by Alan Gurwitt, M.D.

In this report I write about my impressions coming from the two day Chronic Fatigue Syndrome Advisory Committee (CFSAC) meeting. The best source to get your own impressions is the video the links to which are now posted on our website.

Participants

The CFSAC Committee

This is obviously a hardworking group struggling to advance the cause of ME/CFS in spite of both overt and covert obstacles. For years many of their recommendations have been ignored but apparently there has been enough progress to keep them going. A bit of their despair appeared but they did soldier on in spite of the very mixed messages from the federal agencies.

It is not clear to me how their members are selected (see Jennie Spotilla's information from the link in Charmian Proskauer's report) and I do not know the background of some. The chair, Dr. Gailen Marshall, an internist from the University of Mississippi, seemed to be a competent group leader. He showed understanding of the issues and tact and kept the committee on task most of the time. He dealt diplomatically with representatives of the agencies.

There is one vacancy on the Committee. All ten of the members present had a great deal of reading to do as well as subcommittee meetings in addition to the main meetings. There is some question whether members received the written material on time. There were two subcommittees, one focused on research issues, the other on we think on management and treatment

Thank goodness for Eileen Holderman, the sole patient representative, Steve Krafchick, a lawyer from Seattle, Dr. Susan Levine, clinician from New York, and Mary Ann Fletcher, Ph.D., immunologist researcher from the University of Miami. These were the more outspoken members who clearly were proponents we could rely upon. Jordan Dimitrakoff, M.D., Ph.D. a urologist and researcher from Harvard is chair of the research subcommittee and was active at

times during the conference. Three other members were physicians of whom Ann Vincent from the Mayo Clinic was there the second day. They said little. Dane Cook, a Ph.D. from Wisconsin spoke up some. I have no idea where these last four stand in their beliefs about ME/CFS.

It will be important to learn more explicitly how members are selected. The ME/CFS communities should have a larger say in that selection.

The Agencies

HHS was represented briefly by Dr. Howard Koh and by Dr. Nancy Lee who was the Designated Federal Official and at times acted as a sort of co-chair. The National Institutes of Health (NIH) was represented by Susan Maier, Ph.D., the CDC by Dr. Ermias Belay with Dr. Beth Unger on the second day. The regular representative of the Social Security Administration was Cheryl Williams with Mr. Arthur Spencer making the main presentation on the second day. The FDA was represented by Theresa Michele M.D. but on the second day there was an excellent presentation by Rear Admiral Sandra Kweder, M. D. Other agencies reporting were: HRSA (Health Resources and Services Administration), and CMS (Center for Medicare and Medicaid Services).

People Providing Public Commentary

These advocates, some present for one or two days and those who spoke by phone, were allotted a total of 3 hours. They each had 5 minutes. There were many comments, some quite forceful and/or poignant, covering a wide range from comments on the process, some on specific agencies, and personal stories dealing with ME/CFS.

ME/CFS Organizations

We were one of 4 organizations invited. This was the second meeting where groups from the ME/CFS communities were called upon. The others this time were: CFS Solutions of Western Michigan, now, after a merger, called PANDORA (Laurie Chapo-Kroger); Wisconsin CFS Association (Pat Fero); and the IACFS/ME (Fred Friedberg by phone). We each had 5 minutes.

There was extra time during which there were questions from the CFSAC Committee, some on the IACFS/ME Primer for Clinical Practitioners.

Informal Notes of the Proceedings
First Morning, Oct. 3

Before the meeting started a group of advocates gathered in the lobby before being escorted up to the meeting (talk about containment). It included Laura Hillenbrand's father who later made an impassioned plea to the Committee. Bob Miller, from Nevada and a seasoned attendee (whose wife had made the important contact with President Obama resulting in the latter's now well known letter), said it was important to have many advocates as possible actually in the room. He told us that a large group of patients in northern Virginia and relatively close by have unfortunately isolated themselves from others and do not attend.

Howard Koh M.D., Assistant Sec'y for Health of HHS (who was at the DPH in Mass.), provided the welcome and introduction. While lauding the supposedly high degree of government CFS activity he made no mention of the many problems.

The first scheduled talk was by Committee member Dr. Jordan Dimitrakoff (of Beth Israel Deaconess) speaking about biomarkers. He described a large (40 million dollars) 5 year research project on "chronic pelvic pain syndrome" also known as Urologic Pain Syndrome. They wanted to pinpoint biomarkers. The research might serve as a model he claimed (I'm not sure how). He agreed that for this study and for study of ME/CFS a good common case definition is necessary. This was echoed many times during the two days.

Next was Mary Ann Fletcher, Ph.D., who described a study with Nancy Klimas and Gordan Broderick (from Canada) which also searched for biomarkers. The study compared three groups: CFS patients, Gulf War Illness (GWI) patients, and controls. They used an exercise stress model comparing various markers of activity such as apoptosis, lymphocyte function, cytokines, etc. They demonstrated that GWI and CFS were different from each other and from controls, and that all markers and systems were interactive with each other. The two illnesses were different in gene expression. One cytokine, IL-1a, might be a good index in future clinical trials.

Dr. Fletcher added there are pertinent biobanks already available for future research (such as the one left over from the Lipkin studies). Eileen Holderman asked where would the monies

come from. Susan Maier from NIH said possibly by linking to already funded research (which? how?). Dr. Dimitrakoff wondered if ME and CFS are different entities when a single entity is needed. Eileen Holderman pointed out that a generalized term such as urologic pain syndrome takes away from the organization of patient groups such as the more focused Interstitial Cystitis group.

In the public comments that followed, scheduled in advance, Dr. Rosemary Underhill (on the authoring group of the IACFS/ME Primer) spoke to the need to recognize the fact that ME/CFS occurs in small to large cluster groups. Little attention has been paid to that fact. It is a phenomenon that begs to be studied. Indeed, at the end of the second day this was included in the recommendations by the CFSAC Committee. There were other excellent comments from Laurie Chapo-Kroger, Dr. Grobstein, Mary Schweitzer, Rev. Hillenbrand. Note that there were many appeals to the effect that government agencies needed to move faster. For example NIH took 3 years after it had promised to do so to finally put on the State of Knowledge conference (2008 to April 2011)!

NOTE: WASHINGTON is a LARGE city filled with big impressive buildings within which government employees work. They are far removed from where we all live and the realities we patients live with daily. This remoteness shows, more evident in some of the agencies represented than in others. While CFSAC can bring information to the representatives, they and their colleagues need to emerge from their buildings and go out into the field to actually see and talk with patients and their families. Ph.D., MPH and MD degrees may be necessary but are not sufficient to really learn about ME/CFS.

Afternoon Session, Oct. 3

NIH, represented by Susan Maier. She stated that NIH received 30.9 billion dollars for medical research!! Of this ME/CFS received a miniscule 6.3 million or 0.02 percent. There are a total of 29 institutes within this huge agency of which 19 have joined a trans-NIH working group. It wasn't clear which combination put on the State of Knowledge conference in April, 2011. While she repeatedly stated that NIH is ready to fund new research proposals, few applications have been made. She seemed to imply that the reason there weren't had more had to do with the failure of researchers to apply than with any fault of NIH. I believe that implication is quite wrong and misleading for the following reasons:

- Dr. Mary Ann Fletcher made it very clear that key researchers who have applied in the past were turned off by the experience, including unexpected obstacles thrown up by NIH, so are not reapplying.
- It is not clear what attitudes prevail at NIH towards ME/CFS research.

- The personal experiences of two fine researchers I know who described rejection of their applications for what they considered to be unwarranted reasons.
- The presentation by Susan Maier left out details on how new applications could be made. Information from her was reluctantly given.
- There has been a lackluster past history of support and arbitrary decisions in regards to ME/CFS actions.
- When many present indicated that a major increase in funding is necessary, for example $100,000,000, Susan Maier seemed to find that totally unrealistic —yet that, if not more, will be what it will take.

There did not seem to be a positive and actively helpful attitude at NIH in regards to ME/CFS. I doubt that anything will change at that agency from within. They really don't mean it. A fire needs to be lit and perhaps the only way that will happen is from the outside. It needs to come from the President, Congress, and from concentrated focus on the part of ME/CFS advocates. Yes, there are major problems at the CDC, but the funding needed for major scientific advances to occur would best come via a reformed NIH. Advocacy groups need to find out exactly how the application process works and to alert potential researchers but there may need to be a huge change of attitude at every level of this agency.

In contrast to the NIH the **FDA** seems to have fairly quickly reacted to patient advocates. Their representative, Theresa Michele, spoke of the large response from the patient community leading to the Stakeholder's Meeting on Sept. 13th. She stated that the advocacy community could have an impact on future drug development. She mentioned a docket (I missed the number) that has been opened for which comments are needed by November 1st (!!).

At that point Dr. Sandra Kweder (Rear Admiral, in uniform) gave an excellent review of many aspects of the agency. The FDA regulates 25% of all products sold in the USA. She gave a brief history of the FDA which now is the largest regulating agency in the federal government. She pointed out that the FDA can encourage the development of therapeutic drugs but can't require that development. For any new drug there needs to be a strict definition and well designed criteria to measure improvement. These must be objective measures. There also needs to be a very detailed description of the tactics used for research. Focusing on ME/CFS, she described the realities of what is needed: well established criteria or biomarkers. However there is not a "core" ME/CFS, meaning a well accepted definition, an accepted method for measuring how patients feel or function, and accepted biomarkers for objective measures. (Note: none of these are beyond reach). She contrasted the state of knowledge of ME/CFS with fibromyalgia for which there are now 3 medications available. Very important was her statement (if I heard it correctly) that the FDA could advise but the research community needs to develop the tools for study of ME/CFS as well as research definitions.

Dr. Fletcher pointed out that in her opinion there now are biomarkers for ME/CFS. Dr. Kweder did agree that there are not top flight biomarkers for some medical conditions such as migraine headaches, so perhaps strictly accepted biomarkers may not be necessary.

The last part of the afternoon consisted of many excellent public comments, including from our own Donna Pearson and others. There were some common themes: The CDC Toolkit is unacceptable and harmful, the history of the CDC is disgraceful, HHS is providing lower funding than they did in 1993, and a target funding level of $100 million is needed.

Second Day, Morning Session, Oct. 4

The initial speakers were from 2 other agencies: Alaine Perry from The Center for Medicare and Medicaid (**CMS**) and Beth Collins Sharp from the Agency for Healthcare Research and Quality (**AHRQ**). The AHRQ runs the National Guidelines Clearinghouse, which has the website www.guidelines.gov to which physicians can link for information and clinical guidelines for a variety of illnesses and diseases. The IACFS/ME Primer has been accepted by the Clearninghouse and will be posted there soon.

CDC, represented by Ermias Belay Ph.D. Dr. Belay described activities at the CDC. Dr. Beth Unger was there this day as well. Dr. Belay started out by acknowledging the great need for educating primary care doctors. He referred to the 30 minute video available from Medscape: “CFS: the challenges in primary care” followed by CME questions as one effort. The problem that physicians report back is the limited time for patient visits. Two other videos deal with diagnosis and management of CFS and Sleep Problems. They are scheduled to release a video in November called something like “Back to School/CFS”. Who specifically is preparing this is not stated; that worries me.

Dr. Belay also reported that a series of patient vignettes are in preparation for release in June 2013, for use in medical schools via a medical education portal. The fact that the CDC is doing something for medical student education is good if the information is accurate and well presented.

And then a statement about the infamous Toolkit. Both Drs. Belay and Unger said that after

much debate the CDC has decided to keep the current version on their website! There will be a revised version sometime in the future, but no date was given. No explanation was given. This was an absurd decision on the part of the CDC. CFSAC, advocacy groups, etc. have all called for taking down the Toolkit until a much revised version is prepared. The current version is harmful!! Why there wasn't a big protest by CFSAC is puzzling.

The CDC is attempting learn more about CFS/ME patients via working with selected clinical practices, including: The Open Medical Institute (OMI-Kogelnik, Charles Lapp, Dan Peterson's group, Lucinda Bateman's group, and Podell's practice). Nancy Klimas's new clinic will also be involved as will Ben Natelson's in New York. They hope to have 450 patients closely studied. How useful this study will be is hard to say. Very good clinicians are involved.

Dr. Belay then gave a long list of agencies with which they are trying to collaborate.

Impressions about the CDC: It is a mixed bag. They have an abysmal decades-long history in relation to CFS. Hopes were high after William Reeves left. Dr. Beth Unger has certainly been an improvement in many ways. She has reached out to many ME/CFS organizations over the past year for suggestions and information, including our Association, but the promised feedback was poor. They are initiating some promising projects, the outcomes of which only time will tell. Their decision about the Toolkit was ridiculous, because the Toolkit still contains information that is harmful to patients. What became clear at this conference, consistent with their past pattern, is their determination to remain in control of everything including information and decision making. I can understand the need hold the reins tightly to maintain their command of the issues and policies, but those reins are too tightly held.

Next up was Arthur Spencer of the **Social Security Administration, Office of Disability Evaluation** . Requests for SSA appearance at the CFSAC meetings have been made for quite a while. Mr. Spencer provided a clear, detailed, and probably helpful description of the process used for evaluating disability claims. There are five steps in relation to questions re qualification. (My notes are a bit scanty and may not be accurate.) The 1st is: Is the claimant engaged in substantial gainful employment? Basically if the claimant is still working disability is not granted. For this stage substantial provider information is necessary. Specific findings of ME/CFS are needed to demonstrate that the applicant is unable to work. "A one shot consultation" may not be sufficient. A diary of your daily activities can be very helpful but it need not be in great depth. The 2nd criterion is: Do you have a medical impairment? The 3rd was: Does the impairment meet or equal those impairments/illnesses listed on their "medical listing." ME/CFS is not a listed condition but the impairments may be sufficient to be equivalent to those on the list. The 4th criterion: Can you go

back to any past relevant work within your RFC (residual functional capacity). And the 5th criterion: Can you perform any other type of work within your RFC.

The SSA evaluators usually require at least 6 weeks of training.

In a review of the SSA experience from 2001 to 2011 in relation to ME/CFS, while the average national allowance for other conditions was 35%, it was only 21% for ME/CFS. The older the claimant the more likely disability would be granted. However if the claim was pursued up the ladder of reconsideration steps such as going to an administrative law judge the percentage of success increases to 70% (!!). So, one needs adequate medical evidence, a personal diary demonstrating one's limitations, and a lot of persistence. One additional note: no specific case definition is used, according to Mr. Spencer.

I thought this presentation was quite straightforward. Spencer simply spelled out the criteria and steps and what is needed. I am sure others will be better informed than I am. Comments will be welcome.

Public comments followed. Dr. Lily Chiu asked for more prompt availability of meeting information, and the acceptance of international expert input. Others have commented on Billie Moore's poignant description of the hopelessness experienced by some with ME/CFS because of an accumulation of overwhelming factors and the dangers of suicide that may follow. Mary Dimmock (perhaps speaking for someone else) focused on the dismal past history of NIH. Others reiterated the target funding goal of $100 million.

Second Day, Afternoon (and last) Session, Oct. 4

The four organizations invited to appear began this session. We (Massachusetts CFIDS/ME & FM Association) spoke first followed by the others (mentioned above). A copy of our presentation has been distributed. We also provided copies of our CD on pediatric ME/CFS to each committee member. I read our comments and Charmian Proskauer, who had created them, showed the slides. All presenters were informative but 5 minutes is 5 minutes. As an hour had been set aside (we hadn't known that) there were several questions from the Committee including quite a few on the IACFS/ME Primer of which I am one of the authors. I answered as best as I could as Rosemary Underhill had already left.

The next to last subject was discussion of finding pathways towards selecting an American case definition for ME/CFS. I found this discussion wide-ranging but rambling. Dr. Nancy Lee stated towards the end that government agencies can't dictate a specific definition. Such a definition must come from the "medical community" (which medical communities? and how might that be arrived at?).

Steve Krafchick, a lawyer with a MPH degree, in effect implied that was a cop-out, stating that speaking positively about certain definitions already out there would at least lead in the right direction.

He is right in my opinion. I think the government agencies were not happy about accepting either of the two Canadian definitions but unless they get moving fast it could be years before we have a useful American definition. The work on this illness is international. There is no reason why an international definition couldn't suffice. The CDC has so messed up for years, contaminated as they were by their psychobabble leanings and overly broad definition that I doubt they could come through. BUT a good case definition is really needed ASAP.

The last item was drafting their recommendations. The discussion was confusing and rushed. See Jennie Spotila's and Charmian Proskauer's reports for what they believed were the recommendations

Charmian and I agreed that attending the CFSAC Meeting was important. I want to join her in thanking the Board for making this trip possible. Being there and observing first hand as well as meeting Committee members, government representatives, and other advocates was key in gaining further insight. For me the number one problem currently and for years in the past is NIH. We know the problems with the CDC—there are many—but with time and further strong and pointed advocacy perhaps there can be more changes.

I came away feeling the NIH, as the largest potential funding source for research, has simply not made a sufficient commitment to ME/CFS in the amount of funding and positive sense of purpose. Others have documented these failings. While there may be limitations on NIH's total funding the message was that they could fund more ME/CFS research if there were more applications. If so, they need to figure out, along with our own advocates, what is getting in the way and actively encourage new applications and new researchers.

The CFSAC Committee is doing its best and has brought about some change. We need to know more about the NIH funding selection process and how advocates can best support CFSAC in working with NIH to provide more funding for ME/CFS research.