Rough Notes on NIH Community Call March 8, 2016 (Not a transcript)

UPDATE: A full transcript of the call is now available at http://www.meaction.net/2016/03/09/nih-telebriefing-update/

Collins: This institution is very committed to this area of research. We want to move the research agenda forward, both intramural and extramural

Intramural: We've received IRB approval and expect to begin enrolling individuals this summer. I have great confidence in Avi Nath. A website describing it went up this morning. It's a remarkable opportunity to bring the full power of this remarkably interdisciplinary research hospital to bear …

There's a lot of heterogeneity, of course. Choice to focus on people with previously good health and then flu-like illness. To limit heterogeneity. We believe that this study has the opportunity to provide new insights that could be transformative for all of those who suffer from the condition.

The Trans-NIH Working Group defining strategic areas of research. Koroshetz will say more. Quite serious about looking for opportunities to expand research and recruit new investigators, with new eyes and brains.

Please take our commitment with great seriousness. Identify most compelling research questions. I understand that many of you have waited a long time perhaps to get this kind of attention. I hope you understand that we are now … Work together and not work apart. We are your partners. We want to hear from you, that's why we're having this call today. We're listening carefully to the suggestions you have.

Koroshetz, he's seen first hand how devastating ME/CFS can be for patients. He volunteered to chair this. I thank Walter for stepping into this space, with considerable vision already.

I'd like to thank everyone for the expression of interest and even concern that people have sent to us. We're very interested in working together with the community to achieve our long-term goal. Shared: to find better treatments for people suffering with ME?CFS. Big picture: Intramural protocol is only one step in the trajectory we need to get on to get answers that are going to be very helpful for patients. It's a long-term quest. A difficult problem – if not, it would have been solved long ago. We need to bring in the best and the brightest from many different areas of science. I don't think we know where the solution is going to come from, so we need to cast a wide net and get very experienced researchers and clinicians and work with the doctors caring for patients. Important to stay the course and look to the long term goal.

At NIH, we have some bureaucracy that's not easy to understand. Simplify: There's an extramural program as well, and funds from that go from the NIH to universities, companies, clinics, to do research. Intramural program where research is done at the clinical center. World's largest research hospital. Tremendous resources. But 90% of funds go out. Long term, need both. You'll hear about the intramural protocol, but also, we have a trans-NIH working group. We don't' know where the solution is going to come from, so ti's very important to have multiple institutes at NIH working on problem. The WG is working to develop plans that will move funds to highly meritorious research programs in the univ community.

Vicky Whittemore describes WG and what it is about and its plans.

VW: Program director at NINDS. I've been working with Koroshetz to coordinate WG. It's really been a pleasure to work with representatives from the 23 institutes and centers. Dedicated and passionate. We're in the process of putting together both a short term and a initiatives for better infrastructure as well as funding for longer-term research projects. Clearly the community has said, biomarkers, underlying causes and mechanisms, and what is causing "brain fog." Timeline: working very hard to present initiative for approval in May timeframe. Moving forward soon thereafter. Looking for input and feedback from community. Putting out requests for feedback on ideas, conference calls after this one, and reach out to research and clinical community.

Koroshetz: Why can't we say what we're thinking? NIH has processes to fund most highly meritorious research. All groups need fair hearing. Can't put info out before it's ready to be made public to everyone. So have to do a lo to of work behind the scenes. Purpose to present fair and open process here at NIH.

It's going to take an army of really good researchers to solve this problem. Can't be individual groups working in isolation. Want to form consortia. Not all doing the same thing. The first horse out of the gate is intramural. Dr. Nath is calling in from Liberia, doing fieldwork on Ebola. Very gratified that Avi can get on and hope his line stays stable.

Dr. Nath: At US Embassy. Thank you very much. I'm delighted to the be PI of the intramural study. When they asked me to consider this responsibility, I was thrilled to be able to look at the syndrome and see if there is an immune or neuroimmune component. This I the area of my expertise. I've seen patients and know how devastating it can be. Literature: Good reasons to believe that it's immune mediated. I designed a protocol to address those issues.

Three phases: Cross sectional study. Send phase: Longitudinal with repeated testing of a small subset of tests. Larger population with different types. Third phase: Intervention study based on the first two phases.

Brian Walitt, a medical officer at something… considerable. Lead associate investigator, helping to coordinate a large number of investigators.

Brian Wallit: Lead associate investigator. Rheumatology first. Hospital immune disorders. Developed a specialty in Me/CFS and Fibro. Research clinic at Georgetown, where I saw patients on a regular basis. Not just in one's head, not an unconscious choice. Not possible to push through. Tried to help patients and learned just how limited options are. Need for restorative treatment that gives lives back. This led me to come work at NIH.

Since here, I've learned a great deal about science, and how research is done here. Very excited to help Avi Nath facilitate the protocol. Believe it will provide answers to role of infection, immunity,… Also try to understand the biology of PEM. I believe these things will move the needle forward. Very excited to be part of it.

Koroshetz: The protocol at NIH has 26 associate investigators in addition, and they bring this really incredible expertise to the table in this study. This ranges from very high level neuroimaging to high level ability to look at cytokines, antibodies… Leo Saligan in nursing institute has been looking at CF in patients with cancer and neurologic disorders. Quite an amazing group. Different from hospital on the outside, because we're all full-time devoted to research. Tools also extraordinary. Veru difficult to bring a very ill patient for research in a hospital, but here, inpatient unit allow to study over multiple days or weeks.

Stepping stone. One piece of the puzzle.

Questions:

Robert Miller: First thanks. Possible treatments, especially Ampligen. What homework has been done thus far re Ampligen? Any talk with FDA? Only treatment ever to be in Phase 3 trials for ME/CFS. That opening for this drug potentially could lead to it being our AZT. Opening the door to pharma for much more research, plus give relief to many suffering patients.

Koroshetz: Goal is to try to get a treatment. To start, we are going to challenge our investigators to survey therapeutics that have been tried. Those are more short-term wins should they prove effective. New therapies are longer-term. We have an open door policy for people to come and propose… We have met with many investigators and Hemispherix company people. They have presented data from previous studies. Serious consideration. There's a process at NIH for funds to go out, so it's peer review. We're working with taxpayer dollars, so the process is very important to uphold. Will be having discussions on clinical trials as they come forward.

Donna Pearson: There is substantial confusion between the disease that you're studying and others that cause chronic fatigue. I know the name is not an issue that people want to talk about in research. But that's the best way to distinguish. Does the current study have the potential to determine if encephalomyelitis is in fact a portion of the disease?

Nath: We're not looking at every single aspect of the disease. In our population we can tell you if there's evidence of inflammation, and if so, … inflammatory process in the brain. Encephalitis requires infiltration of the cells. Inflammation of brain exists in Parkinsons' and Alzheimers. Do think we'll get closer to that definition. Whether we're able to establish it beyond doubt, not from this study. Animal studies have better chance. Take lymphocytes from patients, inject it into animals and see if we can reproduce the disease. Those studies have much better chance of answering that question.

Koroshetz: a couple of points. The protocol at NIH is interested in getting at the bio basis of the illness. Eventually, that bio basis is what moves the definitions and allows breakup in the heterogeneity in the disorder. That's a long process. I would urge people to stay the course there. Clearly, this protocol which is looking currently at 40 patients, what they find will need to be validated in other groups of patients to make sure it's a real finding that can be generalized. That's the next step. One reason we think organization is important is that many studies have discoveries that are never followed up on to know if they are generalizable. The expectation is that there are multiple different types of mE? CFS. Something we find here may not generalize. These are people who developed it after a flu-like illness. ??, Allergic, traumatic exposures. This is just one piece of the puzzle.

Cort Johnson: Ron Davis has taken on a similar… Is it possible for Davis to follow up on findings that you get up and visa versa? Funding?
Q 2: exercise study. Stevens at Workwell has worked on this for years. Working with her?

Exercise protocol is designed to induce PEM. Maximal effort exercise intervention. Designed to provoke symptoms, not provide a treatment. Unger at CDC, talking to them about proper ramps and so forth. But open to suggestions to all people with experience. Happy to reach out to others with useful things to add.

Nath: Davis's study is not exactly the same…

Koroshetz: Yes, he's been in contact with Davis and a number of other investigators. They will be sharing data. As we mentioned, we're hoping to set up a series of investigators around the country who can work in concert and share data, particularly with regard to looking at generalizability. History of biomarker studies: a lot of things don't replicate, so really need coordinated approach to make sure it's a real finding.

Chairman Proskauer: Why only 40 ME/CFS patients? I realize that it's a very deep study, but with 40 patients, does that have the danger of falling into the category of just another pilot study with numbers that are too small to be meaningful?

Nath: Screening, then admit for a week. It'll take at least a year to study the 40 patients. If you increase it more and more, it'll take longer. Also, we're selecting very precise pop. If we don't find a neuroimmune signal in 40, then it's unlikely to be a driver of the disease. Enough to find immune abnormalities that we're looking for. Then longitudinal study, with patients all over the country.

Koroshetz: At NIH, a culture to try to learn as much as you can from every single patient. There is undiagnosed disease clinic, they found causes for many of these patients. They're all different . With in-depth analysis, there may be very robust findings in one or a small group of its that will be very important> Definitely not epidemiological study. NIH is in deep study of small numbers of patients. This is just one step.

Joni Comstock, ME Advocacy. Emphasis on severely affected patients. So sick they can't care for themselves. We were dismayed that the design was well underway without input from clinicians, researchers, pts and advocates. Deficits showed us that … have not been clarified. We delivered a petition with 725 to stop the study and start from scratch with stakeholders input from the beginning. Because of misconceptions, we expect the NIH to engage experts from moment of conception. Input throughout process, including planning and implementation… through publication. Do you intend to respond directly? How do you plan to incorporate our concerns?

Koroshetz: Our intent is to get input from a wide variety of folks with expertise and experience. We have been doing that from the beginning. Through WG, through CFSAC. Multiple meetings with experts and advocacy groups. It has been a challenge for us, and we may not have reached out to everybody. It's been difficult to know who everyone is. That's the reason for the se calls. This is only the beginning. We will learn from patients. The history on medicine is, as you work with patients, they teach you. The major teachers really have to be the patients who have made the sacrifice to join the protocol and come in and work with the doctors. The protocol itself, Brian can correct me, it's always a work in progress. It gets pus up, approved, amendments, move forward. Protocol will have to be tested. Bringing in control persons first to test it.

Truth of the matter, the scientists at NIH have to e powered to work with their patients to get at the bottom of the biologic nature of ME/CFS. We can't take all patients. The very severe, homebound patients, tit wouldn't be wise to start there.

Walitt: PEM requires pushing patients a bit. Taking a homebound pop and stressing them more… Untoward consequences. It's definitely a very important pop to study, but for next phase.

K: Clinical Center does have capacity to bring people in in very poor condition. 24 hour nursing. So we could potentially get to it at some point. But unwise to start there.

I apologize for perception that we're not listening, because we are very much listening. We'll continue to listen and communicate.

Lily Chu: Co-vice president for IACFS/ME. Individual views. Two points: About study itself, about staff. When I was reviewing the literature for PEM, a lot looked only at fatigue. Website: diary of people recording symptoms for at least a week, but it says fatigue symptoms. PEM is more than fatigue. Problems thinking, sleeping, sore throats, muscle pain… I'd suggest more symptoms than fatigue, plus open-ended area for others.

Timing: Period of two days with blood tests, etc. Reading literature and analyzing data, I see that timing of PEM varies a lot. Testing for peak of PEM. Might be several days after.

Staffing: really glad you have experienced people including Dr. Lipkin. Concerned about Dr. Walitt and Dr. Gill. Gill, in 2011, he had a lot of slides about GET and CBT and not ordering certain tests like tilt table. There are some concerns there where a lot of the community had concerns about Dr. Gill. I even wrote him a letter before his talk. I hope his views have changed. If people interpreting the study have certain biases – we all do – those need to be recognized when they interpret.

Will staff be reading IOM, P2P…?

Walitt: What exactly PEM is has been poorly explored to date. We're going to try to induce it and describe it as it happens. This will be done qualitatively, speaking to patient – maybe even qualitative study of their words, plus bio before and during hospitalization. All sorts of different bio measurements to capture different aspects. Timing – true, taking into consideration.

Nath: Throughout the protocol, there will be seminars, etc. so that the team that is working on the protocol becomes well aware of existing and emerging literature. Speakers to have cutting edge knowledge.

The other thing, there's no element of subjective bias, because we're looking at immune abnormalities. My lab, center for immunology. Over 150 people involved.

Koroshetz: NIH is a very unusual place. The people here… have the strictest scientific lines. I rarely if ever have seen what you might call a personal bias affect a study. Everybody here is really devoted to getting to the bottom of the problem. I don't see any chance that this is going to be corrupted at all. There is very little incentive, and it's a

career breaker if that ever happens. I really do not feel that this is a concern that the community should worry about.

Nath: Protocol won't allow that.

Jennie Spotila: Thank you, esp to FC. Three questions:

1. K: Commitment that RFP with set aside funds is going to be a part of the strategy?
2. N or Wa: Why Lyme disease? There's a lot of overlap in chronic Lyme and ME/CFS. Reliability of testing. If looking for post-infectious group, maybe influenza
3. Whitt: How to systematically incorporate input into study and formulation of strategy? These are good tools, but shouldn't be only one.

1. Couldn't commit to that until we have a plan.
2. Nath: The reason for Lyme is two: 1. Patient pop of convenience, because Marquis? Specializes in it. So he has a well-characterized pop of pts. Knows whether they did or did not get better. Easy recruitment. This isn't chronic. These are individuals who had an infection and then fully recovered. Normally also develop infections and recover. Here…?? Already studied at great length, so use information that already exists.
   Walitt: Onset of Lyme has specific physical findings, like rash that helps us understand exactly when the infection started.
3. We're talking about having a period of time at each meeting, with input or potentially presentations from the community. Using our website to push info out and to get feedback. Also, always open to thoughts from community. Thinking about workshop ideas, with patient and clinical and research comm in organization. Welcoming patients to attend.
   Nath: Looked into legalities about pts advisory committees. Absolutely committed to … We want to come up with a system where we can get continual input as study moves forward. The protocol is a process of evolution. A lot of changes occur, so continual input is necessary. Happy to receive that and work with pt and advocacy groups.
   Koroshetz: Patients who enroll will have a lot of influence on how it moves forward.

Wilhemina Jenkins: Thank Dr. Walitt especially. I wonder if Dr. Walitt, to ally fears and concerns of community, can talk directly to that himself. PACE: We are very concerned about the problem of bias within a study. IT has been shown to affect the results. How his own view of the illness will be incorporated within the study or will not affect it.

Walitt: Me?CFS bio disorder. In every system, there have been abnormalities compared to healthy volunteers. If it's all in your head, that's only because your head is part of the

body. My role, I'm a facilitator of research, helping to coordinate scientists and medical professionals. To provide care and… for patients as they go through the trial. I don't have a bias.

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Rivka Solomon: I've been sick for 26 years, much homebound and bedridden. At least a million other patients in this country. We need equitable research funding, commensurate with degree of disability and pop numbers. We need probably something along the lines of $250 million a year to address this illness properly, and that doesn't count the 30 or so years we've missed.

Koroshetz: The amount of research funding does not match the burden of illness, with this and others. We have probably 300 different neuro diseases. The process by which NIH deals with how to allocate scarce resources is this tried and true process where investigators submit grants, get peer reviewed, scored, NIH takes on mostly highly meritorious, go down until we run out of money. Need in ME/CFS, funds to fertilize the research and get it going. To get a large number of highly motivated and well-trained investigators into the field. That's what we're planning to do in a fairly short time. To get it on par, we need those apps to come in and compete in a fair way with the other disorders. There's a short-term process that we need to stimulate with funds for ME/CFS, but our hope is that this will spread, that the community will start working with investigators at universities and clinics across the country. We have to utilize the NIH resources as best we can for the long term. We can't do it alone, we need to do it with the patients and advocacy groups, working hand-in-hand.