Science to patients (Wetenschap voor Patiënten)
Chat: **Q&A**

During a chatwing-session on June 19, 2015 Prof. Alan Light answered the following questions.

Q: What could be the cause of disorientation? I.e. mean moments of poor recognizing of (familiar) surroundings and not knowing the way home.
And what is your advice for patients which suffer from this dysfunction?
A: The ability to focus your attention is affected by many factors. Adequate ability to quickly increase your blood flow to the appropriate region is one of them. This can be very much affected by mental fatigue.

Q: And what is your advice for patients which suffer from this dysfunction?
A: To include coffee or other caffeinated beverages, movement (unfortunately ME patients should not overdo this). Another possibility for at least some ME patients might be treatment with pregabalin (Lyrica). There are also some drugs that enhance cognition that I can't remember the name of that should be very effective like Provigil.

Q: Is it advisable to measure the blood flow with ME-patients?
A: It would be interesting to know the brain blood flow, but it is not an easy thing to measure, and can be inferred simply by the symptoms, so probably it wouldn't be commonly measured.

Q: If the blood flow to the brain is decreased with 28% when sitting or standing, what is happening? Can it cause permanent damage? Or do you have to lay down the rest of your live?
A: We call that orthostatic intolerance. It is very common in ME. What is happening is, that your cardiovascular system is not getting the proper signals to increase your blood pressure enough to properly supply your brain.
The temporary effect should not cause damage it you do not become unconscious. Going upright very slowly will help. There are some drugs that could help. Ask your physician about midodrine, and propranolol.

Q: Can the brains be damaged because of a low blood flow in the long term?
A: It is possible to cause long term damage to the brain with a low blood flow. The exact conditions that will do this I do not know.

Q: Probably the blood flow of ME/cfs patients is abnormally low. Can you explain why this occurs?
A: The blood flow is low because there is improper signaling from the systems that should detect fatigue. Either they are always on, or maybe not responsive enough.

Q: What is an auto-antibody and what does it do exactly?
A: An autoantibody is a protein that your immune cells make that attacks your own tissues.

Q: Why is it no longer possible to multitask with ME. Before I got sick I could do six things at the same time. Now only one.
A: The mental fatigue is stopping you from being able to do multiple tasks. Your brain is not properly increasing blood flow in the appropriate areas, and your overall brain blood flow may be low.

Q: And why should they (auto-antibodies) attack one's own tissues? How come?
A: The auto-antibodies were likely made to try and attack a pathogen like a bacteria or virus. However, they were similar to your own tissues, which normally does not happen. But if you have a specific mutation, it is possible.

Q: Can you tell more about this specific mutation?
A: The mutation we don't know for sure, but some data suggests that it is found in about 1/3rd of the population, and it is in a major histocompatibility gene that normally should protect your tissues by preventing the development of the auto-antibody, or telling the immune cells not to attack the beta 2 adrenergic receptor containing cells.

Q: And that mutation you get from birth or is it developped later in life?
A: You likely have the mutation from birth, but it could also be a somatic mutation that is tissue specific.

Q: Why would immune cells produce auto-antibodies against specific parts of the fatigue system? Why is this system out of order?
A: It turns out that one of the autoantibodies made has a protein sequence that specifically attacks the B2 adrenergic receptor, which is a key part of the fatigue system. This sequence is also nearly the same as the protein coat of the StrepA bacteria. This might be an explanation. We are currently trying to verify this.

Q: In webinar 64 you tell that you found a group of about 20% of ME/cfs patients with extreme high levels of inflammation genes. Could this possibly mark a subgroup of ME/cfs patients with certain characteristics?
A: Yes

Q: Could those high levels of inflammation genes point to patients in early stage of the illness, as M. Hornig recently proved "new" patients to have more problems with an overactive immune system?
A: Yes, that is a likely explanation.

Q: Can the subgroup of patients with extreme high levels of inflammation genes be related to the remarks of M. Hornig about patients in the first three years of being ill with an overactive immune system?
A: Yes, this is likely.

Q: If patients have very low levels of inflammation genes does that mean they are in a further stage of the illness?
A: Sorry, I cannot easily answer this. We have found at least 3 types of ME that seem to have very different characteristics. There are likely more.

Q: In webinar 64 you said that in some subgroups of about 20% of the patients you found a pretty extreme alteration in the immune-response after exercise, with some of them a clear

increase as well as decrease in inflammatory genes. Were those patients which obviously had a more severe form of ME?
A: Not so much more severe overall, but sicker at the time we measured them for sure.

Q: This might be an odd question, however. I suppose viruses have genes as well. Can the effect of viruses on the human body be seen through the character of their genes?
A: Yes, that is exactly what Lipkin and others are doing.

Q: This statement was made. Could you comment? “I find the assumption on heredity rather premature; to come to definite conclusions other relevant influential factors like environment and behavioral factors need to be ruled out first. It would be interesting if the Utah Database would be extended with that kind of information, this could lead to true epigenetic research, which is the future of medicine.”
A: We have shown with the data base, that at least some ME is hereditary. This may be only a small percentage of the patients, like with Alzheimer, but it does give us clues as to the mechanisms that could be causes. We would very much like to extend these studies. I work with an epigeneticist, and we would like to pursue this in the near future.

Q: The modification of genes in order to get them back to a normal situation sounds rather futuristic. Are you already experimenting with this?
A: Crispr caspase has made gene therapy possible in animal models. It is not ready for human use yet, but the possibility has created some ethical dilemmas already. You can find this online with some human embryo studies.

Q: Can epigenetics become a means to upgrade the immune system in such a way that in the long term it can expel pathogens by itself?
A: Epigenetics alone won't do this, but gene therapy directed at the epigenetic targets might. This is still 4-20 years off, however. We first need to find the targets.

Q: How many people are getting better from cfs?
A: Unfortunately not many, and it is hard to tell because relapses can occur many years later. I believe the last estimate I saw was less than 20%.

Q: Wasn't there a study that most people get better within 1,5 years, and that after that the odds are much smaller?
A: That is true. It is of course a semantic problem since ME requires a time of 3-6 months

Q: Women’s immune-system is more active than men’s. De Meirleir said that up till the age of about 11 the prevalence in boys and girls is equal. Is that in line with your findings or didn’t you research children with ME? And Dr. Bateman either? That might lead to the conclusion that the hormonal system might play a role in the severity of the symptoms and maybe the character of the symptoms as well. Could you think up why?
A: We haven't looked under age 18. Dr.Bateman would probably agree with Dr. Meirleir

Q: Is it possible that there is something like a "point of no return"? I mean if patients are so severely ill that it is impossible to recover?
A: I don't believe that is ever impossible to recover if we truly know the cause.

Q: EBV resides in B cells, are those the same B cells that rituximab attacks?
A: Yes