages. It has served as a catalyst for important advocacy initiatives, like those embarked on by the Norwegian health ministry. The Association also played a direct role in helping Japan form its first national ME/CFS conference. It maintains close contact with the CDC, through Dr. Elizabeth Unger, and overall, it has shown a good, strong reach into a lot of areas, concluded Ms. Proskauer.

MassCFIDS will evaluate on-going advocacy initiatives, participate selectively, and provide opportunities for patients AND their family members, relatives or friends to participate. Our goal is to expand advocacy in Massachusetts.

Back to top