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Subject: Full Erythromelalgia Relief in 17-Year Old Male

I think we have discovered a possible simple and inexpensive solution that may work for some diagnosed with EM. After 13 weeks of a horrible hands and feet EM with my 17-year old son, we seem to have stopped it completely. The solution was all topical and to avoid cold. Our final treatment routine that worked was a routine of applying 1% Amitriptyline 0.5% Ketamine cream four to five times a day, the application of the vasoconstrictor Phenylephrine (found in Preparation H), and total avoidance of cold and water for just the hands and feet (affected area). If we could go back in time we think we could have had it under control in just a couple of weeks with zero oral drugs.

For my son, I believe the Amitriptyline/Ketamine cream has knocked it out, but only after three days of application and a total avoidance of cold and water. I believe the application of cold to relieve the pain was keeping the Amitriptyline/Ketamine cream from doing its thing. Instead to control the pain we topically used the vasoconstrictor Phenylephrine (Prep-H) on the areas that were red. Prep-H was the only thing besides cold that provided any pain relief and allowed us to avoid cold and water.

Please note, I'm an engineer and not a medical doctor so I might have some terminology wrong, and I'm not giving medical advice. I'm just basing this information on my observations of what hasn't worked and what has worked in our experience. I have read all I can on EM, and I haven't seen this approach or explanation offered before. Hopefully this experience and approach helps somebody.

Quick Summary:

I took the approach to EM that it isn't a neurological problem but is a cooling system controls problem localized in the hands and feet. The body is cooled through the skin by vasodilation and increased sweating on a scale of 0 to 10 in intensity based on how much the body needs to get rid of heat. My hypothesis is that there is a localized malfunction in the hands and feet where vasodilation goes to 10 and sweating is 0. After two months of watching all the failed efforts to control my son's pain with nerve drugs, I felt the doctors were going about the problem backwards. They were trying to stop the neurological pain instead of stopping the increased blood that could be causing the redness, heat, and burning pain.

We were told time and time again that the redness followed the neurological disorder and was a result not the cause. What if they are wrong? I thought, the pain is described as a severe burning feeling, so what if it is real, and instead of treating the nerves, let's reduce the redness and heat with a vasoconstrictor and see if he gets some relief. What could it hurt to try? My initial goal was just to reduce his pain level down to below 5 so he could function.

These ideas came to me on a Friday evening, so I quickly searched for an over-the-counter vasoconstrictor. I found nasal decongestants and Preparation H both contained a different

vasoconstrictor drug. I purchased both and rushed home. I found my son writhing in pain, feet scorching red almost up to the ankle with toes and sides of the feet being the worst – his report was the pain was a 9.5 – mind you this was over 9 weeks straight of this condition at this point with no relief aside from temporary nerve blocks we had tried in the hospital five days earlier. I had him apply Preparation H on both feet. After about five minutes, the red color changed and he reported the pain was down to a 3! Burning hot to the touch had changed to just warm. Tops of his feet lightened up, and after about a half hour the flare was out completely for the first time. From this point on, at any sign of a flare up he applied Preparation H. The result for the first week was no pain above a 5 on a flare-up and flare-ups were quickly put out or minimized and the frequency of flare-ups decreased. After the first week, flare-ups stopped completely! It has now been five weeks and counting without a flare-up, his skin has peeled off, and he is running and working out to gain his strength back that was lost. Time will tell if this works long term, but it seems we have it under control for now.

Long Story:

I'm a licensed Mechanical Engineer in the state of California specializing in control systems. In late March, 2017 my 17-year old son was diagnosed with EM. Like many, it came on suddenly and horribly. We struggled to first get it diagnosed, but mostly to find him some relief from the constant 9 to 10 pain in his hands and feet. Nobody had heard of EM--neither us nor the doctors, and no one had experience treating it as it is so rare. We spent the first five weeks with sleepless days and nights, wailing pain, frustration, helpless, and a shotgun-treatment approach of 20+ pills a day. Only very cold water seemed to relieve his pain for short periods of time. I became obsessed with EM to understand it and to find some relief for my son but could find none.

As things got worse and worse, we finally took him to the Kaiser Oakland Emergency room, and after rounds of heavy narcotics with barely any relief, they admitted him to the pediatric floor. We spent five days watching the doctors chase his pain with narcotics and by adding more drugs to his growing list – at the peak he was up to 25 pills a day of five different medications without any sign of relief. On the fifth hospital day with frustration levels at their highest, pain management was turned over to the anesthesiologists. They wanted to do a Ketamine IV or an epidural, which my son refused due to the need for a catheter and the thought of being paralyzed from the waist down. The thought of a Ketamine IV didn't match anything we had read on this condition, so we resisted. Last, they offered a bilateral nerve block in both legs at the knee. This made perfect sense, so we gave the okay and 30 minutes later they were performing the procedure. Finally he had full pain relief! The pain was gone and the feet were dead to the touch, but he was also unable to move them because the anesthesiologist had it turned up too high. However, the EM flare-up was extreme, and his feet looked like they would explode. If EM is a neurological condition, why after the nerve blocks were in place and the nerves completely cut off, didn't the EM let up but maybe got even worse? The doctors had no answer.

The going understanding of EM is that it caused by a neurological problem that is not fully understood. I decided to throw that idea away. Instead, what if the pain is the result of a real burning of the skin due to the increased blood and overheating? If so, all the nerve medication treatment was trying to block real pain and wasn't successful. From The Erythromelalgia Association (TEA) website:

“Erythromelalgia is a rare and frequently devastating disorder that typically affects the skin of the feet or hands, or both, and causes visible redness, intense heat and burning pain.”

and

“The characteristic of cooling bringing relief to EM sufferer’s pain is a hallmark trait of EM.”

Visible redness, intense heat, burning pain and no relief from any nerve drug but physically cooling the skin provides temporary relief. What is the redness? It is increased blood. What is the pain? Is it the result of trapped heat from the increased blood? If we stop the increased blood then shouldn’t the pain be reduced providing relief? For my son’s case, the answer was YES!

Skin provides the main cooling mechanism for the body by opening blood vessels (vasodilation) to increase heat in the skin while the sweat glands release moisture that evaporates taking the heat from the blood away. It does this on a sliding scale of say 0 to 10 based on how much the body needs to shed heat. EM in this case is not the entire body but is just the localized skin in the lower portions of the hands and the feet. To me, an engineer, this localized cooling control system in the hands and feet is broken or malfunctioning with a vasodilation of 10 and sweating of 0 and seems to be spontaneous. So, how do we fix it?

When a control system is broken, engineers look at the three things: input (sensors –does the body need to get rid of heat?), controller (computer or in the body the brain), and the actuator or device to change something physical (vasodilation and sweating). For example, a F-16 fighter jet is considered a “fly by wire” control system jet. The F-16 doesn’t have mechanical linkage between the pilot’s control stick and the control surfaces on the wings and tail. Instead, it has a joystick the pilot moves that provides input to a computer system that interprets the inputs from the pilot and then sends signals to the control surfaces to do what the pilot wants.

Consider a problem where the pilot holds the stick in the straight and level position but the F-16 suddenly climbs out of control despite the pilot holding the control stick neutral or even pushing forward which should cause the plane to descend. To diagnose the problem, engineers will look at the stick to see if the problem is the inputs. Next will be the computer system to make sure there isn’t something wrong with the programming. Last checked will be the actuators on the tail elevators that physically make the plane climb. If the joystick is good and the computer is good, then the problem has to be the actuator in the tail. Maybe a loose wire or a short is causing the actuator to malfunction.

What if EM is similar? Why are just the hands and feet burning rather than the entire body? What if the blood vessels in the skin of the hands and feet are malfunctioning on their own—without the brain telling them to do anything — and going to a 10 on the cooling scale causing full vasodilation while the sweat glands stay at 0? The result would be localized extreme redness and heat resulting in non-stop burning pain. Sound familiar?

If this hypothesis is correct, then constricting the blood vessels should provide nearly instant relief. We do not want to do this orally for two reasons: 1) we do not want to constrict blood vessels throughout

the body as this could cause a dangerous increase in blood pressure, and 2) the problem is only in the hands and feet, so why treat the entire body – the rest of the body is fine; let's not mess with it.

There is a small study that shows Midodrine cream has helped relieve pain. What is Midodrine? A vasoconstrictor. Let's go further and find a more powerful vasoconstrictor that is over-the-counter and proven highly effective for near 75 years – Preparation H (0.25% Phenylephrine HCl – tube costing \$6.99). There are multiple formulas for Preparation H, but we just want the one with Phenylephrine as there are no long term negative effects on the skin. (Others formulations contain Pramoxine which I think can thin the skin after long term use.) For my son's situation, Preparation H with Phenylephrine worked and it worked fast! Here is a summary:

- 1) No oral medication helped; if anything they made his overall condition worse. We weaned him off of all oral drugs after 14 weeks, and his overall wellbeing returned to normal. Trying to wean off of some of the neurological drugs like Lyrica has been horrible with twitching, sleepless nights, mood issues, etc. It took nearly three weeks to wean him off the prescribed 300mg per day dosage.
- 2) 1% Amitriptyline 0.5% Ketamine cream worked for us! Prior to the vasoconstrictor, we found others had success with this cream and applied it to his hands and feet. After two days, no change. The third day his hands started changing and went from burning red to a waxy yellowish color and a tingling, but the flares went away (stick with this cream – do not stop it and keep a constant layer on). The feet however remained the same. My thought is this was due to the cold treatments on the feet during flare-ups. What if the cold treatments along with the thicker skin in the feet kept the medicine from absorbing in the vascular portion of the skin? What if he was washing off the cream? His hands didn't undergo the same intense cold treatments because he was able to tolerate the pain better in his hands. As soon as we stopped the cold treatments in his feet (nerve blocks), three days later we started to see the changes in his feet that we saw in his hands. However, when we stopped the nerve blocks the flare-ups returned after a day (I believe because we again used cold to relieve his pain) and continued until we started using Preparation H.
- 3) Burning pain is real and is caused by uncontrolled vasodilation in the lower portions of the hands and feet. Applying a vasoconstrictor can relieve the pain by constricting the blood vessels and reducing the heat, all without applying cold. Do this topically and locally on the red areas do not take it orally. This allows the 1% Amitriptyline 0.5% Ketamine cream to do its thing and “reset” the blood vessels, if you will...
- 4) We believe the overall solution for our son was to avoid the cold treatments, apply 1% Amitriptyline 0.5% Ketamine cream four to five times a day. Apply Preparation-H (0.25% Phenylephrine only active ingredient version) at any sign of a flare-up. The combination of the Amitriptyline/Ketamine cream and Preparation H seems to fix the malfunctioning blood vessels in the hands and feet, returning them to normal cooling operation. Why? I don't know. This is something we have yet to understand. My thoughts are that the problem is in the microvascular

system of the skin where it thinks it is getting a signal to vascular dilate but it isn't. Is it the Amitriptyline, Ketamine, or Phenylephrine that is resetting the microvascular muscles? Again, I don't know, but at this point, I don't care because the combination of them all seems to work! At least it does for my son.

- 5) Normal Life. For my son's case, we have found Preparation H can minimize the flare-ups if not stop them completely. For the future if he wants to play sports, go for a jog, or deal with a hot day, he can apply a thin layer of Preparation H to his feet and hands and go! Keep a tube in his bag and if a flare-up starts, apply the vasoconstrictor and minimize it. No ice packs, cold water, cold air, air conditioners or fans needed. However, over 5 weeks and counting with zero flare-ups.

Maybe this solution will not work for others with EM; however, it has given my 17 year old son his life back. He was unable to function, writhing in misery, unable to put pressure on his feet, unable to concentrate on anything, missed 9 weeks of school, dropped 25 lbs. of muscle, and nearly destroyed our overall family. Now, five weeks after starting this topical localized treatment, the flare-ups have stopped, he is running, eating, putting muscle back on, concentrating, and overall is starting to look like his normal self again. We are looking forward to his senior year in high school. I hope our experience and different approach to treatment can help provide somebody else with relief.