

"Providing an opportunity for multiple myeloma patients and their loved ones to come together to exchange information for mutual support, comfort, and friendship"

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July 2023 Myeloma Newsletter

Upcoming Meeting Speakers

Dr Natalie Callander will be our featured speaker for September. Hope to get an update on the Trillium Research work.

MMRF nurse navigator will present at the March 2024 meeting. More info to follow.

Dr Timothy Schmidt, UW Carbone Cancer Center will be our featured speaker at the July 18th meeting. He will join us at 4:30pm. Hoping to get him to talk about his clinical trials.

I now have these educational tool kits.

The Multiple Myeloma Research Foundation has a new educational tool kit! I have requested 20 copies and will let you know when they are here. This will be helpful for newly diagnosed group members. It is titled "Your Myeloma Journey Guide".

Included in the tool kit:

- Multiple Myeloma Treatment Overview
- Multiple Myeloma Disease Overview
- •Caregiver Guide
- Precision Medicine Booklet

- Myeloma Booklet
- Autologous Stem Cell Transplantation Booklet
- Immunotherapy Booklet
- •Patient Resource Guide

This is interesting research and worth sharing in this newsletter.

REVERSING T-CELL EXHAUSTION WITH ANTIOXIDANTS

(Clinical trial information- Lymphoma)

Can exhausted T-cells get re-activated by antioxidants? Can antioxidants be used to improve CAR T-cell therapy outcomes?

Memorial Sloan Kettering Cancer Center (MSKCC) doctors in New York City, Drs. <u>Santosha Vardhana</u>, MD, PhD, and <u>Craig B. Thompson</u>, MD found <u>evidence</u> that balancing the body by reducing excess oxidative stress with antioxidants reverses T-cell exhaustion to help the T-cells work effectively at multiplying and destroying cancer cells. Their work is testing this concept in lymphoma.

T-cells are the patient's own cancer-killing immune system cells. CAR T-cell therapy helps enhance the patient's T-cells to more effectively kill cancer cells.

One of the reasons CAR T-cell therapy has had limitations in effectiveness is that the T-cells get exhausted, which causes them to stop multiplying and destroying cancer cells.

A strong correlation has been found between T-cell exhaustion and high <u>oxidative stress</u>. Reducing excess oxidative stress with antioxidants allows the T-cell's mitochondria not to be impaired by fatigue and be able to do their job of converting energy stores into energy, keeping the T-cell working.

Drs. Vardhana and Thompson's findings are now being further reviewed in MSK's lymphoma clinical trial using Yescarta combined with antioxidant N-AC (NCT05081479) led by Dr. Gunjan L. Shah, MD.

The success of the CAR T-cell exhaustion reversal is hoped to be replicated for other diseases like myeloma.

Clinical trials like these will be the best way to identify new strategies that can extend the promise of CAR T therapy.

Further research will help define the appropriate dose of antioxidants to administer alongside CAR T-cell therapy for patients, allowing the cancer-killing immune system cells to work well while maintaining an appropriate oxidant/antioxidant balance

Just a quick note on the next article - Interesting dynamics to how the body reacts to Dex. A bit technical but hang in there. It all makes sense in the end.

The Best Time to Take Dexamethasone and Why

From the HealthTree Foundation

Understanding the Physiology of Dexamethasone

Cortisol is an adrenocorticoid produced each day by the adrenal gland. It is essential to life, is a major factor in controlling our reaction to stress, and significantly affects our moods, energy, digestion,

immune system, and emotions.

The adrenal gland, like many others in the body, is controlled by the pituitary "master gland" which constantly monitors body hormone levels, regulates glandular activity, and controls adrenal hormone production. Other endocrine organs such as the thyroid are also regulated by the pituitary gland.

Our "master gland" produces TSH (thyroid stimulating hormone) to stimulate the thyroid gland to greater function when it senses there isn't enough circulating thyroid hormone passing by.

In a similar manner, the pituitary monitors adrenal glands (located above the kidneys). Cortisol serum levels are diurnal, meaning they naturally fluctuate by the time of the day. Endocrinologists take two serum cortisol levels when checking adrenal gland function, one at 8:00 AM and one at 4:00 PM.

Typically, the morning level is much higher as the adrenal gland responds to ACTH, a regulatory hormone that stimulates the adrenal gland to produce cortisol.

Dexamethasone Timing in Multiple Myeloma Patients

Why does all this matter? It matters because dexamethasone is chemically similar to cortisol.

If we take a high dose of dexamethasone at bedtime, there is still a significant blood level of dex in the morning. When the pituitary discovers there is plenty of steroid in the blood passing by it decreases ACTH production. This tells the adrenal gland to not produce any cortisol on the morning following an evening dex binge.

To further help understanding consider what happens when cortisone (dex) is taken four days in a row, the way it often used to be prescribed for myeloma. For four mornings, the adrenal glands are told by the pituitary to stand down. They do nothing. Now assume the myeloma patient adjusts their dexamethasone schedule and abruptly stops daily cortisone.

The pituitary tells the adrenal glands to get to work, but they have become lazy, unresponsive, and do nothing. The pituitary begins screaming by producing high levels of adrenal-stimulating hormones (ACTH), but the adrenal glands respond with "yeah, whatever". In time, they slowly respond and again produce daily cortisol, the way they are supposed to do every morning.

In the meantime, however, the patient has no physiologic cortisol and, therefore no stimulus to increase metabolic activity when the rest of the body is begging for help.

Another great example of this is surgery. Anesthesiologists always ask their patients if they have been taking any steroids. If they have, the doctor expects that there may be a blood pressure problem or a wake-up problem because that patient's adrenal glands have become lazy and unresponsive. The worst of these possibilities leads to "Adrenal Crisis", which can translate into a true medical emergency.

The Bottom Line: When to Take Your Dexamethasone?

The bottom line, therefore, is that it is much more physiologic to take all corticosteroids (dex, prednisone, prednisolone, Solu-Medrol, etc.) in the morning when the body expects there to be an elevated steroid level.

You will get much less adrenal gland suppression if you take steroids (dexamethasone) in the morning than if you take them at night.

It is much wiser to take all steroids in the morning hours, not at night. You will probably do OK if you take them at night, but your pituitary and adrenal glands will follow a regular physiologic routine if

you give that steroid dose in the morning.

While dexamethasone might bring about a cleaner house or a shopping spree, it can also bring about severe mood swings and unwanted rapid weight gain. If you are experiencing side effects from the dexamethasone that significantly lower your quality of life (or the quality of life of those around you), please talk to your doctor about a dose reduction. No physician or treating medical team wants you or your family to be so negatively affected by treatment.

As always, speak to your care provider on how to take your meds. Another resource is your pharmacist.

Our virtual meetings are on the Zoom platform.

Our meeting for July 18, 2023 will be from 3:30pm to 5:30pm. Dr Timothy Schmidt will be our featured speaker. He will join us at 4:30pm.

Join Zoom Meeting

https://myeloma-org.zoom.us/j/84457667535?pwd=V0lJTDNQU2FOZ1hMUkFaRmJBc0Qzdz09

Meeting ID: 844 5766 7535

Passcode: 678275 One tap mobile

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+1 669 900 9128 US (San Jose)

Meeting ID: 844 5766 7535

Passcode: 678275

Find your local number: https://myeloma-org.zoom.us/u/kyMbCRs05

IMF Info Line – If you or someone you care for has Myeloma, you have questions. Probably, lots of them. You can search the Internet all you want, but other than asking your doctor, there is no better way to get your questions answered than to call the IMF Info Line. Missy, Judy and Paul know their stuff and they want to share what they know with you. Just ask anyone who has called the IMF Info Line. Patients or caregivers are welcome to contact the Info Line staffed by trained specialist at 800-452-CURE (800-452-2873). The Info Line is staffed between 9am and 4pm Pacific Time, 11am to 6pm Central time or infoline@myeloma.org.

The Trillium Fund was established by our founding support group members to facilitate Multiple Myeloma research here in Madison at the Wisconsin Institute of Medical Research. If you or your family wish to donate or send a memorial to this program, checks can be made payable to the "UW Foundation – Trillium Fund" and sent to UW Carbone Cancer Center, University of Wisconsin Foundation, 1848 University Ave, Madison, WI 53726. Donations may also be made online at www.supportuw.org/give (Trillium Fund in Multiple Myeloma Research – 112903576). For any questions, please call Janie Winston 608-512-6068 or email at Janie.Winston@supportuw.org.