FootSteps

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THE NEWSLETTER FOR MEMBERS AND FRIENDS OF THE ERYTHROMELALGIA ASSOCIATION

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Researchers to test backup drug

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Because of this high level of interest among readers of* FootSteps*, the researchers are providing the following update on the status of this trial. They wrote:

"Several patients participated in the clinical trial of the novel analgesic drug held in The Netherlands in June 2010. Data collected were extremely encouraging, showing the study drug (XEN402) with a positive signal for pain relief.

However, at the dose tested in this trial, some patients experienced side effects including dizziness and drowsiness. Although the side effects were transient and resolved quickly, they were noted as severe in some individuals.

Xenon Pharmaceuticals Inc., the Canadian pharmaceutical company sponsoring the trial, has developed a backup drug expected to have milder side effects than XEN402, while still retaining pain relief properties.

Because of the development of this backup drug, the researchers decided to close the current trial and instead pursue the improved backup drug. The first Phase II efficacy study in patients to test the improved backup drug is expected to begin in early to mid-2011."

You can contact the researchers at joostphdrenth@cs.com.

More trials ahead for people with IEM

"There are number of pharmaceutical companies interested in developing drugs against IEM pain," said Joost PH Drenth, M.D., Ph.D., Radboud University, The Netherlands.

Those with inherited erythromelalgia (IEM) have a genetic mutation that causes their pain. The companies are searching for drugs that block the effect of the mutation and relieve the pain of IEM.

Their hope is the drugs will also benefit people with other pain syndromes, Dr. Drenth says. Any new drugs will need to be tested first in people with IEM. If they are not effective at stopping the pain of IEM, it is doubtful they will help others.

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Memorial Fund honors Jim Read

TEA has established a Memorial Fund as a tribute to James M. Read, III. Money donated to this fund will be restricted to benefit EM research.

You can donate to this fund online today. Or you can write a check to TEA and send it to TEA, 200 Old Castle Lane, Wallingford, PA, USA 19086.

(Thanks to TEA member Meg Edelson, who suggested creating this fund.)

Member directory live on website

TEA's member directory is up and running on the new TEA website—erythromelalgia.org or burningfeet.org.

Directory profiles include names, addresses—e-mail and mailing—including cities, states and countries, and phone numbers. In addition to first and last names, the directory can be sorted by city, state, or country.

Members often use the list to find and network with others in their geographical areas.

Only members can view this information. But if you want to, you can opt out of the listing that is visible to members on the site. (See directions below.)

Those without computers wishing to opt out should write to Gayla Kanaster at 2532 Fremont St., Tacoma, WA, USA, 98406.

If you opt out, your profile will be kept intact for administrative staff to use.

New members create their own profiles when they join. The directory is used to create mailing lists, like the one used to mail *FootSteps,* among other uses.

HOW TO OPT OUT

- Log in to the member side of the website with your user name and password
- Click on "manage account" in the upper right corner of the screen
- Click on "Edit profile" under "My Profile" on the next page
- Then on the new page, click on the "manage profile" option (third choice to the right) You'll see three questions on this page that concern information in your directory listing
- Using the pull-down menu to the right of each question, select "NO" for information you do not want listed on the website
- When you are finished, click "Update" at the bottom of the page
- You should almost instantaneously receive an e-mail confirming the changes

Research Update

Drenth pursues new genetic finding

Mutations in SCN9A—the same gene with mutations that cause inherited erythromelalgia (IEM)—were recently found in a small number of patients with unexplained small fiber neuropathy (SFN).

Joost PH Drenth, M.D., Ph.D., and his research team at Radboud University Medical Center, The Netherlands, made this "exciting discovery" earlier this year.

Following up on this finding, Dr. Drenth and colleagues in a new study are defining how prevalent SCN9A mutations are among people with unexplained SFN.

TEA recently donated $15,000 to help fund this new study in which the researchers hypothesize that a significant number of people with unexplained SFN carry a disease-causing SCN9A mutation similar to the mutations causing IEM.

If this hypothesis is proven, the study will establish inherited SFN as another one of the group of pain syndromes—that includes IEM—caused by mutations in SCN9A.

It also would mean an expansion of that group, leading to a wider recognition of the role of SCN9A in pain.

SFN is a common disorder causing intense burning pain, tingling and numbness. It is estimated that 15 to 20 million Americans have some kind of neuropathy and many of these have impairment of the small nerve fibers that control pain and temperature sensation.

SFN remains unexplained in 50 to 70 percent of patients.

Dr. Drenth's team is first identifying a study group of 80 people with unexplained SFN. Next, each study volunteer's DNA will be sampled and their SCN9A gene "sequenced" to identify any mutations.

The researchers will then assess the characteristics of the mutations.

Dr. Drenth expects to have the results of this study by the end of 2011.

Dr. Drenth

In 2001, Dr. Drenth was the first scientist to identify the location of the gene linked to IEM on chromosome 2. He and his colleagues subsequently found mutations to this gene in the families of people with IEM.

Dr. Drenth and his team continue to study IEM and the "myriad disorders" that feature pain or the absence of pain.

This kind of genetic research involves studying DNA–each person's hereditary information–that has only been possible because of technological advances made in the past 15 years.

TEA Gifts Researchers

TEA recently gave $15,000 each to the EM research programs at Yale and at Radboud University in The Netherlands.

The gift to the researchers in The Netherlands is being used to help fund the new study searching for genetic mutations in those with unexplained small fiber neuropathy.

The second gift went to research on inherited EM under the direction of Stephen Waxman, M.D., Ph.D., Director of the Yale Center for Neuroscience and Regeneration Research.

In recent years, the Yale team has made notable advances in EM research in studies in families with inherited erythromelalgia (IEM). Yale was the first to prove that genetic mutations are responsible for EM pain.

The goal of the Yale research now is finding "more effective therapies, and ultimately cures, for all people with EM."

"We are acutely aware that, in the majority

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Q&A with Julia and Steve Berkhout — *Fans of TEA*

Julia and Steve Berkhout willingly worked around a 13-hour time zone difference from Dallas to their home near Perth, Australia to share their EM experiences and insight via telephone. (After U.S. Daylight Savings, it's now a 14-hour difference.)

Q: What inspired you to create Facebook (FB) Fans of TEA?

Julia: After Steve was diagnosed with EM in 2004, we were looking for more EM information all over the Internet. In 2008, I was fairly new to Facebook and wanted to put something rare like EM onto it. Every story you hear, people have had EM for years before they know what they have.

Q: How did the EM start?

Steve: In 2002, I started to come home from work with really hot, sore feet. I had been an automotive mechanic and then started mining granite for concrete products. I worked my way up the ladder from operating machinery to being the site supervisor and spent a lot of time on my feet. I should have been to the doctor a lot earlier, though—Oh, I thought, "I'll walk it off." I had severely flat and sore feet so, in 2004, I had two foot reconstructions and tarsal tunnel decompressions. After the operations and during my rehab the pain continued to get worse and, after 4 to 5 years, a pain specialist finally diagnosed the EM. It affects my eyelids, ears, hands, arms, face, groin, and now predominantly my feet. I also have Raynaud's and am deaf in one ear, which affects my balance. My dad's feet get hot when in bed; the same with a brother. Another brother is starting to get a burning sensation in his feet at the end of the day, and I hope it's not the start of EM.

Q: Describe getting the EM diagnosis.

Steve: It was great because there was finally some light at the end of the tunnel: they're onto it. But when we got home, after spending time on the Internet and finding that there's not much that can be done about it, I was knocked straight back down again.

Q: Fans of TEA benefits?

Julia: Steve is 45; I'm 38, but I always struggled to keep up with my energetic workaholic husband. Now, it's the other way around. I have a back problem, so I can understand a little about the pain. People pop in to *Fans of TEA* to exchange ideas, treatments and feelings with people who understand. It's hard to talk to people about EM until they've experienced chronic pain. Others don't mean to be ignorant; they don't have the same frame of reference.

Q: What to avoid on Fans of TEA?

Julia: Venting is okay, as long as it's not prolonged. It can help. But you don't want complaining all the time. It is meant to be a positive site for all who use it—to share and chat.

Q: How has EM changed your life?

Steve: Dramatically. I spend most days indoors in air conditioning. It runs all day, all night, all year. EM challenges me to the fullest extent of my capabilities to get through every day and night now. At first, losing my job just killed me. I had disability income protection insurance, but it has run out.

Steve and Julia Berkhout with dogs Tonka and Misty.

Q: How do you deal with EM?
Steve: On bad days I just tune out and try to do things to take my mind off of the pain; our dogs are a constant source of comfort. I tried all the treatment options and ticked them off the list, one by one—"That one makes it worse: ow, ow, ow." The pain does take it out of you. You can only physically and mentally overcome what you can overcome. We're about to sell the house to move south to a cooler summer because of my EM.

Q: How do you find the courage and strength to move forward?
Steve: My mindset. I don't know; I just do it. Julia says I'm the strongest person she's come across. If anything, this daily challenge has made us closer. We are in it together, just like in the traditional wedding vows we made twelve years ago—"For Better or for Worse/in Sickness and in Health." We met at work; Julia was also a mechanic before she had her back problems.
Julia: I am now self-employed to give me some flexibility in my hours.

Q: What's it like for you to watch Steve cope?
Julia: It depends upon how he is doing. It upsets me to see him in so much pain—it's apparent in his facial expression. I feel for him and wish I could take the pain away. But he always has a smile for me. I've become a lot stronger emotionally.

Q: Advice for others?
Julia: You can't take the pain away, but you can always be there and help them with things. I make him feel loved and needed.

Q: With EM, I can't…
Steve: …be on the phone very long; do jobs around the house; swim or exercise; socialize normally; work, not even on the performance/sports car I built from the ground up. I sold it after 20 years. I can't get a full night's sleep, sleep in a warm bed, or even lie close to my wife in bed because of her body heat.

Q: …But I still can…
Steve: …cuddle with Julia on a really cold night, and I can occasionally ride my motocross bike for about one hour on some days, in the winter and spring. The breeze feels good, and the engine vibrations numb my feet.

Q: Has EM changed you?
Steve: It puts a whole new perspective on life. We have a very strong marriage—that is helpful. I appreciate everything she does for me. The little things that you take for granted are more important. I don't stress about things too much.

Q: How can others join FB Fans of TEA?
Julia: It's simple—just sign up for free on facebook.com, create a user name and password, and log in. Go to the "group" section and type in *"Fans of TEA."*

Q&A Rapid Fire

Q: Why FB Fans of TEA?
Julia: I hope it is valuable for people to hear other people's stories—not to compare, but to get the "aha" moments of clarity. Nice to know you are not the only ones.

Q: Words of wisdom?
Steve: Be cool. Find out what works for you – trial and error, as everyone's symptoms differ. Research treatments for your doctor and try anything within reason. Some approaches make it better, some worse. Work out your own pace, and learn your boundaries. It helps to realize that others are fighting their own private battles, no matter what they are.

Q: What is not thwarted by EM?
Steve: Concentrating on the track/speed during an hour dirt bike ride. The exhilaration clears my head and takes my cares away; the engine vibration numbs my feet. Enjoying the company of my wife and dogs. And, my sense of humor.

—Jan Coopman

Your stories — everybody has one

Send your story to Gayla Kanaster, GaylaKanaster@aol.com or 2532 N. Fremont St., Tacoma, WA, USA 98406

Cindy Alexander writes: My story is a little different from others with EM. My cherished aunt suffered from EM and spoke of the pain she was enduring, a pain incomparable to anything else.

Others in her immediate family also suffer with EM. My cousin was incorrectly diagnosed with arthritis at a young age as were his younger brother and two sons.

With the unexpected loss of my aunt last year, I began to look into this disease, initially by joining TEA and getting the EM bracelets for my family as a tribute to her.

I have worked in the Canadian Not-For-Profit and Charity Sector for more than 20 years, employed in accounting roles. After experiencing a major downsizing in 1996, I began to look beyond the finance role I had been doing.

What I found was missing in my experience was a passion for a cause, which I see so often in others. Despite experience in many types of organizations, I found my connection to their missions somewhat lacking because I had no firsthand experience.

With EM, there is much that can be done. More of my family members now suffer from similar symptoms (including me). Before I was even aware of the "burning feet" symptom of EM, I went from someone who slept with my feet totally covered to now not being able to stand covers on my feet during the night.

Testing and waiting for results is an endless process here, but there are many resources in Canada that could help TEA increase EM awareness. I welcome the opportunity to work for this cause to try and make a difference. I believe that every person who is aware of EM brings us one step closer to ending EM—a journey one step at a time.

IN MEMORIAM

James M. Read III, who began the EM Yahoo Group, died May 19, 2010, in Boise, Idaho, U.S. He was one of a small group of people with a similar set of symptoms—and a diagnosis of EM—who connected on the Internet in the mid- to late 1990s. Little was known about EM then.

In 1999, this online group founded TEA as a nonprofit organization, primarily to raise funds for EM research. Jim was one of the original members of the TEA Board of Directors and suggested creating the EM Yahoo group. He managed this "list" singlehandedly for many years—an often difficult, time-consuming job, though he found it satisfying to bring people together in this online community.

According to a "Your Story" he wrote for the *June 2005 FootSteps*, Jim was a Ph.D. clinical psychologist who taught wellness and maintained a private practice for 33 years. He called himself the "barefoot shrink," and worked sitting in a chilly office so he did not have to stand or move around much.

He loved to run, but switched to cycling as daily exercise. He had warmth, redness and swelling in his feet for over 20 years, but credited exercise with keeping his symptoms bearable.

In 2005, Jim was diagnosed with ALS (Lou Gehrig's disease), which he knew to be fatal in just a few years.

Happily married for almost 40 years, he is survived by his wife Heidi, two adult children and a granddaughter. He was 63.

Heidi says, "Jim's favorite quote was from Dag Hammerskjold, 'Life only demands from you the strength you possess. Only one feat is possible—not to have run away.'"

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TEA donates

of cases, EM occurs without a family history," says Dr. Waxman. The team at Yale now is investigating two new lines of research that are moving toward helping those with EM that is not inherited.

One recent discovery is a "polymorphism" within the EM gene that occurs in 30 percent of the normal population.

This polymorphism does not cause pain, but instead causes an increased risk of developing pain in certain circumstances.

"We are aggressively following up on this new finding," he says. The researchers want to better understand how the polymorphism increases susceptibility to pain.

And they want to identify other polymorphisms that increase the risk of developing painful disorders like EM.

The second new line of research involves finding out why some people with IEM do not begin feeling the painful symptoms of EM until they are teenagers or young adults.

The researchers want to know what prevents pain from occurring at earlier ages. (See Research Update, *FootSteps, Vol. 11, No. 1, 2010*, for more information on Yale EM research.)

How do clinical trials work?

When a pharmaceutical company develops a substance it theorizes will have an effect—such as relieving the pain of IEM—it must sponsor scientific experiments to prove the new substance (drug) works before it can be approved for use by governmental authorities.

These experiments are called clinical trials and they are conducted in phases. The trials at each phase have a different purpose and help scientists answer different questions.

Clinical trials are overseen by physician scientists usually working in university medical centers. For example, Joost PH Drenth, M.D., Ph.D., is the principal investigator of the Xenon-sponsored trials of experimental IEM drugs. The trials are taking place at Raboud University Medical Center, The Netherlands, where Dr. Drenth is a faculty member.

Xenon Pharmaceuticals, Inc., is the Canadian pharmaceutical company that developed the current experimental IEM drugs and is sponsoring the trials.

In **Phase I trials**, researchers test the experimental drug for the first time in a small group of "normal" people to evaluate its safety, determine a safe dosage range, and identify side effects.

In **Phase II trials,** the experimental drug is usually given to a somewhat larger group of people. Those in the study group this time must have the disease or condition the drug is intended to help, so scientists can see if the drug is effective and further evaluate its safety.

(The Xenon-sponsored trial in June was Phase II.)

In **Phase III trials,** the experimental drug is given to larger groups of people with the targeted condition to confirm the drug's effectiveness, monitor side effects, and collect information that will allow the experimental drug to be used safely.

(Because IEM is very rare, the size of these groups will be smaller than the size of Phase III groups for most other drugs.)

Governmental agencies like the Federal Drug Administration in the U.S. will approve the drug's use only after Phase III trials are completed successfully.

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