Wetenschap voor Patiënten
(Science to patients)

Webinar 50: Introduction / experience with ME

Prof. Leonard Jason. Broadcast September 2th 2014

My name is Lenny Jason and I am a professor of psychology at DePaul University in Chicago. I'm also the director of the Center for Community Research. I've been at DePaul University for the past 39 years.

How did you get involved in ME?

I initially got involved in ME-research in the early nineteen nineties. At that time people were talking about this disease as the 'yuppie flu'. What I found was that the CDC had done some prevalence research, called the four-city study. And they had estimated that fewer than 20,000 people had this illness. I was very skeptical of that research, and when I looked at their methodology as a research psychologist, it was significantly flawed. For example, they had referred people into their study who had been identified by doctors as having ME. And yet as we know lots of physicians don't even think this illness exists. So how can they refer such people into their catchment prevalence study? So basically looking at that research I was skeptical, realizing the CDC at that time was getting several thousand phone calls every month about severe fatigue and possibly ME. And I decided that I would try to work with some colleagues on a prevalence epidemiology study with adults.

What kind of research did you do regarding ME?

After looking at the research literature, we found that basically there were better ways of estimating prevalence than through ascertainment methods by physicians. So myself, Judy Richman and several other colleagues wrote a NIH grant. We were able to get funding to actually sample 26,000 people. And in that large sample, a community-based sample, we tried to find out how many people might have ME. What we found was that the rates were much higher than what the CDC had estimated. So by the mid-late 1990s we were able to make projections that approximately a million people had this illness. That was one of the first large studies our group did. But it took us ten years to work on that basic epidemiology, from writing grants, getting it funded, doing the research, to publishing it. So it is a long term commitment to do this type of research.

What are the most important discoveries you made?

I think one of the important things that we learned was that not less than a million people had this illness, rather than the 20,000 which were estimated. So it wasn't really a rare disorder, but the 'yuppie flu' was really a myth. The people we found having this illness did not tend to be yuppies. In fact we found people who had lower incomes had more likely to have this illness. So folks belonging to minorities, colored people, were more likely to have

this illness. Those were important findings, both the prevalence as well as the numbers. And that led us ultimately to make statements about this illness that we really needed to have more public resources devoted to it. In part because it wasn't a rare disorder, just affecting a bunch of middle-class individuals who were possibly lingering or doing something else. This was a serious illness, affecting a lot of people, many of them not having resources and suffering other disadvantages besides this illness.

What research are you into currently?

In terms of the work we're doing currently, certainly we thought that in terms of epidemiology it was important to find out the prevalence rates for adults. We're now in a way trying to do some community-based prevalence studies with young people, with pediatric ME. And that work we're going to be doing for the next five years. We're also going to be doing research on college students who have mononucleosis and will test them when they're healthy. Looking at what happens when they develop mono, and trying to follow them as to which ones recover and which ones don't. So with Ben Katz at Children's Hospital in Chicago I'll be doing this work on those two very large projects over the next five years.

Is your research psychological or also physiological?

The current research that we're doing implies that we want to get a look at all the different parameters. In terms of what are risk factors for those who end up getting this illness versus those who don't. And particularly looking at them before they get ill. That's a very important factor. Some research that we're just publishing for example looked at mononucleosis in youth. We basically found that there were no psychological factors predicting as to which ones would get more severe ME in the future. What we found was that the severity of the illness they got actually was the only thing that was a significant predictor. So that's an important factor suggesting that there might be more biological factors that involve both the initiation of this illness as well of its maintenance.

Wetenschap voor Patiënten
(Science to patients)

Webinar 51: Criteria and diagnosis, part 1

Prof. Leonard Jason. Broadcast September 2th 2014

What would you call this disease and why?

The British started calling this illness ME many years ago and there's been a regression back to CFS in 1988 through the CDC in the USA. I think there's been a movement to change that, and actually some people are calling it ME/CFS as a transition term. But I ultimately think this illness should be called ME, for Myalgic Encephalomyelitis. I think that's the legitimate name for this illness. In a sense it got hijacked thirty years ago and it needs to revert back to that original name.

Does the name CFS trivialize this illness and why?

The name CFS is a terrible term with which the CDC came up many years ago, in 1988. If you think about someone who is coughing and you would say he suffers from 'chronic cough syndrome', people would say 'who cares, everybody coughs. It just isn't a big thing'. However if we call it bronchitis or emphysema, people would say 'that really sounds as a significant issue'. So the name counts. And you can't use a name for an illness that trivializes a condition. Chronic Fatigue Syndrome is one of those names that ultimately has to change.

Our group actually did some research looking at attributions. We called it ME and we gave a case description. Then we gave it the name CFS and after that we attached the term Florence Nightingale Disease. We did the same case study and we found that names do make attributions and they do significantly make a difference in how one thinks about those cases. We did this research with medical interns as well as psychology undergraduates and we found, attributions undergo changes, based on the terms that are used to describe cases.

What is wrong with the CDC-criteria?

The CDC-criteria are often considered to be the same as the Fukuda 1994-criteria. They were assembled by consensus of a group of people. I think consensus based case definitions contain problems, specifically with four symptoms required out of eight possible ones. You can miss some of the cardinal symptoms of this illness. For example, three cardinal symptoms are post-exertional malaise, memory- and concentration problems and unrefreshing sleep. However if a person has four other symptoms and not these three cardinal symptoms, he can still get the diagnosis CFS. That's the major problem with an illness category when the cardinal features of the illness are not required to be diagnosed.

What criteria do you use in your current research?

Our group actually looks at several criteria and tries to have people fill out a questionnaire. And then we actually look at how a person meets the 1994 Fukuda-criteria, how they meet the new 2011 ICC-criteria for ME, as well as the Canadian ME/CFS criteria. So we try to compare and contrast those three. But I must say, there's limitations with all three. And consensus based efforts are probably not really the best way for us of characterizing this illness.

What's the difference between your primer of 2013 and the ICC/ICP of 2011-2012?

The IACFS/ME put out a primer that uses the Canadian consensus criteria of 2003. We found that there had been a good amount of research that at least had suggested that this particular case definition selected a smaller group of patients that had more functional impairment. So we decided to focus our primer around the case definition that had been around for ten years. It most importantly specified the core cardinal symptoms of post-exertional malaise, memory- and concentration problems as well as sleep difficulties. So that's why we decided to kind of write a primer and focus it around a case definition that we thought was an improvement of the Fukuda 1994-criteria. In fact there was another case definition, the ICC, that did come out in 2011 and 2012, but there hasn't been as much research done at that particular case definition. So we decided to use the one that had a little bit more been used by the research community.

Wetenschap voor Patiënten
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On Friday September 5th 2014 Prof. Leonard Jason answered questions in a chatwing-session. These are the Q&A of this session.

Q: What do you think of a new name: Viral Mitochondrial Syndrome
A: I think that name is interesting, and part of the problem is that there are now dozens of possible names. It might be good to do an international poll on this but my guess is that ME would be the clear winner, given the historical issues involved.

Q: But that only involves the brain, and perhaps a bit the spinal cord, and I think the same problem happens in all places
A: Good point.

Q: You propose to go back to the original name: ME. What is in this name that justifies the use of it?
A: There is now growing evidence for the inflammation and that is part of the name. Just as important as the name is how we define those that have this illness. A critical issue for us all.

Q: You did research after the prevalence of ME. Can you tell if there are large differences in percentage of numbers of patients between countries, continents, and different climates?
A: I like community based studies, and sorry to say there have only been a handful. One in Africa did come up with comparable rates as in the US; and that one was done in Nigeria.

Q: And is it more common in places where everyone gets vaccinated?
A: Wish I could answer that question, but as I mentioned there are just a few really good epidemiological studies that were based on community samples, so would have to be somewhat guarded about what we know regarding your question.

Q: In all the research you know of, has there ever been any connection seen between CFS and spine disease (degenerative disc disease, etc.). I contracted both about the same time as CFS. The spine issues may have started before but it's hard to recall symptoms since it's been 30 years when CFS started "suddenly" overnight.
A: The two illnesses could have been connected, and it is clear that folks with ME also can have other illnesses that might be associated or independent.

Q: Can you tell how many patients with severe mono get severe ME? And how likely is it to get ME after having been mono patient before?
A: A very good question, and we are now recruiting literally thousands of healthy participants to watch over time which ones develop mono and recover and which ones do not. I will hopefully better be able to answer that question in a few years.

Q: You mentioned your interest in ME started with a very shallow CDC-report on ME in the early 90s. Did someone request you to comment on that report?

A: Yes, many patients were rather upset about the Yuppie Flu stigma and all that went with it. We had dialogues with multiple parties in the Chicago area and around the US and even were provided some pilot funds by the large national US CFS organization. That helped us refine our methods so we could successfully compete for the NIH grant, that we eventually received.

Q: A doctor once told me that mono absolutely could not be the/a cause of ME because many people would be positive for mono when tested. So she thought there could be no relation. What can I tell this doctor?
A: We do know that many people do get mono and recover but we also know when asking patients about their illness, they mention they got mono first. What is needed is a prospective study and that is what we are now doing.

Q: Currently you are researching students with EBV. How solid are the evidences that EBV may cause an outbreak of ME? Or would you formulate this differently?
A: We are currently recruiting thousands of college students so that we can determine the link between EBV and ME.
Q: Just EBV or also other HHV's?
A: We are studying EBV

Q: Do you think you'll find EBV in the blood (of those you're following now who have mono and later on develop ME) or anywhere else eventually? And how?
A: The EBV study with students is funded by NIH, and we will have to see what the outcomes are, and that will take a few years.

Q: None of the sets of criteria for ME fit their purpose. What set of criteria would you suggest and why?
A: There are currently multiple case definitions (CFS, ME/CFS, ME) Each has different criteria. Over 20 have been developed but rarely guided scientific method. This is a major problem.

Q: According to you what criteria are the best to characterize ME? And do you make a difference between ME and CFS?
A: I do make a distinction between ME and CFS. The Fukuda criteria are general and do not require core symptoms, such as post-exertional malaise. ME would require specific symptoms, such as neurocognitive and post-exertional malaise.

Q: Would it help scientists, doctors and patients if there was a single set of criteria that was used by everybody?
A: What is needed are the following three things: provision of operationally explicit criteria (i.e., consensus within the scientific community on a particular case definition), operationalization of rules for determining when a symptom meets threshold for counting as a problem, and structured interview schedules to ensure the necessary information is elicited from an interview
Case definitions are a set of rules that allows investigators and clinicians to determine who has and who does not have an illness. It is critical for the scientific community to develop a consensus on this issue.

Q: In your first talk you talk about epidemiology. Do you suspect ME to be contagious or do you believe ME could be a hereditary illness?

A: Some people are genetically at risk and when they are exposed to particular viruses or environmental conditions, they are more likely to develop ME. We have done some work with families of patients with ME and we did find that the families had particular medical conditions.

Q: And that genetic predisposition isn't established yet, is it?
A: I would agree that more research is needed to determine the genetic predisposition to get ME. I think we'll get more good research in this area in the future.
Q: By the Lights, or also others?
A: The work by the Lights is great, and they are true pioneers in this field.

Q: Could you mention somebody, a scientist or group of scientists, that is in charge, or has so much authority, that he/she could "organize the reassembling of many scientists in order to find the consensus that is so much needed?" Who must stand up?
A: I think we need an international movement that brings together the patient community and government officials to bring about the change, and scientists need to provide the data that are convincing. I think we're at a point where this is possible.

Q: It is really encouraging to understand that you think we come to the point of creating an international movement. Thanks!
A: Real progress often takes time. Change can be gradual and uneven, and there will be setbacks along the way. Patience and a long-term commitment are critical aspects of social change movements.

Q: Many ME patients with depressive feelings are getting antidepressants by their GP but these are very addictive. Are there other treatments than AD to cope with a depression?
A: There are probably a number of things one might do to help with depression, but I would not want to get into them without knowing more specifics about the person and what they are dealing with.

Q: Do you think it would be helpful to look not just at the presence or absence of a symptom but also at the severity, frequency and variation in severity (at worse vs at best) as a measure for treatment?
A: We indeed believe that it is critical to use well-validated measures that include frequency and severity of symptoms because an individual might have a very severe symptom but it may occur so infrequently that it is not a major problem for that person. In addition, some problems occur often but are not that severe, so they also would not reach the criteria for being a problem.

Q: What do you think is the prevalence of ME? Literature says 0,1 percent, but 1 percent is more likely. The lighter, reversible cases included, one might think of 10 percent?
A: My best estimate is that about 4-5% of the population has six or more months of fatigue. About half of these individuals have clear medical reasons for their fatigue such as cancer. If you believe the Reeves 2007 data, then a little bit more than 2% of the population has CFS. If one uses more specific criteria, such as the Canadian criteria, then far fewer would have ME.

Q: Might there be similarities in ME and fatigue problems which occur with cancer?
A: One of my colleagues in the nursing department at DePaul is now studying fatigue following treatment for cancer. We need to know more about this and I'm hoping he will get funded to continue his research in this area, and then maybe we will better understand how

ME and cancer fatigue differ. We are now hoping to study how ME differs from a number of other illnesses, such as Lupus and MS.

Q: Is there any other medical condition that you know of where people experience PEM? I was just wondering if it is unique to ME and in itself can be used as a variable that discriminates between different conditions? Or would you include severity/frequency of unrefreshing sleep and cognitive issues in that mix to discriminate between conditions?
A: There are other conditions that could elicit PEM, and that is why we ask patients about 54 symptoms, and we hope that this larger group of symptoms will help us find the clusters of symptoms that differentiate different medical conditions from ME.

Q: Do your colleagues take ME seriously?
A: Yes, my colleagues do take ME seriously, but I recognize that many people still are very skeptical, but those people tend not to interact with me, as they know my opinions on this issue.

Q: Can you give a link where I can find the DePaul Questionnaire? I really can't find it.
A: The link to our questionnaire: https://redcap.is.depaul.edu/surveys/?s=tRxytSPVVw

Wetenschap voor Patiënten
(Science to patients)

Webinar 52: Criteria and diagnosis, part 2

Prof. Leonard Jason. Broadcast September 9th 2014

What do you think to be the cause of ME?

There are certainly lots of opinions about the cause of ME. There are individuals who certainly have a viral kind of beginning, sometimes mono(nucleosis). There are other people that have some type of accident that causes their onset into this illness. There are other people who have some type of environmental toxin or exposure to molds.

So there actually are quite a few different types of things that seem to precipitate this illness. It's very possible that these individuals might have some genetic predisposition to this particular ME illness. Just as other types of chronic illnesses have been found to have some genetic predisposition. But I would say that at least at this point, it sounds like there are a number of triggers that could be the precipitants of individuals manifesting ME.

What is the reason for the stigma that is associated with ME?

There's a terrible stigma associated with people who have ME. A lot of people wonder why is this the case? Our group at DePaul University has actually put together a scale that measures stigma. So that we can get some clues as to what's going on. We certainly have a society that values energy and stamina and endurance more than anything else. It's probably more important than even money, if you can believe it. And if you don't have those qualities of energy, you are a person who's probably more discriminated than any racial or any other type of group in our country. Because energy is what makes the American dream. People who have fatigue are seen as being deficient somehow.

And the reason is that everybody feels fatigue at some point. Sometimes it is through a marathon race, but sometimes it's through having several jobs. Ordinary fatigue that most people experience is something that probably goes away when they go on a vacation. Or when they're not stressed because of so many responsibilities. So most people think of fatigue in completely different ways than patients who have ME. So when a patient with ME kind of says that he doesn't have energy or endurance or stamina, others react "I have all that things I have to do, and I keep doing it. Why can't you?". And worse than that: 'You don't look like you're sick'.

The combination of those different characterizations leads to incredible societal negative attributions towards patients, which makes them almost like the 21st century lepers. Like how it might have been like two hundred years for people with that other disease.

Do you diagnose ME by Exclusions? What do you include?

I think that it's important to diagnose ME not just by exclusions but also by inclusions. We need to understand a person has core symptoms of this illness, like for example post exertional malaise. That has to be there for this illness to exist. And yet some of the questionnaires say you need to have 24-hour difficulties after you've exercised with some symptoms including fatigue. Those questionnaires are problematic and I'll tell you why.

A lot of people don't push themselves because they're so sick. So they don't have to experience post exertional malaise, because they've learned in some ways to really hold off. And they form a little bit of an energy bubble, as their 'envelope' - about which we'll talk another time. So it's possible that some individuals would experience post exertional malaise if they were pushed. If they had to do exercise, if they had to do the daily tasks that most people do. But since they're not doing that, some of them don't even experience it. So if you ask the question if they do experience it, they'll say no. But the reality is they would have it, if they would have to do daily activities.

So all I'm saying is that we have to be so careful to phrase the questions in the right way to tackle these types of complex symptoms. If you put a person on an exercise bicycle and really do a challenge, then you'll find post exertional malaise. Particularly not after one day but after two days. Because after one day they're able to push themselves enough to look good and some of these oxygen exchanges will be ok. But when you do the testing it's the second day that you see the post exertional malaise. So again both with exercise, with challenges as well as with self-report questionnaires, one has to be so careful about how one asks the questions. So that we identify people who really have the core symptoms.

Clearly you don't want to bring people into your studies, or into your practice who have another illness. So if they have MS, if they have cancer fatigue, if they have other types of fatiguing illnesses that are due to medications, you want to exclude them. If there is a psychiatric reason for their fatigue, like major depressive disorder with melancholic features, you want to exclude them as well.

You want to find people with ME, solely ME and not something else. To get a diagnosis of ME, I think you have to have three cardinal symptoms. Post exertional malaise, neurocognitive problems like memory and concentration difficulties, and unrefreshing sleep. Those symptoms I think need to be there. Not that there aren't other symptoms that could be there as well. Like some of the immune, neuroendocrine and autonomic. But I would say the three that I first mentioned are critical.

What is the DePaul Symptom Questionnaire? And what is its focus?

Over the last fifteen years our group at DePaul University has been working on developing ways of using self-report questionnaires to assess patients' symptoms. Our most recent effort is called DePaul Symptom Questionnaire. We've actually put that on an electronic system called 'red camp', that is available now to anybody in the world and which they can download. This is a 54 item questionnaire that according to us measures some of the current symptoms of many patients that have these types of illnesses.

Each symptom is rated for frequency and severity on a five-point scale. We've been doing some basic research on this questionnaire, making sure it has some good reliability and also validity. We feel pretty comfortable that this scale could be used by people both in clinics as

well as in research settings. And we have some investigators from different parts of the world that are currently using our scale.

Can the DePaul Symptom Questionnaire be used by anyone?

The DePaul symptom questionnaire could really be used by anybody. It could be given to patients at a clinic, it could be given to researchers, to their subjects, the participants in studies, where patients could fill it out. The thing that we like about the questionnaire is that we have built an algorithm which forms a pattern of looking at the responses. After a person actually fills in the particular questionnaire we can score which case definitions they meet. That gives us the ability to use the questionnaire to focus on people in terms of how many symptoms they might have for the critical case definitions.

Wetenschap voor Patiënten
(Science to patients)

Webinar 53: ME versus psychiatric disorders

Prof. Leonard Jason. Broadcast September 23th 2014

Confusion about ME and (major) depression, what is the difference?

Our group has been spending quite a few years trying to look at the differences between major depressive disorder and ME. To put it real briefly, if you have a person with a major depressive disorder and would say to him: "if you were well tomorrow, what would you do?", that person would say: "I don't know".

If you ask the same question to a person who suffers from ME, he will start compiling a list of things he would want to do but hasn't been able to because he has been sick. So there's an issue of real self-reproach. People with ME don't have that kind of negative personal feelings about themselves. People with major depressive disorder do have that type of negative feelings about themselves. There's self-reproach, expectations for the future and also exercise. People with major depressive disorder often feel better with exercising. We know that with people with ME exercise often induces post exertional malaise. So there are clear differences between these two illnesses and they have to be differentiated.

Are there biological differences between a major depression and ME?

There are a number of studies that have actually also found physical differences, biological differences between people with major depressive disorders and ME. For example cortisol levels generally tend to be lower in people with ME and higher with people with major depressive disorder. Asking the right questions, even with self-report questionnaires one of our doctoral students was able to discriminate 100 percent between the two groups. If you do it right. So that's why questionnaire development is so important. Because if you ask the right questions, you can really discriminate people from these different illnesses, which is critically important for the research that we and others do.

The best research looks at things from a multi-dimensional perspective using multiple disciplines. For example, you want self-report questionnaires to be brief, so that you can find out what the basic symptoms are the person has. But then you want to follow it up with a physical examination, so that you can rule out other illnesses. If a person has lupus or MS you want to rule them out. But you also want to use challenges. For example, putting a person on an exercise challenge with the max or sub-max test. That would show some of the genetic markers that might differentiate patients from people who aren't patients. What we really want is the best sources of data, so that we can really do comprehensive evaluations of self-report and medical domains. So that we can better characterize this illness. And if you miss one of these domains, you miss an important area of functioning in helping to understand these people.

Are there other psychic disorders which can be confused with ME?

Besides major depressive disorder with which ME can be confused, and I think often is confused, there are other types of psychiatric illnesses that can be confused with ME. For example somatization disorder is something that has been confused with people who have ME. There are also anxiety disorders that have been confused with people with ME. What I'm suggesting is that if you go to a physician to get a medical examination, you really need to have structured psychiatric interviews to make sure you have particular disorders or not. Because we want to differentiate those people. Physicians unfortunately have not been trained to do a psychiatric evaluation. So often they don't know if a person has a major depressive disorder. Or a somatization disorder. So you really want to have a comprehensive psychiatric as well as a comprehensive medical examination before you determine whether a person has ME. Because you want to exclude other causes of the person's illness.

Which role does depression play in ME and how is it to be treated?

Every chronic illness has higher rates of patients who have a depression. So there's no reason that people with ME won't have some depression as well. Not all patients with ME, but some patients will. Just think about it. If you have an illness that a lot of people don't understand, a lot of people don't believe in, it's very debilitating and you are often questioned about it. Those are all reasons to feel discouraged. So you might suffer discouragement, almost hopelessness at times. That does occur. And I think we have to understand that that's the same thing that occurs with any type of chronic illness. The depression that occurs with any chronic illness starts with the people around that individual legitimizing what they're experiencing. The support systems around a person have to be examined. And if you have individuals - whether they are parents who don't believe their child is ill, or workers who don't believe that individuals are ill - and if there is discouragement and skepticism, that's going to be a deadly type of influence. That has to be removed if you're going to begin to treat an individual's sense of hopelessness or despair for being victimized with an illness that's so poorly understood by society.

When a person has ME I think it's important to treat all the symptoms that that person has. For example, if they're dealing with pain some types of medications might be used. If a person's dealing with any other type of symptoms, all types of medications should be considered. What a patient needs to have is the best possible team that works on the different issues. It might be a nutritionist, it might be someone who deals with physical therapy, it might be on different issues that the person needs help with. And we should empower patients to put together a treatment team to meet their needs, which are often divers. That's the key to success, using both pharmacological and even non-pharmacological interventions to come up with a treatment program that meets each individual's needs.

Resemblances autistic disturbances, MS, Parkinson & Alzheimer with ME

We don't have a lot of research yet, in terms of comparing ME with lots of other conditions. I think we need that type of research, because that will help us understand some of the similarities and dissimilarities. In terms of MS for example, one of my colleagues, Matthew Sorenson, and I are just finishing a paper that's looking at brain proteins in MS. And we have found for example that individuals with ME tend to have the same level of low brain proteins, called BDNF, as people with MS. That's one of the primary biological markers of MS. And what does BDNF brain protein make? The myelin sheath, that allows the electrical impulses to go to the brain. So again it's possible that MS and ME have some similarities that we really don't know that much about yet. But I think in the future we will do more comparative biological research to help us understand this.

Wetenschap voor Patiënten
(Science to patients)

On Friday September 26th 2014 Prof. Leonard Jason answered questions in a chatwing-session. These are the Q&A of this session.

Q: In webinar 53 you say that it has been proved that patients with ME have lower levels of cortisol and patients with a depression have higher levels of cortisol. Can you explain this difference?
A: Low levels of cortisol result in an overactive immune response, so this is very compatible with what we see in patient data. To be more specific, it is really a reduction increase of cortisol when one is waking up to about a half hour later that the results seem to apply to.

Q: Are you any further into discovering any medication apart from painkillers or antidepressants that will work for ME?
A: Lily Chu published some results of the influence of different medications last year as part of the FDA and you might want to check out her findings. You can find them here: http://www.cfstreatmentguide.com/blog/patient-survey-results-for-fda-drug-development-meeting-for-me-and-cfs-99-of-patients-not-getting-better

Q: Has your group discovered more biological differences between ME and depression?
A: Our group has found self-report differences between patients with major depressive disorder and ME. For example, patients with ME have PEM that is severe as well as other core symptoms. Patients with major depressive disorder have self-reproach, and this is generally not found in ME. What is found in ME is sometimes demoralization that can occur when so many doubt the legitimacy of their illness.

Q: Why do people with a depression have high levels of cortisol?
A: There are a number of theories about low cortisol in patients with ME, and it probably has something to do with the HPA axis which is probably deregulated. My guess is that this is centrally mediated and we are most interested in better understanding why this might occur.

Q: You say that if one asks the right questions, it is possible to distinguish ME from depression. What questions have to be asked? By whom? And does your group develop such a questionnaire? To me it seems a very important attribution for examination.
A: Yes, it is important to develop reliable and valid questionnaires that allow us to ask questions that can discriminate between those with ME and other illnesses. Our group has developed an instrument that is called the DePaul Symptom Questionnaire and we have made it available to investigators around the world.
It has good psychometric properties and we now have a dataset of about 1,000 people who have filled it out, and this is the type of sample that is needed to do the types of statistical analyses that are needed. As for questions, we now have a detailed questionnaire that assesses 54 symptoms. For each one, we try to assess the frequency and severity, as we feel both are important to assess.

Q: I totally recognize the great desire to be able to do all things I would like to do. It is often difficult to deal with this lack of satisfaction. It is frustrating (and of course I try to learn and deal with it). Has this to be distinguished from depression and lack of self-esteem?
A: Yes, frustration and disappointment for not being able to do all things because of energy limitations can cause a person to feel a bit demoralized, but this is different from a person with depression who is feeling like they do not want to do anything, even when they have energy.

Q: It is really good, and hopegiving, to understand that your group already is that far in developing the questionnaire. Hopefully this will be used in the Netherlands at short notice.
A: Yes, our questionnaire is now being used from Japan to Norway, and even Iranians are using it. Several large projects have incorporated it as well, so if we can encourage investigators to use similar, reliable instruments, we do much to reduce some of the confusion in the field.

Q: Can you give advice for ME sufferers who are pregnant? What is to be expected? And are there any precautions that can be taken?
A: There are reports that some people who are pregnant have reduction in symptoms. This might be due to the immune system calming down so that it does not attack the fetus. This is very preliminary, and it is important for researchers to better understand this.

Q: How can differences between ME and somatization disorder become clear? Same for anxiety disorders?
A: There are many psychiatric disorders that can cause fatigue. The most prevalent is substance use disorders, but other important ones are depression and anxiety. Just as we expect to have a good medical examination to determine whether a person has ME, we need to also expect that a good psychiatric screen occurs for patients so that we can be sure that they have ME and not some psychiatric disorder.

Q: You are calling PEM one of the three main symptoms of ME. What do you exactly mean with Malaise, the M of PEM?
A: Malaise is not a great word, because it can be misinterpreted. What occurs after exercise is that a person experiences severe symptoms in multiple domains that include physical, cognitive, and other symptoms, but PEM has been used for so long that it is now very prevalent in the literature. The ME-ICC uses PENE instead (post exertional neuroimmune exhaustion).

Q: I suffer from neurocognitive damage because of ME/cfs. I notice that it is becoming more and more difficult to keep a conversation going. I cannot think of what groceries are needed, etc. Question: What should I do to keep this from becoming worse? Question: What can I do to improve?
A: Sorry to hear about the intensification of symptoms. One long-term follow-up study suggested that cognitive symptoms can become worse over time. The IACFS/ME primer has some useful material that you might want to take a look at. You can find it here: http://www.iacfsme.org/LinkClick.aspx?fileticket=Pil0KeDIc2M%3d&tabid=509

Q: You say that if a patient with ME becomes depressed as well, this is often due to the reactions of people that surround this person. This makes very clear the general need for information and education. Does your group develop a program for this issue?
A: We have worked with a buddy program for many years to try to support patients that have ME. There is a need for more information and education on how patients can deal with

individuals in their social environments who sometimes do not understand their illness.

Q: My condition is continually getting worse. How can I improve this, while staying within my limits?
A: Our group has worked with the energy envelope, which is a concept that was developed by a patient many years ago. We believe that this is similar to pacing with some differences. Clearly, our approach involves helping people monitor and stay within their available energy resources. Often, in my experience, patients are engaging in more activities than they have available energy. This is understandable because they have so much less available energy with the onset of ME. Learning to stay within the energy envelope has been shown to have positive results in a number of our studies.

Q: Where can I found these studies, Leonard Jason? Are there links on the web?
A: Link to a energy envelope study:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3596172/

Q: I read that patients with ME often do not respond well to medication against depression. Is this correct? And if this is the case, why is this? What alternative medication or treatment they can use?
A: As a psychologist, I do not prescribe medications, but from the research I have looked at, it seems that the evidence is unclear for antidepressants. Some people say it helps, and others that it does not.

Q: Can ME/cfs be a negative influence to arthritis? Can it speed up the process?
A: A person with ME can certainly have other illnesses, such as arthritis. Just as a person with heart disease might have arthritis or a person with cancer might have arthritis, so it is possible that a person with ME might also have arthritis or other illnesses. The tragic situation for so many patients with ME is that when healthcare workers learn that a patient has ME, they often stop thinking about all the other potential illnesses that the person might have and that might need to be attended to. This is again part of the stigma that is attached to people with ME.
Q: But does arthritis worsen due to ME/cfs?
A: ME certainly can result in multiple dysfunctions in the body. It would make sense that this could lead to other illnesses. One of my graduate students is now doing her dissertation to try to find out what happens when people die after having ME. Clearly, many people have a number of illnesses that occur after having ME, including cancer and heart disease.
Q: Is that the main reason why ME patients have a lower life expectancy?
A: In one study we published, we found that about one third of people who had died after having ME died of heart disease, and another third died of cancer. Their deaths were much younger than would have been expected from national death rates with these illnesses. We now want to look more closely at this.

Q: Your current research is on risk factors. What risk factors do you expect to play a part in getting ME?
A: One risk factor might be exposure to molds. Another risk factor might be getting mono. These are just a few of the important risk factors that we need more research on.

Q: Is there anywhere to donate your body to science for the study of ME?
A: I hope that there will be places that allow patients to donate their bodies to and this will be critical research for the future.

Wetenschap voor Patiënten
(Science to patients)

Webinar 54: Treating and managing ME

Prof. Leonard Jason. Broadcast October 7th 2014

What is the role of a psychologist in the treatment of ME?

Psychologists and mental health professionals have an important role to play in the treatment of any patient with chronic illnesses, ME included. What we need to do as mental health professionals is first validate the patient's experience. We have to listen and become an ally of that individual. And we should really try to understand what they are going through, to build an empathetic bond.

That's so important because particularly patients with ME have often been so victimized by the medical community and others, so that particular relationship is critical to let that person know we believe in him. And that we care about him. I think without that basic trust you make very little difference, and you as a mental health professional will actually be harmful to the patient, without building that trustful relationship.

How can it be avoided that the psychological approach gets the upper hand?

Patients with ME need to have the best team possible, involving multi-disciplines, to have a good chance of getting quality care. You can't just send someone with ME to a psychiatrist or a psychologist. The reason being they probably need many other services to help them deal with the many different symptoms of this illness. Just think about it: if a person with cancer came to a medical doctor and the doctor would say: "Go and see a psychiatrist or psychologist, that's all you need.", that patient would be terribly upset. And that's exactly what's happening with patients with ME throughout the world.

What are useful treatments for ME in your opinion?

There are many different types of treatment for ME. And I'm going to talk a little bit more about what I think of a kind of lifestyle area. The reason is that I'm a psychologist. But in the medical area there are also many good treatments for symptoms like pain and sleep difficulties.

But in terms of lifestyle issues, patients often feel like they have the energy of maybe 10 or 20 percent they had formerly in their lives. So their battery, their storage of that kind of electrical life force has been reduced. And yet due to their obligations they often have to do twice as much work as they have the energy for. And that's a problem.

So in terms of lifestyle management, how do we get patients so far that they're not doing too much? So that they won't exhaust themselves and possibly enter into post exertional

malaise. So I think learning them how to stay within their energy envelope, as we call it, is critical to allow that battery not to get further depressed, depreciated . That's I think what we need to do. A lot of patients are somewhat like a yo-yo. So what happens is they are really sick, they don't do much, they're really careful, and then they feel a little bit better and they do too much. And then they crash. That's a yo-yo effect. Everything possible to let that not occur is really critical in the lifestyle management of patients with ME.

What are the advantages and disadvantages of CBT and GET?

Cognitive behavior therapy is something used with all types of medical illnesses with some very positive results. Why is it so controversial with patients with ME? Because often that's all which is being provided. For example, if a person with epilepsy who needs medications, is said 'we'll just use cognitive behavior therapy', that patient would absolutely be furious. But that's what's happening with ME patients.

They're having needs that are far beyond just psychiatric issues. They have somatic problems. They've got physical dysfunctions. They've got irregularities that are biological. They need the best of medical care and treatment. And yet they're being siphoned to a very narrow type of perspective. That's why they're upset. Because they're not being given what's appropriate medical care. They're being given inappropriate medical care, that isn't meeting their needs.

What is pacing, what is enveloping, and what are the differences?

A number of people have been talking about pacing. Some developments Ellen Goudsmit in Great Britain has written about. We in the United States have used a term called the energy envelope. I think there's a lot more similarities than differences between these approaches. What they both are suggesting is that we need to help patients learn to manage their available energy in a very sensitized tailored contextualized way. For example someone has a battery that's loaded for twenty or thirty percent while he once had a battery that was a hundred percent. Now it's just a fraction of that. How do you do all the tests of life on such a small amount of available energy?

So what we try to say is pacing or staying with the energy envelope, is trying to stay within that available energy, to not exceed it, to not push oneself. Because if one does, ultimately I think one experiences more crashes, more post exertional malaise, which I think ultimately causes more oxidative stress to the brain. And I think it will have some very negative consequences for the patient. So pacing and an energy envelope are the appropriate types of lifestyle changes that can cause improvements. Not cures, but improvements to many patients.

Wetenschap voor Patiënten
(Science to patients)

Webinar 55: Symptoms of ME and treatments

Prof. Leonard Jason. Broadcast October 21th 2014

What is the role of the nervous system in ME?

I think that there is evidence that the nervous system is aberrant in patients with this illness. Certainly some of the work of Alan Light and Kathy Light at the University of Utah suggested that when one puts individuals on some type of exercise with submaximal challenge, one does see some of these types of genetic markers. I do think that there are nervous system domains that patients can have significant problems in. And I think that they are directly implicated in this particular illness.

What we see with most patients is a sympathetic dominance over the parasympathetic system in a sense that their body is 'tuned up'. We often see the symptom called 'being wired'. That's a very common description of patients. They are exhausted but they are still wired.

So in a sense their system is upregulated and I think everything we can do to help patients to downregulate that system is healthy. It's very interesting that lots of the pharmacological things people at times try, including Klonopin and similar things seem to begin to help to downregulate the system. I do think there's an upregulated system in many patients.

What is the role of the blood circulation in ME?

Many patients with ME have a supply of blood that is lower than in healthy people. And when they challenge their body they suffer so-called orthostatic stress when they stand up. They often don't have enough blood flowing to their brain. Individuals sometimes feel they are fainting and they don't feel well. That's because they're not getting enough blood to flow from their bodies up to their brain when they stand up. There seem to be some major circulatory issues among patients. Orthostatic intolerance is one manifestation of that.

How do you measure post-exertional malaise?

Post-exertional malaise can be measured by asking the right questions on self-reported questionnaires as well as by exercise challenges, whether by letting people exercise on bicycles for ten of eleven minutes, or even up to twenty minutes in a submaximal challenge. I think it's important to look at both what people say as well as what people do in a laboratory setting, to bring the best of both together to understand this complex symptom called post-exertional malaise.

What is the role of infections in ME?

Many patients begin to get symptoms after some viral infection. So it does seem certain, as in some samples up to seventy percent of people report having had some type of viral infection. Ultimately the best way we are going to understand the role of these types of infections is longitudinal prospective studies.

An example is that in Chicago we're currently involved with Ben Katz, who's at Childrens Northwestern. Over time we're going to follow thousands of college students who are healthy, to see which ones develop mono and which ones recover and don't recover. That's the best way for us to be able to identify whether a particular virus or a other types of things might be both involved in etiology as well as in maintenance of an illness.

Are there any markers for ME?

About markers for ME… I think that we could say we are beginning to identify some of them and in the future I think there will be many others. There certainly are cortisol difficulties. It seems that people who have a lesser increase in cortisol in the morning might be a very good marker. Natural killer cell activity has been talked about in a number of review articles. There might also be subgroups of individuals who have other types of markers. In the future we will hopefully be able to discover many more of these and will be able to get them across laboratories.

But again, if you're going to find markers, it's only going to be if you have the same types of patients in different settings. That's why the case definition is so important. We have to identify the same people in different places if we are ever going to find consistent biological markers. That's so important because if you don't find consistent biological markers, it's very easy for people to assume it's a psychogenic, psychiatric illness as opposed to a biological one.

Wetenschap voor Patiënten
(Science to patients)

Webinar 56: Population and social impact

Prof. Leonard Jason. Broadcast November 4th 2014

Is the risk of ME higher due to gender, race, genetics or occupation?

Some people have asked whether ME is different in different parts of the world. Certainly there was an initial myth that ME was more prevalent among yuppies, among people who are white and had higher income. That myth is not true. So we actually know that ME tends to be more common among individuals who have a lower income. That is a very important thing. In the United States we have also found that ME tends to occur more often in minorities, of people of color. So yes we've also done a community based study in Nigeria, and we've actually found rates of ME to be higher than in the United States.

So we think ME occurs in many different places around the world. In terms of which particular groups have higher rates than others we're not sure, but certainly in the United States we've found some differences. And certainly people of lower socioeconomic status are more likely to have this illness.

Whether ME is race related is something that we really don't understand well. Some of the symptoms of ME, for example orthostatic intolerance, do seem to be different in African-Americans versus Caucasians. In terms of us being able to definitively understand some of these factors is unclear. We did find for example Latinos in the United States had the highest rates of ME than any other group. And particularly among women Latinos versus men Latinos. That was kind of interesting. We've also found that Latinos who had been more acculturated, who had been more into American society, had differential rates than those who had not been acculturate.

We do think that genetics probably make certain people predisposed toward having a lot of chronic illnesses, and ME is probably a good example of that. We still have a lot more research to be done on that, but I think eventually we will be able to conclude that. That's my guess. Whether ME is somehow higher in particular groups versus other groups, I think that that's something future research will be able to understand better. I think presently we still are trying to understand some of the risk factors for this illness. The best research that's going to help us understand some of these genetic markers is to actually to look at genetics in healthy people and look over time, to see which ones develop ME and which ones don't. And then look at some other risk factors, both environmental as well as biological. That's really the way we're going to disentangle the role of the genes versus the environment, and see the roles of this different things.

What did you find in long-term studies about recovery rates?

There have only been a few long-term studies involving individuals with ME. It does seem like individuals who have longer illness tend to have more cognitive difficulties and more symptoms. Actually we are working on a paper now, trying to look at people who have had this illness for a longer period of time. There really aren't a lot of studies that have been published in this area. But it does look like length does increase some severity issues.

What functional impairments do you see in people with ME? How severe can they be?

Patients with ME have as severe functional impairments as any of the major illnesses, including cancer. And on and on in terms of different very significant chronic illnesses. So these are very sick patients. Patients who really need the best medical care, and patients who are often provided the worst. We see some of the worst functional areas that people have is the physical capacity to do things. Endurance, stamina, that's probably the area where people have the greatest limitations. Sometimes cognitive confusion, where a person basically can't remember things or can't remember why they're doing something. And that often makes it very difficult for a person to be in a work setting. There's the physical impairment of being able to do things consistently over time and then the next day continue to do that. You see lots of impairments particularly with this post exertional type of testing. With cognitive challenges too it seems to be really very difficult to think and remember things and focus on things. There are neurocognitive and post exertional functional impairments that we see in patients.

What is the cost to the individual and society?

Economic analyses have been sometimes done and in America our group has estimated that the cost might be up to twenty billion dollars a year, for the types of problems that patients have with ME. But the real cost is to the patients who are in a situation that they have one of the most severe illnesses that we know of, and they're actually provided the least comprehensive treatment. So here are individuals who have one of the most difficult problems we can think of and they're questioned about the validity whether they really have an illness. Can you think of anything worse in terms of a personal cost than being so sick and having people questioning whether you really are ill or not.

Funding by the government has been at very low levels. Really needed are places you can go to, to get diagnosed and treated. And in the United States these generally don't exist. If you have cancer, if you have MS you can go to specialized clinics, and you get the best diagnosis and the best treatment. But for example, I live in Chicago and there really aren't physicians who are specialists who treat patients with ME. And that's a problem. So we need to have the type of healthcare that involves services which are available to patients. And right now they don't have that services nor do they have the research dollar investment to provide the types of data that we need to find out which pharmacological treatments are most effective with patients. So in both the research arena and in the service delivery arena we're provided with very low amounts of resources, given the severity of this problem that affects our populations.

What can be done to improve the deplorably situation that patients with ME are faced with?

In terms of what can be done for patients with ME, I actually spent the last year writing a book called 'principles of social change' that Oxford University Press has published. And in that book I really try to indicate what other social change movements have done to bring about change. Including the civil rights movement and other types of groups, like the women's movement. And ultimately it's endurance, it's staying committed to something over long periods of time, it's basically having community coalitions that work and try to really deal with the power abuses that occurred. And it's really looking at some other structural issues that need to be faced. We need to organize. We need to be more effective. We need to basically be able to change the status quo, because the status quo is not working for patients with ME. It's only by us collectively being involved in action that the situation really is going to change. As it has changed for many other illness groups, particularly the people with HIV/AIDS, who really have demonstrated that it is possible to bring about a sea of change in treating and appreciating people who have that illness.

What kind of social support may help?

We need social support for patients that involves the family, parents who protect their kids, guardians, spouses, parents who are able to stand up for the rights of individuals who are sick. And also people in educational settings, as well as social service settings, medical settings and within work settings who provide for the special needs of patients. And we all have to recognize that first of all this is a legitimate illness and we have to be willing to accept some of the limitations that patients have. We also have to validate their experience and work with them in terms of what they need. Individualized approaches are critical. So really the entire social network has to be mobilized. That might involve the person's brother or sister, a person's father or mother, a person's grandparents, the people who work at their church, the people who are their medical associates. Everybody has to come together in a team that makes their life more livable, and actually has the respect and services that they need to make a quality of life. To bring about a change is going to involve not just the patients who have ME, because many of them are sick. It's also going to get involved the people who are well. the people who care, the people who are spouses. It's going to involve a social change movement of people saying we're not going to take it anymore, we're going to make a change. And it's going to be thousands and thousands of people working together to say 'this cannot exist the way things are'. And that's going to be the start of the social change movement. That's not going to be in one country, it's going to be in multiple countries.

Wetenschap voor Patiënten

(Science to patients)

Webinar 57: Future/ teaching about ME

Prof. Leonard Jason. Broadcast November 18th 2014

You published about teaching ME/cfs in US medical schools. What were your findings?

We did an initial study involving medical textbooks. And we found that in the medical textbooks which are used to teach future physicians, ME and CFS were rarely mentioned. And even worse, when they were mentioned they often didn't contain actual information about it. So the basic teaching materials that are being used in our medical colleges are very negligent and often inaccurate. That has to be corrected.

Recently we also did a survey of what does occur in medical colleges in the United States. What we found was again that these topics are underrepresented and that has to change. There has to be more focus on teaching of, application of and research on ME in medical schools. Until that changes, we're not going to have people finishing the medical college who are adequate and providing the coverage that patients need. So this has to be one of the high priority issues that we work on.

You also did this kind of research a few years ago. Have there been changes since then?

The research that we are currently doing, implies our constant learning from the past. We're trying to integrate the type work for example with computers and people who understand artificial intelligence. So that we can use not just the consensus way of making a case definition, but we can use the best sciences in things like data mining and artificial intelligence, to come up with case definitions that might be more specific and accurate and sensitive. That's some of the work we're currently doing and we're also again trying to look at different ways of using multivaried and more complex modelling, to have empiric ways of making decisions in understanding how systems operate. As opposed to try and have just the consensus way of making case definitions or scientific pronouncements.

We think that our research has made a difference. In the nineteen nineties ME was really considered to be a relatively rare disorder, affecting the yuppies and called the yuppie flu at the time our data came out in the late nineteen nineties and early two thousands. The prevalence estimates that are now being used by the federal government indicate that they estimate it closer to ours, a million people having this illness. So we've been able to battle the misperception myth that this is a rare yuppie flu illness. We now think it's a very significant illness that is not a yuppie flu, which affects many more people than we previously thought.

In addition our research has challenged the term cfs and we have championed trying to get alternative terms. There's a number of organisations that are now using both ME/cfs and ME and I think our research has helped to contribute to that shift. Finally there's our case definition research of comparing and contrasting different case definitions and using empirical methods rather than consensus methods to think about what are the core features and how to measure those core features. We think we'll continue to make important contributions to the debate on the case definitions that is currently going on.

Does DePaul University/Rosalind Franklin University teach medical students about ME?

The DePaul University doesn't have a medical school. There's been some talk about maybe some type of alliance with Rosalind Franklin but it is in the very early stages. We have made some efforts to begin to collaborate with people at Rosalind Franklin, but again those are early efforts at this point.

We do think that multidisciplinary efforts are important. So we have an epigeneticus in Iowa that we're working with, we have an immunologist within the nursing department at DePaul that we're working with, we have a computer science expert in the computer science department that we're working with and we have people in different universities that we collaborate with. It's critical for us to think about multidisciplinary research beyond the particular laboratories of our particular settings. And that is going to be the key to research, whether we have a particular medical school or not.

What research are you working on at this moment?

We have several lines of research that we are focussing on. One is the use of our DePaul symptom questionnaire to gather large databases and we think with these large databases of patients versus controls we'll be able to better understand which symptoms differentiate these groups. We're using very sophisticated, even artificial intelligence techniques that are empirically based rather than consensus based in trying to help us inform the decisions regarding the case definition. In addition we're not just interested in self report issues with our questionnaire. We're also looking at data that involve more physiological, biological measures.

For example, we are now looking at college students and trying to find over time which ones develop mono and which ones don't and which ones recover and which ones don't. And we have blood samples of all those particular college students so that we'll be able to look at what they were like when they were healthy and what happened after they got sick. That type of longitudinal prospective research is critically important.

I might add that we also have an epidemiology study going on with paediatric ME and that's going to be an important kind of lesson for us to also look at the biological as well as the other domains that help us understand what are the risk factors and how many individuals within their youth have this illness. That's something that we'll be working on as well in the future.

What other research do you think will be hopeful for the near future?

I think the most important research that will occur in the future is going to involve multidisciplinary efforts that will bring in people from different disciplines, including computer scientists who have mathematical gifts to help us understand decision trees, so that we can figure out what symptoms might be the best predictors of illness. We might be able to bring in also people from the best of the sciences, the best virologists, epidemiologists, people who understand the autonomic nervous system.

So what we really are looking for is how do we get together people with genetic backgrounds and environmental backgrounds and public health backgrounds to participate in these types of rich multidisciplinary efforts. To understand what we think to be the greatest challenge to medicine today. Because medicine knows how to fix a broken bone, medicine knows how to deal with people who have the flu, medicine knows how to deal with many types of illnesses. What's really a puzzle for people are these complex illnesses and as we get insights into the mechanisms that are involved in complex illnesses like ME, we are going to have a new birth of understanding of what persons have to face and how we can better understand the human condition.

That type of research really needs to have adequate funding. We will one day be able to reinterpret different types of illnesses based on what we learned from people with ME.
At the present time there are many economic challenges to countries. I think these are difficult times for both basic researchers as well as patients. But I have faith and I have hope that over time we will recognise that the greatest medical insights will occur while involving patients with the most complex system issues such as ME. And as we get more scientists and researchers to understand this basic fact, my belief is that we will begin to bring together the best scientists in the world to study what I think is one of the most neglected but most important medical illnesses facing our world.