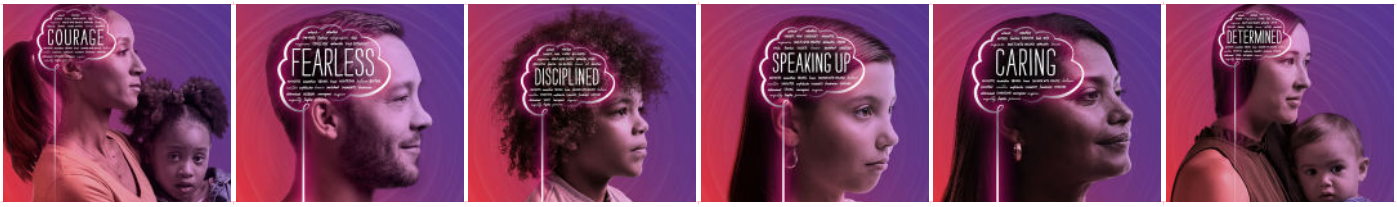
Nehemiah (Nehe) and his family are END EPILEPSY Ambassadors

RESEARCH QUARTERLY

ISSUE 14: JUNE 2020

EPILEPSY FOUNDATION | END EPILEPSY

Bliss and Mia | Jared | Nehe (see cover) | Whitney | Maribel | Katrina and Nico



Our END EPILEPSY Ambassadors and many volunteers share their stories to raise awareness and funding, and also inspire the "next generation" of our mission.

"If you can't fly then run, if you can't run then walk, if you can't walk then crawl, but whatever you do you have to keep moving forward."

~ Martin Luther King, Jr.

WELCOME

IN THIS ISSUE, we celebrate the next generation. Our cover art shows Nehe and his father Juno, who thanks to research in the ketogenic diet and the Epilepsy Foundation, have been able to achieve seizure control. We have an amazing track record in pushing the needle of possibilities for those who come after us — from supporting research since the 1960s to championing the American Disabilities Act in the 1990s and the amendments that followed. In these turbulent times, the Epilepsy Foundation stands with communities of color in the fight against inequality — from leading the conversation on how healthcare disparity in minority communities' influences epilepsy care to raising awareness about epilepsy across all cultures to reduce the stigma and discrimination. Together, we can build a safer and more positive society for all.

This past quarter has been tough. COVID-19 has impacted the lives of people with epilepsy in many ways, including reduced access to health care and treatments, loss of employment, and financial security. The Epilepsy Foundation's ability to raise funds has also been challenged and we have had to reduce our own workforce. Despite this, we are working tirelessly to ensure that the "Next Generation" of the Epilepsy Foundation continues to improve how we do our mission.

We also have new faces leading the charge of the Epilepsy Foundation's mission. Laura Thrall joined as the new President & CEO this past April. She brings over thirty years of leadership experience in the nonprofit sector. Dr. Brandy Fureman was recently promoted to Chief Outcomes Officer to ensure that we continue to be data-driven in our strategies in the public health, advocacy, and research arenas.

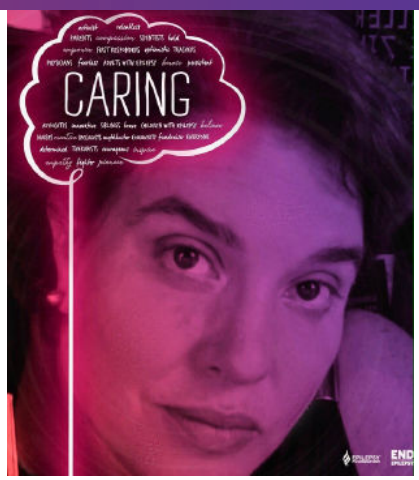
In this issue, we celebrate what the next generation will bring — from supporting the future of wearable devices by partnering with the Danny Did Foundation (page 4) to telemedicine (page 5) to our early career awardees (page 6). In late August, we will be hosting our first ever virtual Pipeline Conference, showcasing over 30 different products being developed for the next generation. Visit epilepsy.com/pipeline2020 to learn more and register.

Uncertainty is something our epilepsy community knows all too well – many of us live with not knowing when the next seizure is going to hit. COVID-19 has added more uncertainty to the mix. During these times, I am reminded of the words of Martin Luther King, Jr. "If you can't fly then run, if you can't run then walk, if you can't walk then crawl, but whatever you do you have to keep moving forward." No matter the circumstances, the Epilepsy Foundation's mission remains — to overcome the challenges of living with epilepsy and ultimately END EPILEPSY for all people.

Kind regards,

Sonya Dumanis, PhD
Senior Director of Innovation,
Research and New Therapies

HISTORY CORNER
WITH DR. ELAINE KIRIAKOPOULOS



BENZODIAZEPINES
FROM CHANCE DISCOVERY TO DRUG DELIVERY

If not for a serendipitous discovery of a class of medicines called benzodiazepines with the potent ability to stop abnormal electrical activity in the brain responsible for seizures, made by Dr. Leo Sternbach, many of the therapeutic options for epilepsy might not have existed.

In 1941, Dr. Sternbach moved to America where his company had set up a position for him as a part of the team at Roche in New Jersey. Dr. Sternbach was asked to lead the effort to bring a new tranquilizer drug targeting anxiety to market for Roche. Following his curiosity, he wondered if the chemical structure of the synthetic dye compounds he had worked on as a postdoctoral student could be altered to allow them to react with the human central nervous system.

His ingenuity and tenacity led to the 1955 discovery of the first benzodiazepine, chlordiazepoxide (Librium), and though he did not know it at the time, this would mark a major breakthrough in psychopharmacology. Testing of his newly discovered benzodiazepine compound demonstrated that along with its ability to reduce anxiety, the compound had robust effects as an anticonvulsant, muscle relaxant and sedative. He went on to discover several other benzodiazepines, including diazepam *(Valium)* and clonazepam *(Klonopin).* Over a decade after the discovery of benzodiazepines, an understanding of how they worked on the brain emerged: by increasing the power of the inhibitory effects of GABA (gabba aminobutyric acid) on neuronal excitation and decreasing the likelihood of seizure activity.

"ONLY WHEN THE SALES FIGURES CAME IN, THEN I REALIZED HOW IMPORTANT IT WAS."

Dr. Leo Sternbach

Not surprisingly, because of their potent ability to stop seizure activity, benzodiazepines became first-line treatment for the management of acute repetitive or prolonged seizures and status epilepticus. In the present-day hospital setting, benzodiazepines are routinely administered intravenously during a seizure emergency.

Most seizures occur beyond the hospital setting, so better drug delivery options are needed to help people with epilepsy manage acute seizures that happen at home and in their community. Drug delivery methods must evolve to serve the needs of caregivers at home who find themselves needing to safely administer medicine quickly, with reliable dosing and absorption.

The history of benzodiazepine delivery for acute repetitive or prolonged seizures outside the hospital setting prior to 2020 in the United States has been limited to intravenous therapy given by 911 emergency medical crew services, off-label use of intravenous form of diazepam injected rectally until its FDA approval in 1997, and a limited use of prescribed pill forms of diazepam, lorazepam and clonazepam. Since the FDA approval of rectal diazepam gel in 2005, there has been more use of this option for the treatment as abortive or rescue therapy, though limitations (social, legal) remain secondary to the invasive nature of delivery. Off label intramuscular or intranasal use of liquid intravenous formulations of midazolam have also been used.

Encouragingly, the obvious need for easily accessible and applied rescue therapies has resulted in the development of innovative drug delivery for benzodiazepines. In 2019 the FDA approved the use of midazolam intra nasal spray *(NAYZILAM®)* as a rescue therapy, and in 2020 the intranasal diazepam spray *(Valtoco®)* was also approved by the FDA and has recently become available for prescribed use. A novel diazepam buccal film *(Libervant)* has shown early promise and is also currently pending FDA approval.

1. Obituary, Leo Sternbach, The Lancet. Vol 366. Oct. 22, 2005.
2. Leo Sternbach, Transcript of an Interview Conducted by Tonja Koeppel at Hoffmann-La Roche Inc. Nutley, New Jersey on 12 March 1986 Philadelphia: Science History Institute, Oral History Transcript #0043

Danny Did

ONE BOY'S IMPACT CARRIES FORWARD

By Tom Stanton, CEO of Danny Did Foundation

Go to DannyDid.org to learn more

In the summer of 2009, Danny Stanton was known as the "little mayor" of Leona Avenue on Chicago's Northwest Side. There, on that street where he lived his whole life, Danny befriended everyone, from fellow four-year-olds to adult neighbors. As the third of four siblings, his place in the world was happy, safe, and adventurous all at once.

His only deviation from good health was his epilepsy. Danny had his first seizure at age 2. Over the next two years, his parents witnessed four seizures, all while Danny was sleeping. Then one morning in December, Danny's mom and dad found him lifeless in his bed. They had never been told that someone could die from a seizure. They only learned of this possibility from the death certificate, which listed Danny's cause of death as sudden unexpected death in epilepsy (SUDEP).

A Movement Begins

After Danny died, his parents established the Danny Did Foundation in 2010 with the mission to prevent deaths caused by seizures. Danny Did exists to help keep people alive until the ultimate solution — cures for epilepsy — is achieved. The foundation's name comes from the last line of Danny's obituary: "Please go and enjoy your life. Danny did."

Our impact has been fueled by partnerships. Over the past decade, our relationships with Partners Against Mortality in Epilepsy (PAME), the Epilepsy Foundation's SUDEP Institute, the Epilepsy Foundation's Pipeline Conference, and Epilepsy Awareness Day at Disneyland have connected thousands of patients and caregivers to critical provider, research and advocate resources.

Intervention Matters

Even though seizures pose a range of life-threatening risks – falling, drowning, cardiac arrest, status epilepticus, SUDEP, suffocation – patients and parents learn little about these risks, nor how to mitigate them. Like other epilepsy organizations, we are committed to changing this through education.

But Danny Did also champions knowledge about, and access to, seizure alerting devices. We know people with epilepsy regularly experience intensive, continuous monitoring in a hospital, only to return home to the cold comfort of a baby monitor. Families and patients need guidance when seeking alternatives. We provide accessible, objective information about technologies that can detect seizures, and alert for help. And, because insurance rarely covers the expense of these devices, we fund grants to support their purchase.

The Device Pipeline

Non-invasive devices for epilepsy are in their relative infancy, but the pipeline is maturing.

Not long ago, the vision of the future was a device that could alert a caregiver to a movement-based seizure. Now, that simply isn't enough.

People who experience multiple seizure types want a system that can alert to all. The next generation of devices will be multimodal, able to detect a range of indicators for seizure activity, such as changes in heart rate or respiration. Beyond even detection and alerting, we believe seizure prediction is realistic in the near future. The Holy Grail is prevention: a system that predicts a seizure and supplies an intervention to stop it.

To foster successful device companies in the epilepsy space, Danny Did is teaming with the Epilepsy Foundation's Innovation Institute to host a product accelerator course in August. Device makers will receive expertise, coaching and feedback. As this industry strengthens, patients and caretakers will gain more effective options to choose from.

Our Vision

Until insurance coverage is a reality, Danny Did is bridging awareness gaps by educating families about their device options, and filling gaps in access by funding grants for families who cannot afford one. It is our purpose to do like Danny did.

Improving Telehealth Practice for Epilepsy

By Kathleen Farrell, MB BCh BAO, Senior Director of Clinical Research

Telemedicine or telehealth visits use audio and video to connect you to your healthcare provider in their office. These are sometimes called "virtual visits." You can see, hear, and talk to your provider, just like you do in the office. The telehealth appointment is private, using secure software to make the connection. You can also have a family member or friend accompany you during the visit, and you are billed for the visit the same as if you were seeing your healthcare provider in person.

While telemedicine was practiced sporadically over the last number of years, perhaps no circumstance could have accelerated its broader application quite like the COVID-19 pandemic. Suddenly, clinic appointments have transitioned to the virtual setting for nearly all non-urgent cases.

Clinicians and patients alike are quickly learning how to use telemedicine platforms (varying widely by practice and region). They are also learning about the mechanics of a virtual visit and how to not only complete the visit but ensure that it is a success.

The scope of considerations and worries is vast. Some of the concerns the Epilepsy Foundation has heard from patients and providers include:

- I don't have a smartphone or computer. What are the other options?
- I am a non-English speaker or am deaf. How will I give or receive the information I need virtually?
- Will my insurance cover this?
- Will I be reimbursed?
- I feel less connected to my patient when we're not in the same room. How can I be clear on important things to share?

The Epilepsy Learning Healthcare System (ELHS), an initiative of the Epilepsy Foundation, includes 12 epilepsy centers in both pediatric and adult practices. Data is captured in an organized way at every clinical encounter and real-time improvements are adopted by providers to improve the standard of care for all people living with epilepsy.

Since the outbreak of COVID-19, these centers have created a Telemedicine Workgroup with the goal of increasing the percentage of telemedicine visits completed by ELHS sites for patients with epilepsy from the pre-COVID-19 rate to 80% by August 1, 2020. In parallel, the ELHS Community Core, comprised of patient family partners (PFPs), rare and local epilepsy organizations, have created a checklist tool for use by people with epilepsy preparing for a telemedicine visit. Gathering follow-up data via community survey will allow testing of modifications to improve outcomes and ensure that epilepsy community members have the best resources at hand.

- Download and use the Telemedicine Visit Preparedness Checklist here: English language version & Spanish language version
- To test and modify this tool to make it most useful, anyone who uses it is asked to please complete a very brief evaluation survey here.

Learn more at epilepsy.com/elhs and become a partner in the mission: all people living with epilepsy will live at their highest quality of life, striving for freedom from seizures and side effects, and we won't stop until we get there.

Please contact Senior Director of Clinical Research, Dr. Kathleen Farrell kfarrell@efa.org for any questions pertaining to ELHS.

Next Generation Scientist Awards

Our Epilepsy Foundation (EF) is proud to partner with American Epilepsy Society (AES), American Brain Foundation, and the American Academy of Neurology to attract and fund some of the best and the brightest in the field.

Since the 1960s, the Epilepsy Foundation has supported the careers of over 3,000 researchers.

Meet the Foundation supported awardees for this year!

AES/EF Junior Investigator Award

Leah Blank, MD, MPH
Icahn School of Medicine at Mount Sinai
Determinants of Guideline Adherent Therapy in Newly Diagnosed Epilepsy

Although national and international societies have made evidence-based recommendations supporting the use of newer anti-seizure drugs with demonstrated efficacy and decreased side effects, these same drugs are often not prescribed. Instead, for reasons that remain unexplained, older anti-seizure drugs with serious side effects are still often used as first line agents in adults with new onset epilepsy.

Dr. Leah Blank will use detailed medical record data from the Mount Sinai health system to understand the patient, practice, and provider characteristics that might influence first drug choice for adults with new onset epilepsy. For example, does the insurance type or care setting impact who gets on which medication first? Dr. Blank will then use national data to determine the effect that these choices have on patient outcomes overall, including drug discontinuation (how long they remain on that first-choice drug) and health care utilization (how likely are they to be seen in the emergency room).

This study will lay the groundwork for the development of an intervention targeted at ensuring that those with new onset adult epilepsy are getting to the right treatment faster.

AES/EF Junior Investigator Award

David Klorig, PhD
Wake Forest University Health Sciences
Evaluating Gene Therapy Strategies to Treat Epilepsy Using a Novel Method

When developing a gene therapy strategy, one wants to know quickly if the treatment worked. Dr. Klorig has developed a new experimental tool that allows him to measure seizure susceptibility in animal models based on brain activity measurements, to quickly assess whether previous impaired brain activity is repaired. He now wants to test whether this tool can be used as an outcome for optimizing gene therapy strategies in epilepsy.

For this effort, he is going to test two different gene therapy strategies involving the potassium channel Kv1.1. The two strategies focus on targeting the gene therapy to different types of brain cells (neurons versus astrocytes). Using his new tool, he can then see how brain activity changes with these two different approaches, and which one will be better for repairing brain activity. This work will reveal important information about how these different brain cells impact seizure susceptibility and could also develop a new way to inform strategy for epilepsy gene therapies in the clinic.

Leah Blank, MD, MPH

David Klorig, PhD

Colin Ellis, MD

Susanna O'Kula, MD

Susan Spencer Clinical Research Training Fellowship

cosponsored by the American Academy of Neurology, the American Brain Foundation, the American Epilepsy Society, and the Epilepsy Foundation

Colin Ellis, MD
University of Pennsylvania
Polygenic Risk Transmission in Familial Epilepsy

There has been substantial progress over the past decade in identifying monogenetic causes of epilepsy. Monogenetic means that the cause of the epilepsy is linked to one gene. However, there is a lot of evidence that many epilepsy cases could be polygenetic, meaning that there are multiple genes involved. For example, there are studies in large families where epilepsy is more common than the general population, but there does not seem to be one key gene that is explaining why that is the case.

Recently, polygenic risk scores were developed for epilepsy that looked at multiple common variants associated with epilepsy across the board. Dr. Ellis will be assessing the polygenic risk scores for two large families where epilepsy seems to be fairly common, to test whether those that have epilepsy have higher risk scores, and whether tweaks to the mathematical modeling for calculating the score improve the algorithm for determining who in the family is likely to develop epilepsy.

AES/EF Clinical Research Training Apprenticeship

Susanna O'Kula, MD
New York University
Healthcare Utilization & Workplace Productivity in Hispanic PWE

Depression affects up to 55% of people living with epilepsy. It is associated with diminished quality of life, worsened seizure control, and an increased risk of premature mortality due to suicide. Unfortunately, depression is often under-diagnosed and left untreated in people living with epilepsy. In under-served communities, there are increasing challenges due to disparities in access to care, language barriers, discrimination and low socioeconomic status.

Dr. O'Kula wants to better understand how depression impacts Hispanics living with epilepsy and to create culturally tailored interventions to address depressive symptoms in this community. A telephone-delivered, group mindfulness-based program (UPLIFT, Using Practice and Learning to Increase Favorable Thoughts) has shown promise in treating depression in people living with epilepsy. This study will evaluate how this program improves workplace productivity and use of healthcare services in Hispanics living with epilepsy enrolled in the program. Dr. O'Kula will also run focus groups to identify barriers and in a follow-on study will test whether addressing those barriers improved outcomes from this initial study.

The overarching goal is to improve quality of life and health of those living with epilepsy, ensuring that appropriate outreach care strategies are used.

THINK BIG with Dr. French

EPILEPSY RESEARCH AND COVID-19

Probably many of you have heard on the news that there are a lot of clinical trials in progress to treat coronavirus and COVID-19. Most big medical institutions have pivoted their research endeavors (both in the laboratory and in the clinic) to focus on COVID-19, our current biggest threat. It might seem that research in other areas has stopped. However, despite all this new activity, epilepsy research has not stopped.

For example, most of the volunteers who already enrolled in epilepsy clinical trials before the COVID disruption were able to continue through video and telephone visits with clinical researchers. Just as people with epilepsy have been discouraged from physically visiting the clinic, in-person clinical research visits have also halted, due to the risk of coronavirus contamination at hospitals. These visits are also being restricted due to the fact that in some locations doctors have to help out in hospitals with overwhelming number of patients with COVID-19.

Starting in May, many hospitals stabilized and started to re-open their clinics. They are doing this very carefully, making sure that the environment is extremely safe. It is very likely that this will allow centers to begin recruiting new patients into clinical trials once again.

Also, while academic research labs have been shut down all over the world for the last few months, they are starting to ramp up again, and will probably be in full swing by mid-summer. Many safeguards have been put into place to ensure that the researchers have a safe environment to work in.

In the meantime, these researchers have used this time to evaluate and publish their data, contemplate new ideas, and innovate new strategies to move forward. Several new potential therapies have started the path towards the clinic and will probably be entering into trials shortly.

There are many reasons to feel extremely hopeful about the future of new therapies for epilepsy.

Featured on Cover

NEHEMIAH (NEHE) AND HIS FAMILY SHARE THEIR STORY TO RAISE AWARENESS AND FUNDING TO END EPILEPSY.

Since Day 1 of his first seizures, Nehemiah's parents have been actively advocating for him. But they haven't stopped there. They've faithfully embodied and lived the spirit of END EPILEPSY — locally in Los Angeles and nationwide — by sharing their story, learning more about epilepsy and treatments, participating in camps and conferences to connect to resources and others, arranging for Nehe's school to be trained in Seizure First Aid, and fundraising with their team for the Walk to END EPILEPSY. Nehe has benefited from programs of the Epilepsy Foundation Greater Los Angeles. Care & Cure's funding to establish Dietary Therapy Programs in three hospitals in LA made it easier for Nehe's family to access this treatment — and Nehe ultimately gained seizure control with the ketogenic diet administered attentively by his Dad. They have **benefited from research and given back to research** — as their story continues to raise awareness and funding to END EPILEPSY.

THE SUDEP INSTITUTE

Biomarker Challenge

Each year, more than 1 out of 1,000 people with epilepsy die from sudden unexpected death in epilepsy (SUDEP). If seizures are uncontrolled, the risk of SUDEP increases to more than 1 out of 150. SUDEP is the leading cause of death in young adults with uncontrolled seizures.

Among the 65 million people worldwide living with epilepsy, nearly one-third have ongoing seizures despite existing therapies.

To accelerate the identification of effective treatments for SUDEP, the Epilepsy Foundation SUDEP Institute is sponsoring a $1 million challenge to develop a predictive biomarker to identify people at risk for SUDEP. If we can know who is at risk, we can develop prevention strategies and intervene before it is too late.

With the help of our partners at InnoCentive, all of the challenges allow us to take advantage of interdisciplinary approaches and alternative perspectives. Through combining and contrasting ideas, the best and most valuable solutions will be identified and financially supported.

PLEASE CONSIDER DONATING

to funding the winning solution – it will be a win for ALL who have a loved one living with epilepsy.

Please, help us reach for the stars now by investing in this winning solution - and help us save lives.

EPILEPSY FOUNDATION | SUDEP INSTITUTE

CHALLENGES TO DATE:

Challenge 1: Advocacy Campaign
Empowering people with epilepsy, $15k awarded

Challenge 2: Self Management Tools
Preventing epilepsy seizures, EpSMon (Epilepsy Self-Management) mobile app created

Challenge 3: Identifying Potential Biomarkers
Predictive biomarkers of epilepsy seizures, $75k awarded

Challenge 4: Bringing Biomarkers to Clinical Practice
Developing predictive biomarkers of SUDEP

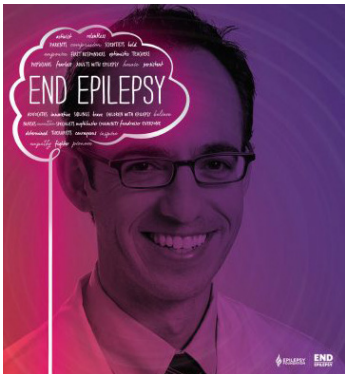
- **Milestone** Project plan, $40K awarded
- **Milestone** Proof of concept, $80K awarded
- **Milestone** Validation data in humans of predictive value for SUDEP $800,000 prize

The Final Milestone of our Final Challenge is live now and open until October 10, 2020!

Biomarkers may be genetic, structural within the body, metabolic, physiological, or something else that is quantifiable.

The winning biomarker will be easily and safely measured, cost-efficient to detect, modifiable with intervention (something we can actively treat or prevent), be consistently associated with SUDEP or life-threatening seizures, and will drive human intervention. For example, the biomarker may identify a high-risk patient group to allow testing of existing interventions such as seizure detection devices.

Learn more go to epilepsy.com/sudep



Innovator Spotlight

MEET DR. SHAUN A. HUSSAIN

The Epilepsy Foundation believes in attracting the next generation of talented clinicians and researchers to tackle the challenges our community faces. This month we sat down with Dr. Shaun A. Hussain, Director of the UCLA Infantile Spasms Program at UCLA Mattel Children's Hospital. Dr. Hussain was an Epilepsy Foundation Care & Cure specialist in 2007.

Q: What made you interested in epilepsy?
A: Although I was always interested in neurology and the brain, my interest in epilepsy was cemented as a medical student. I was struck by how devastating seizures and epilepsy can be. It is not just that individual seizures are scary or dangerous. The sheer unpredictability is particularly unsettling. The exposure to children who were devastated by seizures — and others who were cured — made a lasting impression on me. At the same time, there is a lot of movement going on in the scientific space, making the field an incredibly dynamic place to work. I was drawn to both the promise of what could be done and the potential impact that I could personally make.

Q: What made you focus on Infantile Spasms?
A: The unmet needs for treatment of infantile spasms is extraordinary. These seizures occur early on in life and are especially harmful to the developing brain. Around 10-15% of kids diagnosed with infantile spasms die by the age of two years, due to sudden unexpected death in epilepsy (SUDEP) or lethal infections caused by the condition. At the same time, 20% of children with infantile spasms can be cured. This extreme contrast inspires both fear and hope. The desperate need for new treatments that are both effective and safe was — and is — obvious.

Q: What did the Epilepsy Foundation Care & Cure Fellowship allow you to do?
A: The early support from the Epilepsy Foundation of Greater Los Angeles supported my pediatric training in pediatric neurology and epilepsy. The fellowship gave me the protected time and support to set up the Infantile Spasm Project at the David Geffen School of Medicine and Mattel Children's Hospital at the University of California, Los Angeles (UCLA).

Q: What is the Infantile Spasms Project?
A: The goal is twofold: education and medical discovery. First, awareness is critical. Most people have never heard of infantile spasms, and most pediatricians struggle to remember what they might have learned about it in medical school. Infantile spasms are rare and the average pediatrician will only encounter two or three new cases in their career. This knowledge gap — paired with the observation that diagnostic delays of as little as a week harm long-term development — is a recipe for disaster.

Foremost, I wanted our website (https://www.InfantileSpasmsProject.org) to be a resource for parents to quickly figure out what infantile spasms are, and facilitate their access to effective care. Second, we are spearheading research efforts to better understand the disease, and our primary mission is to identify promising new treatments and move those therapies from the laboratory to human clinical trials.

Care & Cure was launched over 15 years ago by the Epilepsy Foundation of Greater LA with the primary mission of funding the training of pediatric epilepsy fellows. Care & Cure is now going nationwide. Want to support the initiative in your local area? Contact donate@efa.org.

Q: For the awareness goal, what should people know about Infantile Spasms?

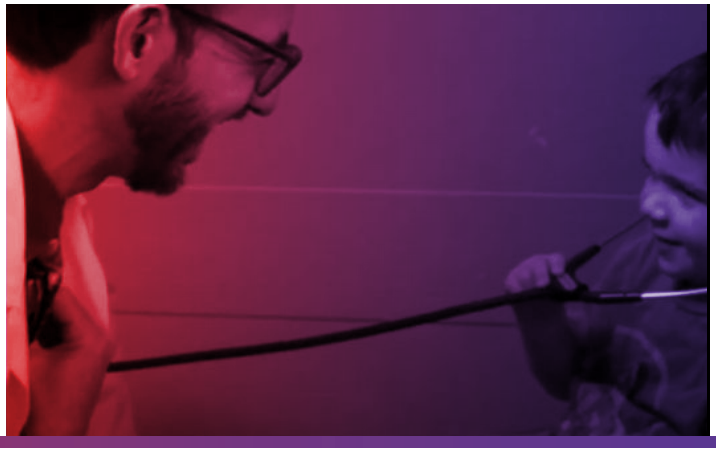
A: Infantile spasms usually begin between 4 and 8 months of age. The baby might have a subtle shrug, or a head drop. There could be a momentary wide-eyed stare. This behavior — "the spasm" — will recur every 5 to 10 seconds in discrete clusters lasting several minutes. The clusters most often occur upon awakening. A big problem for us is that normal babies make lots of weird movements, so it might not be that obvious when it happens if you do not know what you are looking for. It is tempting and easy — even for healthcare providers — to dismiss infantile spasms as normal behavior. Too often, parents tell us that they had a gut feeling that something wasn't quite right, but as first-time parents they also didn't know if they were overreacting. You can go to infantilespasmsproject.org and see video examples. Although infantile spasms are a rare condition impacting 1 in 2,500 infants per year, we want to make sure that everyone knows the signs.

Q: For the research component, what should people know?

A: There are a lot of unknowns but there is also a lot of hope in the field. The biggest problem is that our standard therapies are simply inadequate. The only work about half the time, they are incredibly expensive (one in particular costs about $150,000 per patients), and they are highly toxic, with side effects including potentially fatal immunosuppression and vision loss. Fortunately, there are now a dozen drugs that are moving out of the lab and into early stage clinical trials. For example, researchers are testing whether cannabidiol (CBD) or fenfluramine (fintepla) are effective treatments, to name a few.

Q: Is there anything else that people should know?

A: I am incredibly grateful to the Epilepsy Foundation for their support. Their early support provided the foundation for not only my career, but also many of my colleagues who are now working on solving infantile spasms with me. Thank you for that support and thank you for the commitment that you provide to early careers — it is more impactful than you might realize.



The Quarterly Pipeline Report for March – June 2020

By Sonya Dumanis, PhD, Senior Director of Innovation

As we think about the next generation of therapies, we wanted to also add a quarterly pipeline report to update the community on the next generation of treatments moving through the epilepsy pipeline. Here was the news from the past three months.

CLINICAL TRIAL RESULTS

- Engage Therapeutics announced positive results for its Phase 2b StATES study of Staccato® alprazolam, an orally inhaled therapy designed to terminate an active epileptic seizure. Their findings suggest that Staccato alprazolam can not only abruptly terminate the seizure that is happening (within 2 minutes) but that they also prevent the occurrence of any other seizure for the next 2 hours! Read the press release.
- Ovid Therapeutics had promising initial data from their Phase 2 open-label ARCADE study of soticlestat (OV935/TAK935) in patients with CDKL5 deficiency disorder (CDD) and Dup15q syndrome (Dup15q). The early data demonstrate that soticlestat, a potent, highly selective, first-in-class inhibitor of the enzyme cholesterol 24-hydroxylase (CH24H), shows a reduction in seizure frequency compared to baseline levels in individual patients. Read the press release.
- UCB gave an update on their Phase 2b padsevonil safety and efficacy study in epilepsy (ARISE). Although Padsevonil was well-tolerated, unfortunately, the trial did not meet its primary clinical endpoints of reducing seizure frequency in adults with treatment-resistant focal-onset seizures. Read the press release.

DEA SCHEDULING

- XCopri, a new drug for focal epilepsy that was approved in late November 2019, just got its Drug Enforcement Agency (DEA) Scheduling. The medication was listed as a Schedule V, the lowest designation for abuse. This was the last step needed before the drug could get onto the US market. Stay tuned. Read the press release.

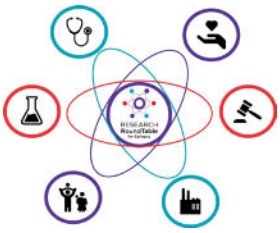
ON THE MARKET

- Valtoco, a diazepam nasal spray intended to treat seizure clusters for those that are 6 and up, in seizure emergencies in patients 6 years of age and older, is now commercially available in the US. Read the press release.

MERGERS AND ACQUISITIONS

- In June, UCB acquired Engage Therapeutics, Inc. (Summit, N.J. (U.S.)), a clinical-stage pharmaceutical company developing Staccato® Alprazolam for the rapid termination of an active epileptic seizures. Read the press release.

Learn more about the Pipeline at **epilepsy.com/pipeline**



Research Roundtable Report

Regulators recommend that sponsors engage with the agencies early in development to discuss options for electronic seizure diaries.

The Research Roundtable for Epilepsy (RRE) is an initiative of the Epilepsy Foundation to facilitate the development and implementation of new treatments and diagnostic tools for people with epilepsy, by collectively addressing roadblocks to research and development. Each roundtable focuses on a single critical issue and allows an in-depth discussion in a pre-competitive space.

The 2020 RRE went virtual on May 14-15, convening researchers, people living with epilepsy, 22 drug and device companies and regulators from the FDA and others for discussions. There were two topics this year. The first was "Approval for focal epilepsy drugs for infants" and the other was "Innovative data capture, including electronic seizure diaries."

At present, anti-seizure medications (ASMs) approved for focal epilepsy in adults can have efficacy from those trials extrapolated to the age 2 years, and can receive FDA approval with addition of only safety and pharmacokinetic data. Regarding infantile seizures, a major question is whether they are a separate entity analogous to the way neonatal seizures are a separate entity, or do infants have focal seizures that are similar to older age groups. And if they exist in a similar fashion, can data from older age groups also be extrapolated down to the 1 month to 2-year population to inform treatment choices. Pediatric epileptologists and researchers shared data demonstrating that the clinical picture of the way focal seizures begin and evolve, their characteristics and symptoms, EEG features and treatment response are similar to that of older children. These data support the possibility that no separate efficacy trials (which would be very difficult to accomplish) would be needed for these young children. In these circumstances, evidence of safety would need to be independently established in the infant age group and could not be extrapolated. If efficacy extrapolation is not possible, there are potential clinical trial designs to reduce or eliminate the need for a placebo group (where a person participating in the trial receives only the standard of care treatment, rather than the experimental treatment plus standard of care, and may experience a worsening of their seizures), for example a PK/PD design.

The group discussed special safety issues in children. The risks of evolution from focal seizures to infantile spasms and other seizure types or syndromes cannot be discounted, although to date there is no indication that specific drugs increase this risk. Cognition is a safety issue of particular importance in infants.

The second part of the meeting focused on electronic seizure diaries: their current use in clinical trials, barriers to completion, and possible alternatives or options to broaden their use. Regulators recommend that sponsors engage with the agencies early in development to discuss options for electronic seizure diaries. People living with epilepsy and caregivers shared their experiences, including their preference for a longer window for completion of seizure documentation (up to a week after the event, rather than the typical 1-2 days), and their reasoning for using various tracking tools such as spreadsheets rather than a particular digital diary tool. Industry members expressed willingness to collaborate to explore the potential of a standardized, more user-friendly seizure diary option.

A manuscript is in preparation, and planning is already underway for another successful RRE meeting in 2021, with the topic to be defined soon.

Learn more about the RRE here or email Dr. Kathleen Farrell, Senior Director of Clinical Research at kfarrell@efa.org.

Epilepsy Foundation Supported Publications

FACTORS ASSOCIATED WITH CAREGIVER SLEEP QUALITY RELATED TO CHILDREN WITH RARE EPILEPSY SYNDROMES

The Epilepsy Foundation is a proud founding partner of the Rare Epilepsy Network (REN), a coalition of more than 30 different rare epilepsy organizations initially coming together to collect data across 40 rare epilepsy diagnoses including affected person demographics and family history, caregiver demographics and quality of life, seizure characteristics, diagnostic history, development and phenotypic characteristics, comorbidities, treatments and more. A recent publication based on REN data is "Factors Associated with Caregiver Sleep Quality Related to Children with Rare Epilepsy Syndromes," published in The Journal of Pediatrics in May 2020. That publication is available here.

Learn more about REN, view the data Dashboard and make research requests to gain insights into the rare epilepsies at www.epilepsy.com/ren

FORECASTING CYCLES OF SEIZURE LIKELIHOOD

The Epilepsy Foundation's My Seizure Gauge Initiative wants to create a seizure forecasting tool. Recently, Dr. Pip Karoly published her work that looked at whether data in seizure diaries could be used to forecast the likelihood of when future events would occur. The goal is to create personalized forecasting from mobile seizure diaries. Check out the publication here.

CRITICAL SLOWING DOWN AS A BIOMARKER FOR SEIZURE SUSCEPTIBILITY

The authors looked at recorded long term brain signals to understand what features in the signal could be used as reliable warning signals before a seizure. They write about a feature known as "critical slowing" that was observed and how it can be incorporated into seizure forecasting algorithms. This work was supported by the Epilepsy Foundation's My Seizure Gauge Initiative. Check out the publication here.

Upcoming Research Grants

SUDEP BIOMARKER CHALLENGE

> Submissions open now
Prize for $800,000
www.epilepsy.com/research

DRAVET SYNDROME FOUNDATION RESEARCH GRANTS FOR POSTDOCTORAL FELLOWS

> Submissions open August 21, 2020
Up to $50,000 for 1 year
https://www.dravetfoundation.org/research-grant-awards/

DRAVET SYNDROME FOUNDATION RESEARCH GRANTS FOR CLINICIANS AND ESTABLISHED INVESTIGATORS

> Submissions open August 21, 2020
Up to $150,000 over 2 years
https://www.dravetfoundation.org/research-grant-awards/

DO YOU HAVE QUESTIONS OR A RESEARCH FUNDING OPPORTUNITY TO SHARE? EMAIL GRANTS@EFA.ORG

WANT TO DONATE FUNDS TO RESEARCH? GO TO: DONATE.EPILEPSY.COM/DONATE-RESEARCH

LEARN MORE ABOUT THE EPILEPSY FOUNDATION'S RESEARCH PRIORITIES AT EPILEPSY.COM/RESEARCH

Clinical Trial Portal List

Clinical trials are the way new treatments are tested for safety and effectiveness before being approved and made available to people with epilepsy.

Go to **EPILEPSY.COM**/clinical_trials to learn more.

Rare Epilepsy Syndrome Trials

CANNABIDIOL AS AN ADD-ON THERAPY IN TUBEROUS SCLEROSIS COMPLEX

This study is looking at how effective and safe cannabidiol (CBD) is in people 1 year to 65 years old living with Tuberous Sclerosis Complex (TSC). CBD is given in addition to their current anti-seizure medications.

PREVENTING EPILEPSY USING VIGABATRIN IN INFANTS WITH TUBEROUS SCLEROSIS COMPLEX

This Phase IIb trial will test whether earlier treatment versus standard treatment with vigabatrin in infants with tuberous sclerosis complex (TSC) will have a positive impact on developmental outcomes at 24 months of age. It also tests whether early treatment prevents or lowers the risk of developing infantile spasms and refractory seizures. It is a randomized, double-blind, placebo-controlled clinical trial design. Infants under the age of 6 months diagnosed with TSC but without history of seizures or infantile spasms may be eligible.

FOCUSED ULTRASOUND FOR TREATMENT OF EPILEPSY

The University of Virginia Comprehensive Epilepsy Program is conducting a research study on the use of focused ultrasound to treat deep lesions in the brain causing intractable epilepsy in adults 18 to 80 years old. The study will evaluate the effectiveness and safety of an investigational device that uses ultrasound or sound waves from outside the head to treat seizures that are not well controlled by medication and are due to a small growth of abnormal cells in the middle of the brain, most commonly hypothalamic hamartomas.

PERAMPANEL STUDY FOR INFANTS WITH EPILEPSY

This clinical research study is being done to learn more about the safety of Perampanel (E2007), the study drug, and how well it's tolerated in infants, from 1 month to less than 24 months old (<2 years), who have epilepsy.

Focal (Partial-Onset) Seizures Trials

XEN1101 AS ADJUNCTIVE THERAPY IN FOCAL-ONSET EPILEPSY, WITH AN OPEN-LABEL EXTENSION

Do you still experience seizures despite taking medications for your focal-onset epilepsy? Xenon Pharmaceuticals Inc. is enrolling adult patients with focal-onset epilepsy into a clinical trial for XEN1101, a novel investigational anti-seizure medication. The study drug is taken once a day and study subjects will continue taking their prescribed epilepsy medications during the trial.

ESLICARBAZEPINE ACETATE (ESL) AS FIRST OR LATER ADD-ON THERAPY FOR THE TREATMENT OF PARTIAL-ONSET SEIZURES

This study is looking at how effective and safe eslicarbazepine acetate (also known as ESL) is in people 18 years of age or older with partial-onset (focal) seizures, when it is added to their current anti-seizure medication(s).

PFIZER A0081096: LOOKING FOR CHANGES IN EYESIGHT FROM USING PREGABALIN

This study will look at people between 18-65 years old, taking their own anti-seizure medications in addition to either the study drug (Pregabalin) or a placebo. The aim is to look for changes in eyesight.

EPILEPSY FOUNDATION'S HUMAN EPILEPSY PROJECT (HEP2): RESISTANT FOCAL SEIZURES STUDY

This study, the Human Epilepsy Project 2: Resistant Focal Seizures (HEP2) is designed to better understand the challenges of living with focal seizures that do not respond to medication and determine biomarkers of epilepsy severity and treatment response.

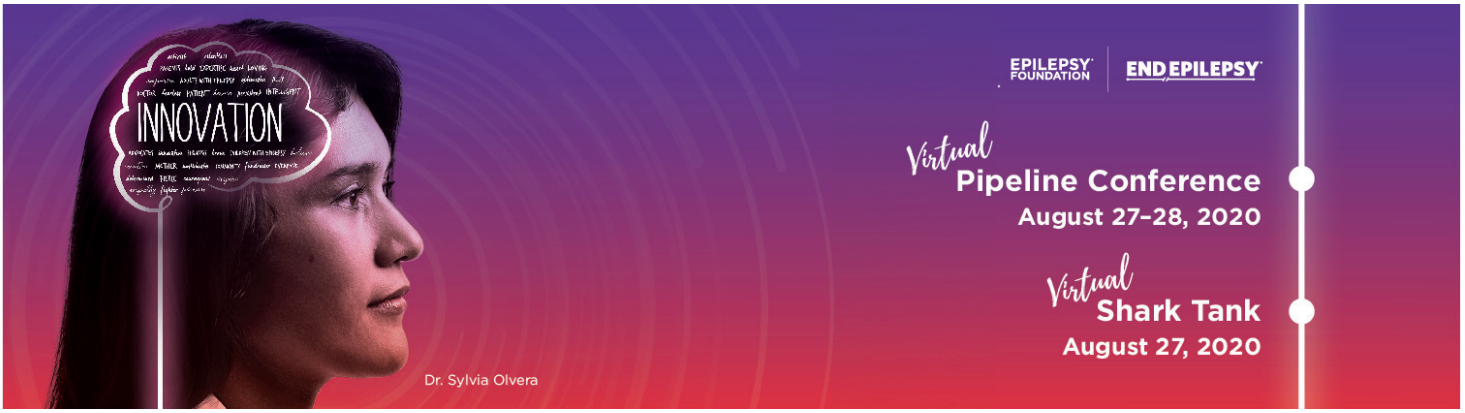
Focal or Generalized Seizures Trials

STEREOTACTIC LASER ABLATION FOR TEMPORAL LOBE EPILEPSY (SLATE)

This study is looking at the safety and efficacy of MRI-guided laser ablation therapy with Visualase™ (laser ablation may also be called laser interstitial thermal therapy or LITT) for seizures coming from the temporal lobe in people who are taking seizure medicines.

EFFECTIVENESS OF INHALED STACCATO ALPRAZOLAM IN TREATING AN EPISODE OF FOCAL OR GENERALIZED SEIZURES

A new clinical trial is looking at how effective and safe orally-inhaled alprazolam (also known as STAP-001) is in people 18 years of age or older with focal or generalized epilepsy when given at the time of a seizure episode. This study is commonly referred to as StATEs (Staccato Alprazolam Terminates Epilepsy Seizures).



Upcoming Conferences

VIRTUAL FIFTEENTH EILAT CONFERENCE ON NEW ANTILEPTIC DRUGS & DEVICES
New Antiepileptic Drugs • July 27–30, 2020
Devices • August 3, 2020
eilatxv.com/

VIRTUAL PIPELINE CONFERENCE
August 27–28, 2020
epilepsy.com/pipeline2020

INNOVATION AND ACTION TO END EPILEPSY® Community Day Conference goes Virtual
August 29, 2020
epilepsy.com/communityday2020

PARTNERING AGAINST MORTALITY IN EPILEPSY
December 3–4, 2020
https://pame.aesnet.org/

AMERICAN EPILEPSY SOCIETY MEETING
December 4–8, 2020
https://meeting.aesnet.org/

CURING THE EPILEPSIES: SETTING RESEARCH PRIORITIES
January 4–6, 2021 • Bethesda, MD
ninds.nih.gov

Have a conference that you want to share? Email **CONTACTUS@EFA.ORG**

TAKE THE SURVEY

NIH-supported research survey to examine impact of COVID-19 on rare diseases community

A new online survey launched by the National Institutes of Health-supported Rare Diseases Clinical Research Network (RDCRN) aims to find out how the COVID-19 pandemic is impacting individuals with rare diseases, their families and their caregivers. Results will help the rare disease research community shed light on the needs of people with rare diseases during the COVID-19 pandemic and other potential health crises, in addition to informing future research efforts. More information here: https://www.rarediseasesnetwork.org/COVIDsurvey

Remembering Charlotte Figi

In April, Charlotte Figi, age 13, passed away. She was the namesake for an early varietal of low-THC, high-CBD medical cannabis (Charlotte's Web). Her success on the treatment launched a movement that led to sweeping changes in medical cannabis laws across the globe. Our heart goes out to her family. Her legacy has made an incredible impact in the epilepsy community and she will not be forgotten. Charlotte's life and tragic early death remind us again of the importance of our mission.

Mission

Epilepsy Foundation is a nationwide network organization on a mission to lead the fight to overcome the challenges of living with epilepsy and to accelerate therapies to stop seizures, find cures, and save lives.

We're mobilizing action to **END EPILEPSY.**