Alpha 1 Antitrypsin MZ Information & Research

News & Research Update

Apr 27, 2024

Website status and research update

Dear Subscribers,

Because the number of subscribers is increasing rapidly, we decided to create an overview/summary of the subjects handled in this newsletter over the past few months. This may be good anyway because it also provides you with a good understanding of the connections between the different subjects.

But first, something about Chemotherapy.

I hope nobody of us has to go through this, but we should be aware that Chemotherapy is extremely hard on any healthy liver and, of course, even more so on an Alpha1MZ liver, which is already under continuous Hepatocyte ER stress.

This means that you should inform your MD of the state of your PiMZ liver and have them consider this during any treatment.

This paper, "Effects of systemic chemotherapy on the Liver," tells it all
https://pubmed.ncbi.nlm.nih.gov/20526005/

“The administration of chemotherapy challenges the tight regulation and balance of all body processes. As most drugs tend to be lipophilic, they are readily taken up by the liver. Under chemotherapy, up to **85% of patients develop liver steatosis**. Steatohepatitis is the more serious event, especially if accompanied by an increase in bilirubin levels.”

I think this says it all and does not need further clarification.

Overview/summary of subjects handled in the past newsletters

1. There are about 35 million persons with Alpha1 genotype MZ, and the “Z” mutation originated in northern Europe and was spread by the Vikings.

2. Alpha 1 Antitrypsin Deficiency is caused by a mutation in the SERPINA1 gene. There are over 200 variants. The normal variant was called M, and the first deficient variant was called Z (Gly342Lys). The Z is abnormally formed and retained in the Hepatocyte ER, causing Hepatocyte ER stress and a gain of toxic function in the liver, reducing liver capacity.

3. The Alpha1 MZ liver is affected by the “Recruitment Secretory Block” effect because Alpha1 MZs carry both the “M” (the normal) and the “Z” (the abnormal). Under stimulation, when more hepatocytes are recruited to produce the AAT protein, more Z protein is produced, which then causes blockage and more hepatocyte stress.

This means that in a PiMZ liver, all zones in a liver lobule are affected, not only the Periportal zone.

4. Research papers show that 25% of the Alpha1 MZ have continuous background inflammation.

5. Alpha1 MZs have a high prevalence of biliary tract issues, which may be caused by the Recruitment Secretory Block, where we see a proven impact on the Pericentral zone of the liver and, as such, on the Bile Acid generation. This is confirmed by biobank data.

6. The already reduced capacity of the PiMZ liver is further reduced by aging, which means that we see most issues starting at the age of ~40 unless there was a liver “event.” These liver events can be medications that are hard on the liver, or even pregnancy, which can be a high load for the liver as well. This is why we see 1 out of 15 Alpha1 MZs with Intrahepatic Cholestasis and Preeclampsia

7. Because of the impaired Bile Acid availability, there is a high prevalence of biliary tract issues, which leads to absorption issues in the small intestines (ileum). This causes Vitamin and Mineral deficiencies and SIBO.

8. Within the group of Alpha1 MZ’s, we see a very high prevalence of Vitamin B12 deficiencies, which will also explain the high prevalence of Neurological issues, which can be very serious and typically start around the age of 40 when the aging of the liver starts playing a role. (Please note that vitamin B12 helps produce a substance called myelin that shields the nerves)

9. Alpha1 MZs also experience an impaired immune system, and we have seen in clinical cases that Augmentation therapy helps to restore the immune response.

10. The good news is that the big pharma is developing medications that are in different phases of clinical trials. These are RNA type of medication to eliminate the “Z”, which will resolve our liver problems, or even convert the “Z” into a “M” which should resolve also the Alpha1 deficiency (Immune, and anti-inflammatory issues).