FootSteps

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THE NEWSLETTER FOR MEMBERS AND FRIENDS OF THE ERYTHROMELALGIA ASSOCIATION

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New EM drug to be tested

An experimental drug intended to block or reduce the pain of inherited EM (IEM) will be trialed in people with IEM in Nijmegen, Netherlands, under the supervision of principal investigator Joost Drenth, M.D., Ph.D.

The drug XEN402 was proven safe and well tolerated in healthy volunteers in phase 1 clinical trials. The next step is phase 2a clinical trials in people with inherited EM. This clinical trial is a study of the safety and effectiveness of XEN402 in treating EM pain.

Volunteers with IEM are needed for the trial group. Only 15 people will be accepted for the study, which must be done by September. (See page 2 for qualifications.)

The study will cover the cost of travel and accommodations for those who qualify. And volunteers may take a companion to the Netherlands, expenses also to be paid by the study.

DRUG MAY BLOCK GENETIC MUTATIONS. Scientists at Xenon Pharmaceuticals developed XEN402 to block the genetic mutations in one of the sodium channels (Nav 1.7) in nerve fibers in the skin. The mutations allow a much-larger-than-normal number of sodium ions to flow into nerve cells, sparking signals interpreted by the brain as pain.

If these phase 2a trials are successful, longer, bigger trials (phases 2b and 3) must be held to prove the drug effective before it goes to the FDA for approval.

Xenon Pharmaceuticals Inc. is a privately held biotechnology company located in Vancouver, Canada.

Reconstructed website launched

TEA launched its reconstructed website – www.burningfeet.org or www.erythromelalgia.org – in June.

The new site does not yet include all the information contained by the former site, but content is steadily being added. A major problem with the web host brought down the former site in late 2009.

TEA hired K-Data Systems, Grand Rapids, Mich., to completely reconstruct the website. This same company will host and provide support for maintaining the site in coming months.

Many TEA members re-registered on the interim website or filled out and returned the form that was sent to their home

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This issue of **FootSteps** *is being underwritten by Xenon Pharmaceuticals, Vancouver, British Columbia, Canada, the company that developed the experimental drug undergoing clinical trials.*

Do you have inherited erythromelalgia?

Currently, there are very few treatment options for those living with EM. But over time as clinical researchers and patients work together, this can change.

Clinical research studies need the support of people like you so new medicines can be developed.

We want to tell you about a clinical research study that will evaluate the safety and effectiveness of an investigational medication for the treatment of pain from EM.

As you know, EM is very rare. That is why this global study is being conducted at only one location: Radboud University Nijmegen Medical Center. Located in the city of Nijmegen in the Netherlands, it is a leading medical center in Europe. Your travel and accommodations are arranged on your behalf. There are no travel expenses for you to incur.

We invite you to take the next steps:

1. **Compare yourself to the study requirements**
2. **Know what the study is asking of you**

The study requires you to:

- Be 18-75 years old
- Have inherited EM
- Be experiencing pain caused by EM
- Be generally healthy (apart from your pain)
- Stop taking your usual pain medications for 9 days
- Not be pregnant or breast-feeding

Your role in the study:

- An out-patient screening visit
- 9 days/8 nights in-patient treatment visit at Nijmegen Medical Center (where you will be closely monitored)
- A follow-up phone call (after you return home)
- Taking the investigational medication according to the study requirements
- Recording your pain levels during your stay at the Medical Center

The study is limited in size (only 15 people will be accepted). It is also limited in time; the study concludes in September 2010. Regardless of where you live, this study is open to you.

Should you qualify, the study will cover the cost of bringing a companion with you to the Netherlands.

For more information about this study please visit the study website: www.RareDiseaseStudy.com
Within the US call: 1-866-304-7030
Elsewhere call: 484-674-6313 (non-toll free number)
E-mail: JoostDrenth@cs.com

Research update

Yale group unraveling IEM 'molecule by molecule'

"EM remains our major focus. We have a wonderfully energetic, talented team, and we are unraveling this disease, molecule by molecule," Stephen Waxman, M.D., Ph.D., wrote in a recent e-mail to Gayla Kanaster, TEA Secretary.

Director of the Center for Neuroscience and Regeneration Research at Yale University School of Medicine, Dr. Waxman leads the effort to analyze the complexities of inherited EM (IEM), and in doing so suggest new methods for the treatment of many forms of pain, including non-inherited EM pain.

In 2004, Dr. Waxman and his group were the first to show how genetic mutations in one of the sodium channels (Nav 1.7) in nerve fibers cause the pain of IEM.

QUESTIONS OF AGE, SEVERITY. Among the questions Dr. Waxman now is working to answer: "Why should an individual with an EM-producing mutation begin to experience pain at age 20? Why does this person not hurt at 15? Are there protective mechanisms that prevent pain at earlier ages? Might they be useful for pain therapy for those with childhood-onset EM, or for pain treatment at large?"

He reports his group is mainly focused on people who developed symptoms in the first few years of life. But recent studies of people with IEM whose symptoms appeared between ages 11 and 20 are providing new and exciting clues about EM.

HAN STUDIED MUTATION OF TEEN. One of the more than a dozen articles related to EM research published by the Yale group in 2009 had as its lead author Dr. ChongYang Han, a physiologist from Beijing working with the group at Yale. (Hosting visiting scientists is a Yale program TEA helped fund in 2007 with a $45,000 donation.)

Dr. Han's study analyzed a new mutation found in a patient who first experienced EM pain in his teens and compared it to mutations found in people who developed symptoms before age 10. His study – published in the journal *Brain* – found differences in how the mutations act that relate to the severity of the resulting EM.

Stephen Waxman

Another question being explored by these researchers: Why do some IEM patients respond favorably to certain drugs and not others? In separate studies, Dr. Waxman and his team have analyzed mutations found in IEM patients resistant to lidocaine (Sheets et al, 2007), and more recently, those responsive to mexilitine (Choi et al, 2009), and to carbamazepine (Fischer et al, 2009). The findings of these studies point the way toward personalized, genetically based treatments.

Recent studies have found a common genetic variation in Nav 1.7 that does not produce pain, but may increase the susceptibility to pain, like the pain of non-inherited EM. "We are aggressively following up on this new finding," says Dr. Waxman.

EM STUDIES HELP OTHER PAIN. "Studies of EM are highly relevant to other pain syndromes in which Nav1.7 is also a major contributor," says Dr. Waxman. He and his coworkers are investigating molecules and mechanisms that control the behavior of Nav1.7 in pain after nerve injury, limb amputation, and burn injuries.

Nav1.7 contributes to pain in all of these conditions, suggesting that drugs blocking Nav1.7, developed for EM, may be useful for other forms of pain.

TEA endorses Kakkis' 'CureTheProcess' campaign

Kakkis EveryLife Foundation believes:

- **No rare disorder should go untreated.**
- **We already have the science we need to treat more rare disease patients.**
- **We need an improved process with new study designs and disease measures to accelerate the development of new treatments.**
- **We need the right people in both industry and FDA to make these changes effective.**
- **All new drugs for rare diseases should be safe.**

TEA recently endorsed the "CureTheProcess" campaign being waged by the Kakkis EveryLife Foundation. And TEA became one of more than 100 organizations that are campaign partners.

Emil D. Kakkis

Founded just last year by Emil D. Kakkis, M.D., PhD., the foundation's goal is reforming the way rare disease treatments – especially drugs – are developed and approved for use.

As we know, effective treatments don't exist for many people with rare or "orphan" disorders like EM. This situation is made even more tragic when the science exists to develop a treatment, but cost and complexities slow or stop progress.

Dr. Kakkis' aim is to expand access to treatment for patients with very rare diseases by improving the FDA regulatory process. The campaign's goal is to give even the rarest of diseases access to the FDA's accelerated approval process.

RARE DISEASE DRUGS FACE DIFFICULT PATH. Despite research advances, treatments for rare diseases in the U.S. still have a particularly difficult development path.

Dr. Kakkis left his post as Chief Medical Officer at BioMarin Pharmaceutical in early 2009 to found the Kakkis EveryLife Foundation. Dedicated to his mission, he funds the nonprofit with his own money.

"I created the Kakkis EveryLife Foundation to 'CureTheProcess' and focus on fixing the problems associated with developing treatments for rare disorders," says Dr. Kakkis, a pediatrician and medical geneticist.

Dr. Kakkis spent more than 18 years researching and delivering new treatments for patients suffering from rare diseases.

According to Dr. Kakkis, there are more than 7,000 rare disorders that together affect more than 25 million Americans.

TEA 2009 annual appeal raises $12,540 for research, operations

Despite the slow start to an international economic recovery, TEA's generous donors answered the 2009 Annual Appeal with gifts totaling $12,540.

This was the third annual appeal sent by TEA. In 2008, appeal donations totaled $14,459. The 2007 appeal resulted in $11,757.

Arriving in mailboxes in November 2009, last year's appeal was sent to the entire mailing list of members, friends, families and former donors.

The $12,540 total includes donations received through May 31, 2010.

TEA 2009 Annual Report: the financials

THE ERYTHROMELALGIA ASSOCIATION

BALANCE SHEET - DECEMBER 31, 2009

ASSETS

Cash and Cash Equivalents	$	98,169
Total Assets	$	98,169

LIABILITIES AND FUND BALANCES

Total Liabilities	$	-
Fund Balances		
Fund Balance - Operating	$	74,571
Fund Balance - Research		23,598
Total Fund Balances	$	98,169
Total Liabilities & Fund Balances	$	98,169

STATEMENT OF ACTIVITY - Year Ended December 31, 2009

Revenues		
New Members	$	3,226
Renewals	$	4,023
General Contributions	$	4,570
In Honor Donations	$	715
Research Fund Donations	$	1,701
Bracelet Fundraiser	$	276
Annual Appeal-Rsch	$	630
Annual Appeal - Unrestricted	$	11,160
Articles	$	34
In Memoriam	$	2,511
Interest Income	$	1,569
Total Revenues	$	30,415
Expenses		
Awareness Support	$	1,000
Copying	$	64
Domain Registration	$	15
Fees/Memberships	$	95
Insurance	$	948
Membership Phone	$	97
Miscellaneous	$	10
Office Supplies	$	500
Paypal Fees	$	187
Postage	$	6,147
Printing	$	3,073
Sunshine Club	$	102
Teleconference Phone	$	285
Total Expenses	$	12,523
Income exceeded Expenditures	$	17,892

By Beth Coimbra, CPA*

TEA manages its funds very carefully. As a 501(c)(3) corporation – a nonprofit – TEA's income comes almost entirely from donations and membership fees. As an organization, TEA seeks to be transparent and fully inform members of its status. To the left is a report of TEA's 2009 financial year.

The top portion of the financial document (the Balance Sheet) is a snapshot of the financial condition of TEA on December 31, 2009. It shows that TEA's Operating Fund totals $74,571, an increase of almost $14,000 over December 31, 2008, and TEA's Research Fund has $23,598, which represents an increase over one year ago by almost $3,000.

The second section of this financial document (the Statement of Activity) shows the sources of income during the year ended December 31, 2009, and the cash used by TEA during the same year. At the very bottom, it can be noted that income exceeded expenses during the year by about $17,000.

The largest portion of TEA's expenses went to the printing and mailing of the newsletter, a highly coveted member benefit.

*Beth serves as Treasurer and President of TEA.

Your Stories — everyone has one

Everyone can empathize with those who have experienced the long road to an EM diagnosis and live with EM's continuing challenges. Most of us have tales to tell. TEA encourages you to write your story. Then, send it to Gayla Kanaster, GaylaKanaster@aol.com or 2532 N. Fremont St., Tacoma, WA, USA 98406.

Richard Eaton writes: By the age of 13, I knew I was different. I told my doctor my feet hurt from standing. The longer I stood the worse it got. All I got was condescension and patronizing looks. It was so frustrating. At 16, working in a fast food restaurant was agony. After work I tried soaking my feet in hot water and that made it worse. But cold water! What relief!

At age 20, I tried a hot tub at my apartment complex. I could not tolerate it for 10 minutes. After I got out, an RN there noticed my "red feet" and suggested I have them checked. I dismissed it. After all, every doctor I saw told me there was nothing wrong. I joined the Navy after college and had to do a lot of standing. A Navy doctor told me I should lose weight. (I was 6' 2", 215 pounds.) Throughout my adult life, for many years working for manufacturing companies, standing was agonizing.

After four trips to the Mayo Clinic and 26 appointments spread over multiple specialties, there still was no answer. I did my own research and found TEA's website. I was a textbook case of EM, but my internist at Mayo dismissed it. Through TEA, I found and called a member in my area who recommended her doctor, Henry Brown M.D., Cape Girardeau, MO. Thanks to him, I finally got the EM diagnosis.

I put more pieces of the puzzle together and went to see Dr. Mark Davis at Mayo Dermatology, who confirmed the diagnosis of EM. Then, a focus on symptoms like progressive chronic fatigue, anhidrosis, and heat intolerance pointed to dysautonomia. I've also had multiple other health problems, including a bad bout of pneumonia, a hip replacement, two TIA's, clots in an internal jugular vein and in my right leg, and chronic urinary and upper respiratory infections. Now my primary care doctor has finally scheduled me for an autonomic nervous system screening.

I'm 51, retired, married, with two wonderful teenagers. I continue to be my own medical advocate and am thankful for the progress made possible by the great people at TEA. My heartfelt prayer is that no one needlessly suffers. I feel blessed to finally have a diagnosis.

LaVonne Taylor writes: My EM first manifested when I was about 13. I had been outside in the cool morning air and when I entered the house, my hands began to swell, tingle, itch and turn a bright red. My feet and hands continued to burn and ache frequently, but I didn't realize that it was a medical condition. I thought everybody felt like I did.

Then, one morning I awoke with a black toe. It hurt terribly – itching, burning, and aching. It turned out to be Raynaud's syndrome.

I started to suffer from severe fatigue and depression. My marriage, the care of two small children and holding down a job were often more than I could handle. As usual, the doctors of that day just sent me home with the dictum: "It's all in your head."

At about 50, I began to realize my achiness, severely sensitive feet and frequent total exhaustion were not normal. I was prescribed

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More of Your Stories

Remember, TEA encourages you to write *your* story. Send it to Gayla Kanaster, GaylaKanaster@aol.com or 2532 N. Fremont St., Tacoma, WA, USA 98406.

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tranquilizers and hormone replacement therapy. The HRT seemed to help a little, the tranquilizers not so much. My feet were still burning and stinging at night. When I first awoke each morning they felt arthritic.

I moved to another city and saw a new doctor. He started me on thyroid tablets, plus injectable HRT. That seemed to help. Later I was diagnosed with fibromyalgia. I mentioned my stinging, burning feet. He responded offhandedly, "Oh that's erythromelalgia. You can take an aspirin at bedtime for that." Pooh-pooh … it's nothing.

It's NOTHING? My whole life I've been suffering and it's NOTHING?

I treat the symptoms and try to be as kind to myself as I can be. I stay active and plan to be active for as long as I can. Mental toughness and positive outlook account for a lot. I am, in my own small way, trying to make people aware of the condition by writing about it on my health sites: www.vonnieshealthspot.com; www.everydayhealth.com/blogs/healthy-aging-and-me; and www.examiner.com/x-35227-Palmdale-Healthy-Living-Examiner

Susan Galloway writes: My EM started at night. I couldn't hold my feet still. They began to feel as if they were asleep and by the end of the day, would be swollen and bright red. I then had symptoms in my hands followed by my ears, when one would turn purple and double in size. I let this go for months, until the uncomfortable tingling in my feet moved to my ankles and I knew it was time for action.

My neurologist diagnosed primary EM in 2005 and made an appointment at the Mayo Clinic. I put my life on hold and flew from Salt Lake City, UT, to Rochester, MN, for a week of testing.

Susan Galloway

I continued to work as a senior buyer for USNANA Health Sciences for another year with unbearable pain and loss of sleep. I also had to give up tennis, swimming and most physical activities. Soon, I was in a wheelchair and on about 15 different medications. I returned to the Mayo Clinic. They put me on a cream made up of nortriptyline, ketamine, and amitriptyline. It did numb my feet, but continued use burned my skin and caused painful sores.

For a while, I saw a family counselor, which did help in handling the pain. I'm now seeing Dr. Kyle Harmon at Summit Pain Management in Salt Lake City. I've eliminated all medications except for 10.5mg methadone 3xdaily, amitriptyline and oxycodone and am trying to cut down my methadone dosage. I avoid using the wheelchair unless absolutely necessary. I've started to use the treadmill three times a week for 20 minutes and walk my two dogs a mile each day, even though painful.

Fortunately, I have my religion, and my husband and family are very supportive. I still enjoy reading, sewing and genealogy. I will never give up. Hopefully, we can all find our own way, after all, isn't that what it's all about?

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New TEA website easier for members to navigate

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addresses. These listings were transferred to the new website's member directory.

If you have not re-registered, please do so as soon as possible. Register online at the new website or mail your name, address, phone number, and e-mail address (if you have one) to Gayla Kanaster, 2532 N. Fremont St., Tacoma WA, USA, 98406.

In general, the new website should be easier to navigate for users and TEA volunteer staff alike. TEA intends to update the site more often and communicate more frequently with online members — one new feature allows TEA's president to send e-mails to the entire membership more easily.

In many ways, the new site functions much like the old. For instance, people are able to make donations using credit cards or a Paypal account, as before.

The new website also will maintain and update the archives of medical journal articles and newsletters. As before, members must sign in with their user names and passwords to access certain member-only information, like the articles and the directory.

When you re-register, you create your own member directory listing, saving time for the TEA volunteers who maintain the online member database.

When registering, you decide if you want your information to be available to other members who might search the list, or if you prefer to keep your listing private.

Members often search the member directory to find and connect with others in their geographical regions.

As always, TEA's volunteer board and staff will be accessible via e-mail and telephone, if anyone has any questions or problems navigating the new website.