

## CHRONIC FATIGUE SYNDROME - CURRENT STATUS

IRVING E. SALIT, MD, FRCP(C)

*Head, Division of Infectious Diseases  
The Toronto Hospital*

*Head, Division of Infectious Diseases  
Mount Sinai Hospital*

*Associate Professor, Medicine and Microbiology  
University of Toronto*

DR. DANIEL FLEMING: The next speaker will be Irving Salit. Irving is an expert on chronic fatigue syndrome and will bring us up to date on this very important matter. He's gone on record as saying the diagnosis of this disorder requires good science, and he certainly is a scientist, as you can see from his curriculum vitae. The media is confusing as to whether this is an immune disorder or an infectious disorder or a psychiatric disorder, and perhaps I will know better after this presentation. Irving has recommended some very innovative approaches to this, and I look forward to hearing about these. Irving, we welcome you to the platform.

DR. SALIT: Thank you very much. I see that you have an International Congress of Life Assurance Medicine, ICLAM. I would propose that if you change the title to International Congress of Life Assurance and Insurance Medicine, then it would be ICLAIM, and that might be appropriate.

Now you've heard about the, with all due respect, very simple topic of myocardial infarction, where you have objective measurements. You're about to hear about another topic where life is much more difficult, because we really don't have any true objective measurements of what's going on. This topic is chronic fatigue syndrome. This illness goes by a variety of different monikers, and these names have changed over the years. Basically, I think that this is the same illness that has been described for many years and had a variety of different names. Several hundred years ago, it was called febricula, then it was called neurasthenia, then chronic brucellosis, hypoglycemia, myalgic encephalomyelitis, etc. The point is that I think we're talking about the same illness that has been described for centuries.

There has been an attempt to put some methodology and some science into this by establishing some objective criteria for the illness. This has been done by the Centers for Disease Control. Just because you make some objective criteria, it doesn't really mean that they're right. But at least it was a start. I don't think these criteria are correct, in that they cannot separate out

chronic fatigue syndrome from other conditions, which is a bit of a problem. But at least for scientific studies, we are aware that we are talking about subjects who at least meet these criteria, and for insurance purposes there is some value in this as well.

So there are some major criteria and some minor criteria. The major criteria for this condition are that these subjects have severe fatigue which is disabling and has been present for at least six months, and you have to exclude a bunch of other causes of chronic fatigue, as well. Then there are eleven minor criteria, and subjects have to have at least eight of these. Most of them have at least eleven and usually have a few write-in symptoms, as well. They are: acute onset, very frequent mild fevers, painful lymphadenopathy, muscle weakness, muscle aching, joint aching, headaches, a variety of neuro-psychological complaints, and sleep disturbances. And one of the important features of chronic fatigue syndrome is post-exertion fatigue. These subjects will one day do something that triggers the fatigue; they'll go to the grocery store to buy some milk, and then they're wiped out for a couple of days thereafter.

This illness has been popularized in the lay press and there is really a lot of nonsense that has been written about it. This is in part due to the fact that there are many lobby groups and support groups who are quite influential. Some of these lobby groups are behind an article in *Newsweek*, which was almost complete rubbish. There was an article in *Time* magazine called "The Malaise of the Eighties." Well, is this really the malaise of the 80's? Yes, it is. It's been the malaise of the 1780's and the 1880's. George Miller Beard, a neurologist, described neurasthenia, which when you read the description carefully in Osler's old textbook, is exactly the same condition as chronic fatigue syndrome (CFS). In Victorian times this was very popular, known as "the vapors" and a variety of other things as well. CFS is nothing new.

What are the clinical features of chronic fatigue syndrome? Two-thirds of the subjects are female; almost all of the subjects are between the ages of 20 and 45, with an average age of 35. There is a disproportionate num-

ber of people who are single, either never married or previously married.

They tend to come from higher socio-economic and employment ranks. They are a fairly well-educated group. At least 10%, and in some studies up to 20%, are paramedical personnel: nurses, social workers, etc.

In my own study, published in 1985, we looked at these subjects. The time lost from work or school averaged about 40% of time during the past two years.

The subjects will tell you that this illness started suddenly on one particular day while they were maybe sitting at their desk, and they have never felt right since. Is that how it actually occurred? Sometimes it did occur that way; it often has acute onset. However, when you look back at the previous six or twelve months, you see that there were some difficulties going on in the previous year which have led up to the current event. In some studies we did, subjects with CFS compared to normal controls, almost all the CFS subjects had one or more stress factors in the previous year, but only 5-10% of controls had that. Some of these are not too dramatic, moving house, serious problems with relationship, major illness in the family, major change in employment, and serious financial problems. Sometimes the change in employment is positive. I've had a number of subjects who were striving for a particular promotion for years, they finally get it, and within three months they have chronic fatigue syndrome.

What is the triggering event? What starts this whole process? Well, there are many defined ideologic factors, most of them are infections. Some of them were noted many years ago; some of them have been noted recently. It's true that many of these infecting agents can be a trigger which will start chronic fatigue syndrome down its relentless course. However, I believe that, in part, because I'm an infections disease specialist. When you talk to rheumatologists or other people, they'll tell you that other things trigger CFS in the same way, and I've seen some of these subjects, as well. For example, I have some medical legal cases in which motor vehicle accidents will trigger CFS, and the illness is identical. I cannot tell the difference. Surgery, allergic reactions, other major events will also be triggers. So this can be post-viral, post-infectious, or post-traumatic.

What are the ongoing symptoms? I give the subjects a check-list of about 82 symptoms, and quite a few of them have every one of those symptoms, again with a few write-in candidates. What are the common symptoms, though? All of these subjects have exhaustion, and they'll tell you that the word exhaustion is totally

inappropriate for what they have. They are so wiped out that initially, after they first become afflicted, some of these subjects can't move; they can't get out of bed; if they have to go to the bathroom, they may be able to make it by crawling on the floor. They can't comb their hair, brush their teeth, or do any of those things. At the beginning, they have hypersomnia; they're sleeping all the time. The initial two or three months, they may be sleeping twenty hours a day. They have malaise; they just feel crummy. Quite frequent is the post-exertional worsening, general weakness, headaches. They feel they have fevers, but in fact when you measure the temperature, there is no true fever noted in most of these people; some of them do have a little bit higher temperature than normal people, but it rarely indicates that they actually have an infection.

There is an inability to concentrate, so-called cognitive impairment; they have trouble thinking, concentrating, remembering. This can be disastrous for people who have to make public presentations. Some of these people have very high positions where they have to give talks, make presentations, and it's very embarrassing for them. They lose their concentration right in the middle, and they don't know what's happening. So this is the cognitive impairment: poor concentration, poor short-term memory, can't think of the right word, and they mix up words.

Sometimes because of those events, even though they might seem sort of minor, these events when they mix up words are very traumatic, and it keeps them out of the work place.

Now we did some studies to examine in these subjects some of their psychiatric problems. Together with a psychiatrist and some psychologists, what we did was we administered some standard psychiatric tests to a group of subjects who had CFS. This was, in fact, the first study to do this. What we found was that a lot of these people met the criteria for major depression. A lot of people weren't too happy with these results, and I got a lot of irate phone calls. The CFS support groups immediately started to hate me, and they haven't stopped since. Well, were we wrong? I don't think so. After our study in 1978, there have been many other studies showing the prevalence of current major depression during the episode of chronic fatigue syndrome is high. Forty to 75% of these subjects have major depression at some point during their illness. Now the more contentious point they hated me for was that we found that by history about half of these subjects, in fact, had major depression even before the onset of the chronic fatigue syndrome. Now, many of the subjects will accept that they are depressed during chronic fatigue syndrome,

because they say, "If you were so fatigued, you would be depressed, too." But in fact, we found pre-morbid evidence for psychiatric illness. Many of the subjects will tell me that they have had major depression, but this is not major depression at all; this is something totally different. In fact, that probably is the case. But there seems to be some sort of link, which we don't really understand. Just as an aside, I'm also a head of HIV clinic, the largest HIV clinic in Toronto. I see a lot of people who have very short life expectancy, and I do not see the same sort of neuro-psychiatric abnormalities that we see in these subjects. So there is something inherent in the illness, which leads us to believe that there is a neuro-psychologic component.

Just to give you an example of one particular study where they looked at over 400 patients just with chronic fatigue, all who came in with severe chronic fatigue. What do these people have? Again, 74% have a psychiatric diagnosis. A very small number have an actual medical diagnosis that you can make. Some have combinations thereof. Only a small number have chronic fatigue syndrome or idiopathic chronic fatigue where you can't find any specific association or cause. That's really the type of illness that we're talking about here. But again, the overlap is really quite difficult, and it's hard to separate them out.

All these subjects have sleep disorders. This is really very frequent. Initially, they're sleeping all the time, and this is for the initial two or three months. After that, it becomes very frustrating, because then they can't get to sleep, and once they get to sleep, they reawaken. We've published some studies on this; the sleep disorder is identical to that seen in fibrositis or fibromyalgia. That is, their brain waves during sleep are a little bit too fast. And this is different from what is seen in major depression.

Now, with respect to diagnostic tests, we've done a number of things to look for abnormalities which might be a little bit more specifically seen in CFS, and we published this study on a kind of a brain scan, known as a spec brain scan. It's basically a nuclear brain scan, but it's also combined with a CT scan. What we found in this spec scan is that about half of these subjects had some abnormalities in the blood flow to their brain. Especially in certain areas in the basal ganglia and some other areas, there is a decreased blood flow; it's more of a generalized decreased blood flow, not really seen in too many other conditions other than major depression.

In addition, their immune system is a little bit abnormal, so some people consider this an immune deficiency. The immune abnormalities are subtle. They're not present

in everybody, and they're not of a very serious nature. I consider them as markers to help us make the diagnosis. I won't go into the details, but basically there are some changes in the lymphocytes, in an enzyme we measure, and some of these other things like IGG, and they have some antibodies to DNA, but it's not the same as the kind of antibodies as seen in lupus. So these are subtle and inconsistent changes.

Well, does this illness exist? That's the real question. There is no doubt that these people have a litany of very similar complaints. They all tell the same story. Most of them have not talked to each other before they come into my office; some of them have. Some have read about chronic fatigue syndrome, but some of them have not. They're not making this up. This is something that is occurring. They have ill health, and it has a standard clinical presentation. Now they may not need your help, but they need help from somebody. They have a problem; there's no question about it. And we just can't presume that they don't exist. Whether this is an infection, a psychiatric problem, or some other organic illness, it doesn't matter, as far as I'm concerned. They have an illness. Many of them are disabled.

So, what do we do? We explain what's happening. A lot of them get some nonsensical explanations in the community. They're told all sorts of crazy things, and that makes them worse, and it often increases their "invalidism." Sometimes it's hard to reverse that. A lot of them get hooked up with naturopaths, and they get on weirdo therapies, and it's hard to get rid of that, as well. But sometimes it's useful, especially if they have fibrositis or fibromyalgia, but it may not matter; low-dose antidepressant therapy at bedtime is often useful, and then we try to increase it. Now this may be a sneaky way of getting them to take antidepressants, by telling them that it's for fibromyalgia, but be that as it may, it often has some benefit, if they can tolerate it. They often don't tolerate it.

I explain a lot of things to them, including the natural course of the illness, which is basically, they're very incapacitated for a couple of months, but everybody improves with this condition, especially if they're doing the right sort of things. By two years, there's about 50% improvement. But there are a lot of people who are quite stagnant, and don't improve beyond that at all. So it is quite variable. But it does depend on other things going in their lives, and I tell them that. They want to know why they're not getting better. They're looking for the magic position to make them get better, but sometimes they just are not facing what the real problem is, and they refuse to do so. Many people just have to make some lifestyle changes. So you see all sorts of situations

where people may be working in one job 40-50 hours a week, and in addition, they have another job at night and on weekends, and they keep doing this for a year or two years, and then they crash. So sometimes when they make some of these changes in their lives, and some of them are pretty obvious to me, and I can give you some pretty glaring anecdotes, and the family physicians are sometimes a little bit too close to the whole situation to actually detect what's going on.

Yes, they're really susceptible to a bunch of health fraud quackery. And there is plenty of quackery out there, and there are a number of physicians in the community who tell these people what they want to hear. They may tell them that they have parasite overgrowth, they have candida or yeast overgrowth, they give them all sorts of nonsensical, expensive treatments, which may be dangerous, and the patients like it for a while. It doesn't help anybody. The common drug which is the darling of the chronic fatigue group now is ephamol. It's about \$30-40 a month, and it's useless. I haven't seen anybody get better on this, but they keep trying it.

Most people improve; they rarely get any worse, and the ultimate outcome is there are no serious effects at all. This does not shorten anybody's life span, suicide is a very rare event. People talk about cancers, lymphomas; that's nonsense. There are studies showing that doesn't occur.

Some people who have CFS have gotten pregnant and gotten better during the pregnancy, a few got worse; for most of them it doesn't make much of a difference.

This is not a contagious condition, although secondary cases can occur in the household, but I think that's due to other reasons.

So, how is this illness caused? Is this an organic problem, is it a psychological problem, or is it both? I think it's both. Basically, there is a life history which all patients bring to their illness. There is some triggering event, psychosocial stresses, which result in chronic fatigue syndrome. So it's a mixture of both. What do they end up with? They end up with sleep disorder, immunologic problems, problems with the brain scan, and some of them have depressive symptoms.

DR. FLEMING: Excellent presentation. We now will entertain some questions.

DR. HOWARD MINUCK, Mercantile & General: I've got two questions to ask you specifically about family history of symptoms such as fibromyalgia, depression, chronic fatigue. Perhaps you can shed a little light on

perhaps genetic susceptibility in a spectrum of diseases that might be related.

DR. SALIT: I don't think there's any specific data on the points about family history of depression. It would be useful to look at, actually, or fibromyalgia. I don't have any of that information. I do have information, though, on other cases within the household of similar conditions. There is no question there is a higher frequency within the household. But with respect to family members, parents, uncles, aunts, etc., I don't have that information.

DR. MINUCK: Do you have any comment about the epidemics that we're sometimes seeing in some of the school boards where you might have 15 or 20 people effected in certain boards.

DR. SALIT: There have been about 40 epidemics of illnesses which resemble this. They used to be called neuromyasthenia or neurasthenia. It's hard to know exactly what these were. Most of these epidemics are dying out; they're quite uncommon these days. They used to occur in hospital settings, again with the same sort of demographic picture here, mainly in females, nursing students, and paramedical personnel. It didn't effect the patients very much. It usually was in conjunction with other epidemics going on in the community. For instance, there might be a polio epidemic. Then in the hospital you have this other illness which was not polio at all. This leads us to believe that some of these are, in fact, epidemic hysteria which has swept through the hospital. In fact, there is usually a basis for it. There may be a flu-like illness, as there always is amongst 5% of the population, and if they start to think they're getting polio, well they get very upset, and then it spreads to other people. So this is one possibility. There are other theories, but none of them are proven. The latest outbreak was at Lake Tahoe, and in that episode it's a little bit hard to know if it was truly an objective illness, although they did find some objective abnormalities, but this is always found in the population.

UNIDENTIFIED: I have a question to epidemiology with regards to different cultures, and have any studies been done with regards to immigrant populations within North America to see if there are any differences in those populations.

DR. SALIT: This has not been fully looked at. There are some studies about prevalence of this in the general population, and it's about 25:100,000 in some of the studies. There is a population-based study going on in England to look at chronic fatigue in the general population, and we may get a better idea about what you're

leading to, but in fact, we've seen this in all kinds of people. It may be a little less frequent in the immigrant population. And maybe the implication to your question is, people who absolutely have to work to keep their families going, do they get CFS? Well maybe they do a little bit less often than some other people who have the luxury of being able not to work. We don't really

know that. I will also answer that by making reference to Arthur Kleiman, a medical anthropologist, who has written a very incisive article in the SIBA symposium on chronic fatigue syndrome which was published last year. Arthur Kleiman has an article in there about different cultures and chronic fatigue.