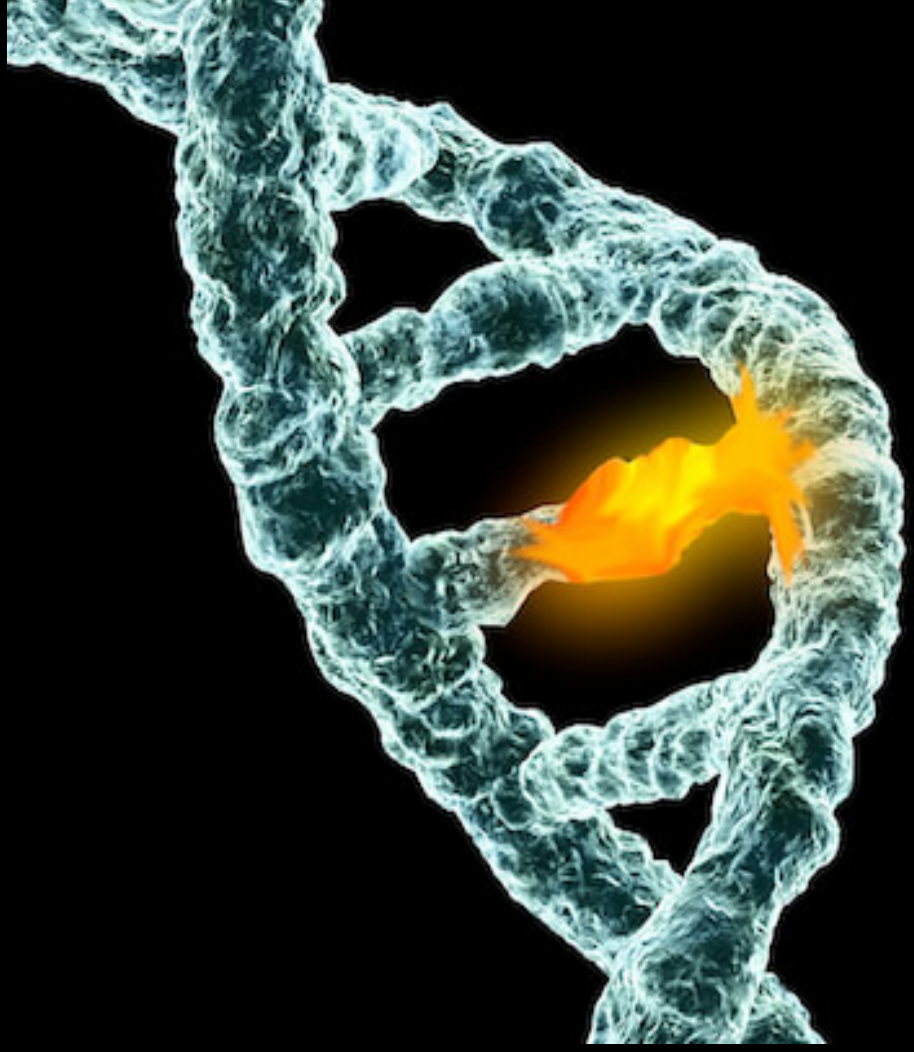


2018 – 2019
YEAR IN REVIEW

THE LATEST IN RESEARCH IN FAMILIAL DYSAUTONOMIA

NYU CENTER FOR Dysautonomia

A MESSAGE FROM OUR DIRECTOR

Over the last 12 months, the Center's research efforts have continued us on the path of finding better treatments. There has never been a more exciting time when it comes to developing new therapies for neurological diseases. In other rare diseases, it has been possible to edit genes, fix protein production, and even cure illnesses with a single infusion. These new treatments have been accomplished thanks to basic scientists and clinicians working together.

Over the last 11-years, I have watched the Center grow into a powerhouse of clinical care as well as research built on training, learning, and collaboration. The team at the Center has built a research framework on an international scale, which means no patient will be left behind when it comes to developing treatments. We now follow patients in the United States, Israel, Canada, England, Belgium, Germany, Argentina, Brazil, Australia and Mexico. The natural history study where we collect all clinical and laboratory data is helping us design the trials to get new treatments in to the clinic as required by the US Food and Drug Administration (FDA).

In December 2018, I visited Israel to attend the family caregiver conference and made certain that all Israeli patients participate in the natural history study, a critical step to enroll the necessary number of patients. Because FD is a rare disease, we need patients from all corners of the globe to participate. Geographical constraints should not limit be a limit to the progress we can make for FD. I am pleased to partner with Mr. Udi Raz, a father and prominent Israeli lawyer who took over as Chairman of the Israel FD Foundation, and shares our vision of a united front in the fight against FD, and sharing information to foster progress. We have identified a third patient from Mexico with the founder mutation whose family were not aware of Jewish ancestry. While we expect to see her soon at the Center, she is now being cared for by a local neurologist, Dr. Alejandra Gonzalez-Duarte who trained at the Center, and graduated from our Autonomic Disorders Fellowship Program. Last week, we identified a 10-month old baby born with FD in Germany.

The Dysautonomia Foundation has been our long-term partner supporting our clinical and research team at NYU. Throughout the years, we have built a strong research program, with the help of Dr. Lucy Norcliffe-Kaufmann and Dr. Jose-Alberto Palma. These two scientists have led the way to a number of discoveries that have changed how we treat FD. Over the last year, their commitment has also enabled us to write guidelines for clinical care and made possible recent research publications that mark a breakthrough in treating lung disease, which remains a key clinical problem to manage. In recognition of their academic contributions to FD, both received promotions this year to Associate Professor. This year, thanks to the support of PTC Therapeutics, we were able to fund a full-time research scientist, Dr. Maria Cotrina-Vidal, who joined our team to help with the natural history study. We are also delighted to tell you that together with Dr. Frances Lefcort, we were awarded an NIH grant to study the microbiome in patients with FD. We hope to learn how this contributes to the gastrointestinal problems that are so frequent in the population.

There is still much work to be done by our committed team and collaborators. Final thanks go to the families and patients with FD that have given up their time to be a part of our research mission and participated in studies. Without you, progress would not be possible.

Horacio Kaufmann, MD, FAAN,
Director of the Dysautonomia Center

Dr. Alberto Palma recognized by the international research community

Dr. Alberto Palma was recognized by the American Autonomic Society as the first recipient of the Felicia Axelrod Investigator Award. The Award, set up in tribute to Dr. Axelrod, recognizes a researcher posed to become a leader in the field of autonomic medicine. Dr. Palma was chosen for his contributions, in particular for his work in familial dysautonomia.

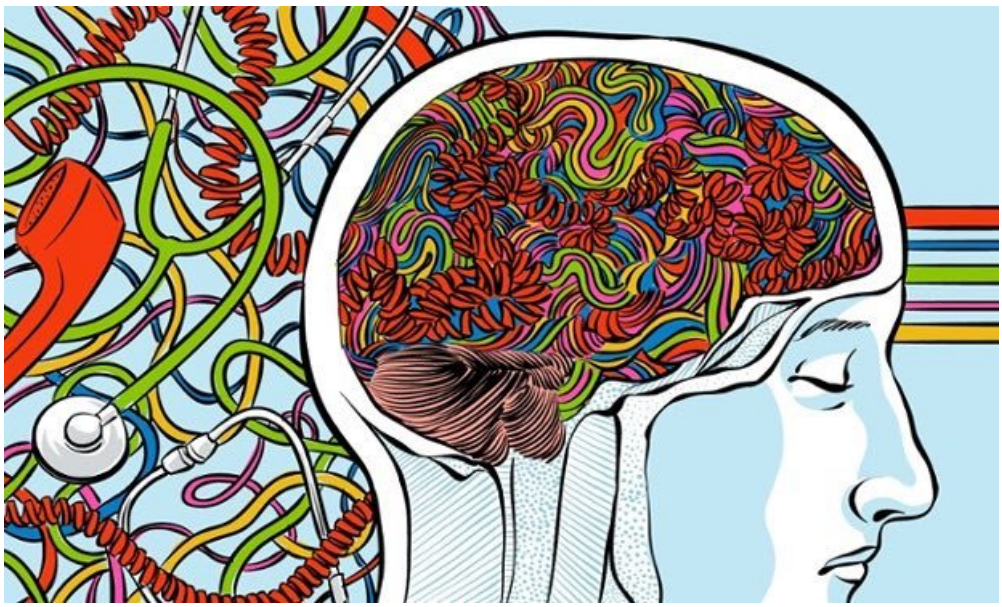
Dr. Felicia Axelrod was a pioneer of research in rare diseases and started the Familial Dysautonomia Patient Registry in the 1970s. Today, registries for rare diseases are now common practice and are recommended as ways to help understand orphan diseases and speed up the development of new treatments. Dr. Axelrod's interest in familial dysautonomia was sparked early in her career. While a medical student at NYU School of Medicine, she began seeing patients with familial dysautonomia and shortly after graduating she established the Dysautonomia Center at New York University. From its humble beginnings, in a single office, she kept meticulous notes on each patient, charting each symptom, each treatment attempt, and every test result for the next 40 years of her career. In the 1990s, she started the first electronic database for patient records, which enable research into the disease to progress at a faster pace than ever before.

When Dr. Alberto Palma joined the Center in 2013, he took advantage of the database and addressed the issues of sudden unexpected death during sleep in patients with familial dysautonomia. The American Autonomic Society selection panel recognized his life-saving work, which has allowed physicians recognize why we should avoid using high-dose fludrocortisone and the importance of using CPAP or BiPAP to help support breathing at night. These recommendations are now part of the new Respiratory Guidelines that were just published that Dr. Palma spearheaded. Dr. Palma has also made significant headway in treating rare autonomic neurodegenerative synucleinopathies like multiple system atrophy. In this regard, Dr. Palma was recognized by the National Institutes of Health and selected as Scholar of the Rare Diseases Clinical Research Network.

Dr. Palma's recognition within the field is a well-deserved honor. Since joining the NYU Dysautonomia Center he has made a real difference in the lives of patients with autonomic disorders. After completing his autonomic disorders

fellowship at NYU in 2015, he joined the Faculty as an Attending Physician and assumed the role of Assistant Director of the Dysautonomia Center. “He is an outstanding example of a clinician scientist”, explained Dr. Horacio Kaufmann, “he takes the time to listen to patients, thinks carefully about their problems, and designs research that addresses the critical issues.”

VISITORS



Long-term collaboration continues thanks to the support of the Familial Dysautonomia Foundation

Dr. Joel Gutierrez is an expert in neurophysiology and has dedicated his career to understanding problems in nerve conduction. By measuring electrical changes, he is able to map nerve connections in the body and tell exactly why the nerves are malfunctioning. Being able to do this requires a painstaking knowledge of human anatomy, electrophysiology, and clinical neurology. Dr. Gutierrez has been working with the Center to understand nerve function in patients with familial dysautonomia for over a decade.

Each year, Dr. Joel Gutierrez has been able to come from Cuba, where he leads the Neurophysiology Department at the Cuban Institute of Neurology and Neurosurgery. He spends time at the Center mapping reflex nerve pathways in patients with FD overtime.

His work is unsurpassed. He has helped us understand why patients with FD have trouble swallowing, a dulled sense of pain, injure their corneas, and struggle to walk. This knowledge has helped the team develop programs specifically designed for the treatment of patients with FD.

He has followed almost 30 patients with FD for the last 10 years testing them on an annual basis. It is an unprecedented piece of information, carefully collected in a very rare neurological disease. “We need patients with FD to come back to be re-examined” he explained, “we are collecting important information that we use to understand why patients have distressing symptoms”.

In clinical practice, nerve conduction studies are used by neurologists to diagnose a variety of medical conditions. The test itself is short and involves applying a small current to the skin and measuring muscle twitch. This painless, quantifiable test is used frequently in the treatment of patients with peripheral neuropathies. It helps us understand acute problems like drop foot or limb numbness. If we can understand how the function of these nerves change overtime we can plan ways to protect and restore them. The Foundation has supported a Visiting Professorship Program at the Center since 2009. Thanks to their continued support, Dr. Joel Gutierrez is back at the Dysautonomia Center. This will allow him to continue his important work in FD.

Past Visiting Professors: Vaughan Macefield, PhD (Australia), Joel Gutierrez, MD (Cuba), Juan Carlos Gómez Esteban, MD, PhD (Spain), Frances Lefcort, PhD (USA)

NEW FACES

Taking on the challenges of FD requires a special team of talented staff who understand the complexities of dealing with an unpredictable and rare disease. Being able to bring in and train new people has always been a part of the Center’s mission. Over the last decade the Center has trained young physicians from Israel, Europe, and South America. Today, graduates of the fellowship training program are now running their own clinics in different countries and caring for patients with FD. The Center has been lucky enough to add new members to the team that will be essential in carrying on the progress in clinical research.

Dr. Bhumika Balgobin is a clinical neurologist with years of patient experience that the Center selected as the 2018-2019 Autonomic Disorders Fellow. The certified Fellowship program provides training in autonomic diseases, including familial dysautonomia. Dr. Balgobin will spend the next few years learning how to care for FD patients and help answer important research questions. She has vast experience as a Physician Assistant in a busy NYC hospital ER and training in electrophysiology.

Dr. Maria Cotrina-Vidal, with support from PTC Therapeutics, the Center was able to bring on board a research scientist to help organize the Natural History Study. This important role was filled by Dr. Cotrina, who was organizing a longitudinal study for survivors of 9/11. Dr. Cotrina will collect and document important clinical data during annual evaluations and help with the recruitment of patients into studies. She has a special interest in nutrition and will be working hard over the coming years to understand this better.

Isabella Schneider began as a volunteer at the Center almost 2-years ago while an undergraduate at NYU. Bella quickly emerged as a talented data assistant who could organize and track information for research using databases. She joined the Center formally as a Research Assistant who helps make our work possible. She is collaborating across medical fields to help understand important issues such as blindness and gastric bleeds.

The Center has a Visitor Professor Program and a Clinical Observership Program for clinicians and scientists who want to spend time learning about FD and gaining hands-on experience. Candidates interested in our undergraduate summer internship program should email a letter of interest to Miguel.Perez@nyulangone.org.

Find out why we need a natural history study and learn how you can do your part.

Speeding up progress in FD with the natural history study

New drugs to halt the progressive aspects of FD are set to enter the clinic in 2019 for testing. Progress in FD is happening at faster pace than ever before and “clinical trials readiness” has become a buzz word in the complex world of drug development for rare diseases. Unlike conventional clinical trials that can test new drugs in large populations, developing drugs for FD requires ingenuity, scale and a different approach. The numbers are way smaller, with only a few hundred children and adults worldwide suffering from the disease. This is where natural history studies come in to play. Classic study designs require half the patients to take a placebo (sugar pill) so that they can be compared to those receiving the active drug. This can be avoided with thorough and abundant natural history data. In this way, the effect of an active drug can be compared to what happened in the natural history study before the patients received the new drug.

The vision

In many ways, FD has become the blueprint for translational research and has paved the way to show how collaboration can blossom into real opportunity. Despite the complexities of the disease, we have a good understanding of how patients with FD evolve overtime and what features of the disease get worse. In 2008, husband and wife team Dr. Horacio and Lucy Kaufmann joined the Center, and started to recognize some peculiar traits that seemed to be worsening overtime. The children with FD could see, whereas the adults were struggling to read. The children with FD were somewhat clumsy, but the adults were falling and unable to walk down the hallway without holding on to the wall. Vision and gait ataxia are now recognized as progressive neurological aspects of the disease.

In 2016, the Kaufmanns launched a new initiative for patients with FD to start a formal natural history study. They built on the original idea of Dr. Axelrod and Dr. Maayan who had been collecting and sharing information for decades. Dr. Lucy Kaufmann explained "We took that initial idea of following patients in a collaboration and decided to plan exactly what routine information we should be collecting each year. We can use this benchmark information to help drug development and drug approvals".

Collaboration

In 2017, the team got the natural history study approved at NYU. In 2019, the study was also approved in Israel and the first international recruiting site opened at Tel Hashomer Hospital. This formal arrangement means that we have an international collaboration that can help patients participate regardless of where they live. More sites are expected to join the study soon.
Successful natural history studies require collaboration, and FD is no exception. When patients are seen, the medical team collects a series of vital pieces of information that track how a patient is at a particular time. That information is like gold. Combining the data from multiple different patients allows one to pick out trends and see what are the unmet needs of the patients. Having a formal natural history study means that the data collection can be standardized so there is less noise. We can train investigators at different sites to collect information in the same way.

Target engagement

Understanding the progressive aspects of the disease have given us a target. We want to keep FD patients seeing and moving independently, explained Dr. Kaufmann. New drugs are needed to fix what is happening inside the nerves and causing the cells of the eye and motor coordinating system to malfunction. We are lucky to have the brightest minds working on the biological strategies to save the nerves, but we still need to do our part.
To test new therapies currently being developed at the bench, we need something to compare to. Since 2010, the Center has been collecting high-definition scans of the back of the eye, which show a progressive thinning that begins at an early age. Putting this information together has given us an understanding of what is the natural evolution of the degeneration of the eye. In other words, it is clear what happens to vision if we don't prevent the nerve loss. With the availability of the eye natural history data, we have a fairly good understanding of why one-third of people with FD go blind. We have to change this. If we develop a drug to save the nerves, we can measure how it changes the natural progression of the disease using the eye as a window.
The same is true for the gait. The team has been rating and recording the way patients with FD move using the same scale for the last 5-years. We can see how they worsen, we can see what are the benchmarks that need to change.

Natural history game-changer

Having this high-quality natural history data available becomes a game changer for developing new drugs and planning innovative clinical trials. Now it is time for all patients to participate. We want to have the clinical information from as many patients with FD as we can. This will help us with the challenges that are faced by research teams that are invested in finding cures for rare diseases in small populations. If we can do this well, it could mean that patients won't have to take a placebo pill during a clinical trial. We can show that a new treatment is slowing or has restored nerve function, if we can compare it to the natural history of the disease.

Your part

Participating in the natural history study is easy. You have to sign permission (consent or assent) to have your data included in the database alongside with “standard of care” treatments, the drugs/therapies that are given to treat the symptoms/complications of the disease.

The type of clinical information collected is routine. It includes vital signs, medications, nutrition/growth parameters, neurological scores, vision tests, blood pressures, blood test results, and pulmonary function tests. These are the tests that all patients with FD are recommended to have routinely for their standard medical care. If they agree, patients and relatives can also give a sample of blood that can be used to measure the levels of the defective protein and mRNA.

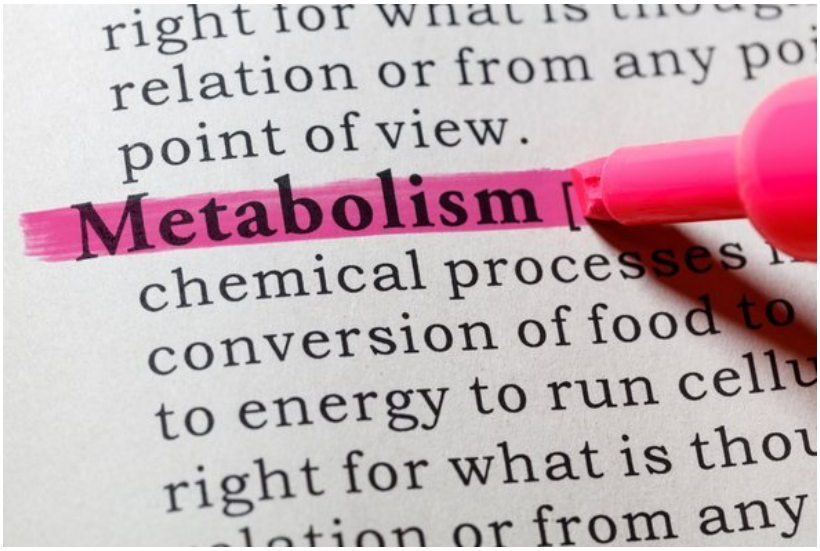
Patients can also send information from their own doctors.

The natural history study is currently approved at the following recruiting sites:

NYU School of Medicine, New York, NY (here)
Tel Hashomer Hospital, Tel Aviv, Israel

Stay tuned for additional recruiting sites soon to be added.

If you want to know more about how to participate in the natural history study, call us at the Center (212-263-7225).



Chronic lung disease has a major impact on metabolism and growth in patients with FD.

New study sheds light on why patients with FD often struggle to gain weight

Our weight is influenced by a number of factors, including our diet, our exercise, and our genetic code. While obesity is a major public health problem, doctors have long recognized that being severely underweight also has deleterious risks. Patients with familial dysautonomia have a single mutation in their genome that results in a whole host of medical issues. For some, it becomes frustratingly difficult to gain weight. Despite having a gastrostomy tube to supplement their caloric intake with liquid nutrition, they remain significantly underweight. The cause for this is unknown. But, a study of 12 patients with familial dysautonomia, performed in Israel in collaboration with the Center, might reveal some insights.

By measuring energy expenditure at rest, the team found that around half the patient population have a hypermetabolic state – meaning their bodies are burning more energy even when they are sitting and relaxing. For quite a while the team had suspected that there were additional factors that accounted for why around 75% patients with FD tend to be underweight. They also noted that a number of patients weren't taking in a sufficient number of calories.

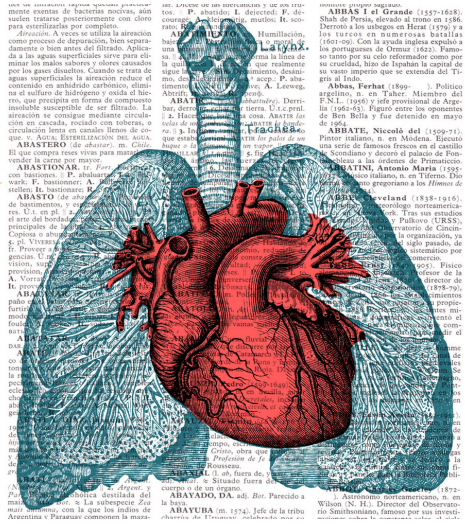
This combination of reduced energy intake and increased energy usage appears to be behind why we see patients struggling to gain and maintain weight. Since patients have a pattern of restrictive lung disease, it is likely that the muscles have to work harder to move the stiff chest wall and allow air to enter the lung. Likewise, if the lung is chronically inflamed, the inflammatory response expends energy and can contribute to weight loss.

> "Around half the patient population have a hypermetabolic state. The increased work of breathing may be driving the higher energy demands."

The results underscore the importance of a multidisciplinary care approach to FD. Some patients may need to work with a nutritionist to make certain their caloric intake is sufficient while at the same time working with a pulmonologist to lessen inflammation in the lung. Such an approach would eventually shift the energy balance back into an even equilibrium, so that there isn't a net deficit.

The study was conducted at Sheba Medical Center in Tel Hashomer, Israel as part of an international collaboration. Lead author of the study, Dr. Bat-el Bar was supported by the Familial Dysautonomia Foundation to spend time at NYU's Dysautonomia Center to train in FD research and clinical care. She and her team are currently recruiting patients for the natural history study.

EXPERT GUIDELINES



How unraveling a complex issue guides medical decisions, so patients get access to the multi-disciplinary care they need.

New expert respiratory guidelines for familial dysautonomia

Scientists have long known that one of the greatest problems faced by patients with familial dysautonomia is the inability to breathe efficiently. Patients have difficulty swallowing, regulating the supply of oxygen to tissues, and mechanical problems caused by abnormal curvature of the spine. The effects can be catastrophic.

The most common cause of death in patients is respiratory compromise, due to life-threatening infections or failure respond to lack of oxygen or the build-up of carbon dioxide. Until now, there were no guidelines to advise physicians how to take care of the lungs of a patient with FD.

From the very beginning it was clear to Dr. Kaufmann that we needed to re-look at how best to manage the respiratory problems of FD from aspiration to dangerous pauses in breathing at night. Over the last decade, medical knowledge has advanced and technology has gotten better. Many of the respiratory problems faced by patients with FD are now fixable or at least can be managed better to reduce the number of exacerbations.

The first step to improving respiratory care was to bring together a group of physicians to discuss the issues and what can be done about them. Experts from respiratory medicine, gastroenterology, speech and swallow and neurology came together with internists, scientists, and therapists to share their experiences. “Soon, we had a working group of 30 people,” explained Dr. Alberto Palma, “we listened to their opinions and reviewed the level of evidence supporting their recommendations.” When the evidence wasn’t there, they looked at the database, which contains the clinical information of all patients with FD seen at the Center. “We looked for patterns and trends to describe how frequent certain issues were and what were the outcomes of the treatments that were prescribed at the time.”

Over the course of a year, the respiratory guidelines started to take shape. The team graded each diagnostic test and clinical intervention according to whether there was strong or weak evidence to support it. The document went through several revisions as the experts all weighed in again.

> “Having the guidelines out there enables other physicians treating patients with FD to have access to the latest medical knowledge”
> – Dr. Horacio Kaufmann.

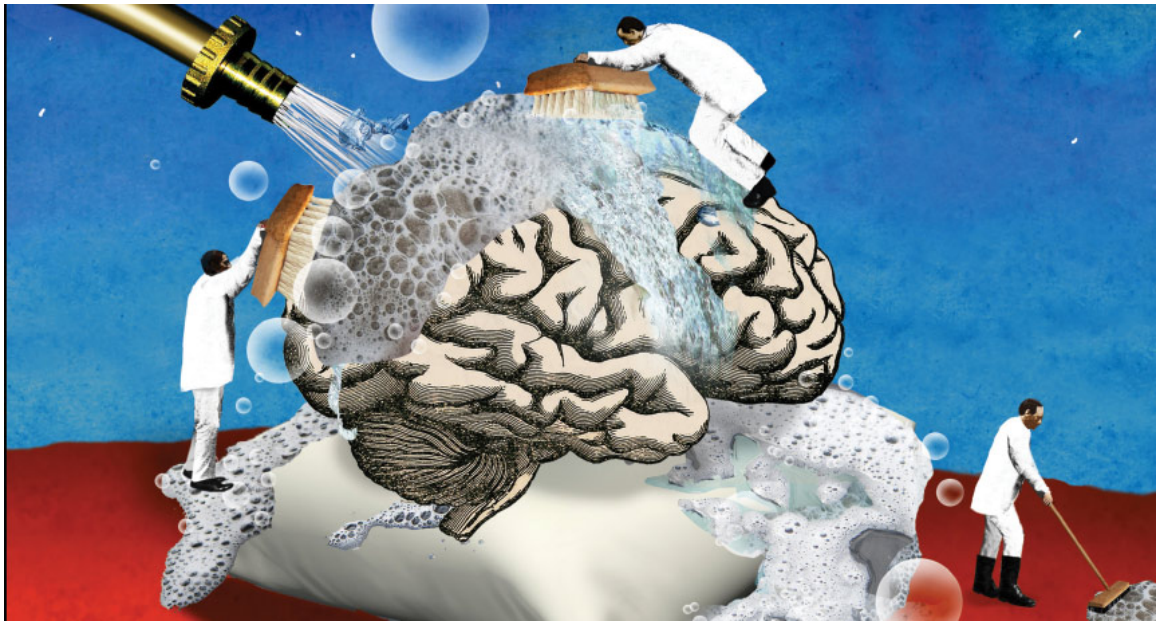
The end result, published this month in the journal Respiratory Medicine, is an important milestone in clinical care. Finally, a physician can sit down and read what sort of respiratory problems occur in patients with FD, why they occur, and what can be done to stop them. The guidelines cover topics like avoiding aspiration, reducing airway inflammation, preventing scarring, overcoming a weak cough, preventing obstructions, and how to provide ventilatory support overnight.

Because patients have difficultly recognizing their symptoms, they often don’t complain in obvious ways. So, the team came up with a list of questions that a physician can ask to screen for the possibility of a chronic lung problem. “Patients can be completely unaware that they have aspirated food, drink or their own saliva into the lung instead of it directing it to the stomach” explained Dr. Palma. “Over the years, these silent aspirations irreversibly damage the delicate lining of the airways, so physicians need to be aware that they should look for signs like a wet sounding voice or colds that linger longer than they should.”

The new respiratory guidelines cover topics like when to involve swallow specialists, how to control saliva, when to recommend a feeding tube, what surgeries may be needed, chest physical therapy, how to monitor patients at home, special precautions for air-travel, as well as the use of antibiotics, inhalers, and CPAP or BiPAP.

All patients born with familial dysautonomia have some degree of lung disease. There has been a huge amount of progress in recent years, and we can take advantage of what has been learned. Dr. Palma added that “Our shared goal is to recognize potential problems early and choose the most effective treatment options to lessen suffering.” Providing expert guidelines for the respiratory care of patients with FD, gives a framework for treatment.

The expert panel included neurologists, pulmonologists, sleep medicine specialists, gastroenterologists, intensive care specialists, scientists, nurses, respiratory therapists, and dieticians. It provides expert consensus recommendations based on the level of evidence for each treatment.



Flushing out carbon dioxide overnight can restore the drive to breathe during the day.

Beyond sleep: The benefits of BiPAP

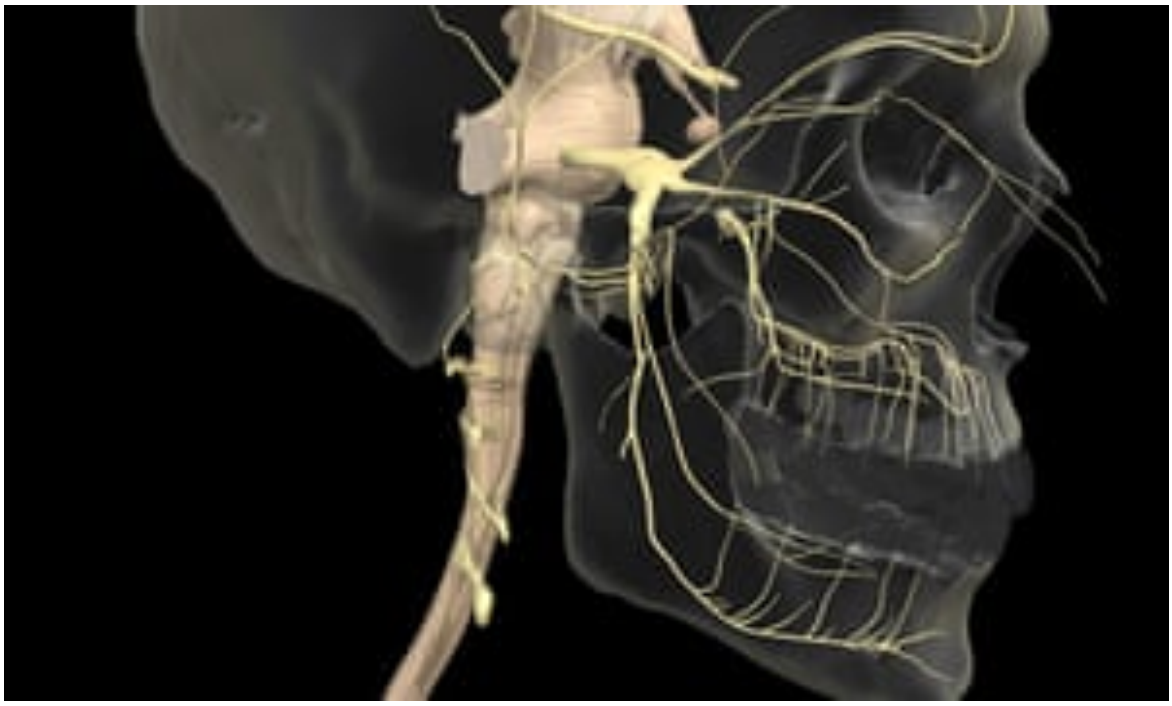
The urge to breathe comes from a physiological drive. Sensors inside and outside the brain are continuously monitoring the internal environment of our blood and effectively regulating daily oscillations in our breathing patterns. Breathing becomes faster and deeper when oxygen levels fall or carbon dioxide levels rise.

While we sleep we are at rest, our energy consumption is less, and our breathing slows. Throughout the night, our respiratory sensors continue monitoring the molecules in our blood, to protect us from having fatal events when we stop breathing. Sleep disordered breathing occurs in nearly every single patient with familial dysautonomia. When they fall asleep at night, their airways can collapse and/or their brain can fail to signal when it is time to breathe. This can lead to snoring, gasping, and sometimes long pauses in breathing. It is very common for patients to awaken in the morning, feeling unrested after frequent awakenings and lethargic.

Overtime, patients become accustomed to having high levels of carbon dioxide in their blood and develop daytime respiratory failure. Walking around with persistently high carbon dioxide levels (known as hypercapnia) blunts the desire to breathe.

A recent analysis of treating patients with FD with CPAP or BiPAP devices shows that this appears to be reversible. These devices, which restore normal breathing, cause a significant reduction in carbon dioxide levels during the day.

Researchers think that the physiological mechanism is resetting of the respiratory (chemo) sensors. CPAP or BiPAP are your back-up that mechanically support your breathing at night. They keep the airways open, ventilate the lung and essentially wash carbon dioxide out of the blood. They suspect that the sensors are being cleaned during sleep so that they work better during the day.



The trigeminal nerve, provides sensory information from the head and neck. A study examining brain MRIs suggests it is possible to measure the size of the sensory nerve bundles

Mapping the size of the sensory nerves

The 12 cranial nerves carry bundles of fibers that enter and exit the brainstem at various levels. The trigeminal nerve is the largest of these nerves and provides the brain with sensory information from the face, scalp, and throat. It controls how often we blink, tear, how we bite, and chew. Each of these things we take for granted are impaired, to varying degrees, in patients with FD.

Brain MRI scans are common in patients with neurological illness and are used by clinicians to investigate a whole host of neurological complaints from seizures to headaches. Over the years, the Center has collected routine MRI scans of the brain from patients with FD and stored them with the hope of being able to understand which particular areas are affected.

Using magnetic fields, we can collect an image of the brain at various levels. The images can create a picture of the brain's contours so you can see structures. The structures in different regions provide a measure of the density of neurons. Not only are they a diagnostic tool, brain MRIs are frequently used in clinical trials to monitor rates of neuronal degeneration.

In collaboration with the Department of Radiology at NYU, the Center embarked on a study to look at the size of the trigeminal nerve in patients with FD. "We had some key questions," explained Dr. Kaufmann, "We wanted to know what happens to the nerve and if it changes overtime". Using routine clinical MRI scans, the team carefully analyzed each of the scans and measured the morphology of the trigeminal ganglia.

Over the years, they built up enough information to compare the scans acquired from FD patients to those in normal controls. When a healthy brain develops, the trigeminal nerve cells bundle together into a ganglia, which is particularly large and amenable to imaging. There are ganglia on both sides that bring connections

from the head and neck. In an MRI scan it is possible to locate the trigeminal nerves, map the blurry edges, and measure their dimensions to calculate the area. Larger areas indicate more nerves.

What we saw in patients with FD was quite remarkable. The size of the trigeminal nerves was much smaller in the patients than in controls. This difference remained even when normalizing for body mass. The trigeminal nerves were about half the size. In addition to having smaller nerves, the patients all had signs and symptoms of loss of trigeminal sensations, including lack of tearing, corneal injuries, and swallowing difficulties. They were, however, no differences in the caliber of the nerves with age.

> "The findings are encouraging, we are always looking for non-invasive ways to follow the health of the nerves. Here you have an image of the nerves themselves measurable in a conventional MRI"
> – Dr. Alberto Palma

The idea that the nerves aren't deteriorating at a rapid rate and appear stable is also important. When looking at the impact of new therapies investigators will need to assess whether they are saving the nerves from an ongoing atrophy or re-growing them. Finding good biomarkers for patients with FD is an important initiative.

Sharing what you know in the hope of saving lives and developing new therapies.

Breathing control in familial dysautonomia

Problems with ventilatory control are a life-long issue for children with familial dysautonomia. Knowing how serious this can be, the team at the Center has dedicated the last few years in grappling with these issues. Following recent key findings the Center's clinical research team was invited to review our current understanding of ventilatory control in patients with FD.

Lack of sensation

At any time, a someone living with FD can stop breathing. This can be caused by a number of issues including sedative drugs like diazepam, sleep apnea, a blockage of the airway. Instead of sensing that this is happening and stimulating the drive to breathe again, patients with FD don't increase their respiratory rate. Put simply, they don't sense what is going on, so they don't respond as they should. The chemoreceptor reflex, which is a system of nerves that control breathing, fail. Patients can severely ill with hypoxia, but because the nerves don't detect low oxygen, they can't stimulate breathing.

Being ahead of the game to prevent consequences

Sleep disordered breathing is almost a universal finding. "In nearly every single sleep study, in which carbon dioxide levels were measured, they were elevated" explained Dr. Palma. Children and adults with FD have pauses in breathing at night or slip into a slow shallow rate where carbon dioxide levels rise. Not surprisingly, the population are at high risk of complications. Sudden death during sleep remains a leading cause of death.

Fortunately, sleep disordered breathing can be treated. We now have more and more patients sleeping with CPAP or BiPAP which normalized their breathing at night. We have children using CPAP and BiPAP at a much early age, building up their tolerance, and protecting themselves against long pauses in breathing or hypoventilation.

As we start to understand ventilatory control in patients with FD, we can start to develop treatment plans that overcome the problems. Understanding that sedative drugs can be useful to break a crisis is important, but ensuring that after taking them, should you fall asleep, you should be wearing a BiPAP mask could save a life. Knowing that fludrocortisone is one way to treat low blood pressure may be fine, but keeping in the

back of your mind that low potassium levels can occur and may cause hypokalemia which can predispose arrhythmias and could worsen hypoxic ventilatory drive is critical.

Having this knowledge out in the literature will hopefully help others understand FD better. Before, anyone wanting to know about ventilatory control in patients with FD had to go back to the original studies from the 1960s. The article summarizes those classic early findings and takes a fresh look at the reasons why ventilatory drive is abnormal in patients with FD. The article also helps treating physicians see that non-invasive ventilation is an important therapy, that patients should be using.

> "Understanding why breathing is poorly controlled and what we can do about it is an important priority"
> – Dr. Alberto Palma

The review article combined the expertise of staff at the Center together with physicians in Israel, a new generation of clinical scientists leading the forefront of FD research and treatment. Things are moving at a faster pace that before. This knowledge helped shape the new respiratory guidelines which breakdown the current treatment recommendations for lung disease in FD.

With still more to do, investigators and clinicians at the Center remain focused on finding ways to improve quality of life in patients with FD and share their knowledge with basic scientists and doctors working on the disease. The idea is to get this information in to the hands of others, explained Dr. Kaufmann, so they can either use it to develop a new therapy or apply it to saving the life of a patient in need of help.

ABSTRACT

Resting Energy Expenditure in Patients with Familial Dysautonomia: A Preliminary Study

BY BAT-EL BAR, LUCY NORCLIFFE-KAUFMANN et al.,
March 2019, J Pediatr Gastroenterol Nutr. 68(3) p 422

OBJECTIVES: Familial dysautonomia (FD) is a rare hereditary sensory and autonomic neuropathy characterized by chronic lung disease and cyclic vomiting due to hyper-adrenergic crises. Most FD patients are in a depleted nutritional state; however, the phenotype of the disease is quite different between patients, as for the severity of lung disease and the intensity and frequency of these pathognomonic crises. In this study we wanted to investigate whether resting energy expenditure (REE) levels are increased in this population, and if correlations exist between REE levels and phenotype severity.

METHODS: Data was collected from 12 FD patients (6/6 m/f). REE measurements were conducted by indirect calorimeter. Measured REE % predicted were correlated with pulmonary function, severity of the scoliosis, serum C-reactive protein, yearly frequency of hyperadrenergic crisis, hospital admissions and the use of nocturnal noninvasive positive pressure ventilation.

RESULTS: Mean REE was 112 ±13% predicted with 50% being in a hypermetabolic state (REE/HB>110%). Body mass index (BMI) was below normal range in 75% of patients, and reduced energy intake was also decreased in 75%. No significant correlations to disease severity factors were found. When dividing the subjects to REE levels above or below 125% predicted, Patients with REE above 125% predicted presented with significantly lower inspiratory capacity (42.7% predicted vs 62.8% predicted; P = 0.04).

CONCLUSIONS: Hypermetabolic state was described in 50% of FD patients. The Low BMI is explained by combination of relative anorexia and increased REE. The REE levels are related to the underling respiratory disease.

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doi: 10.1097/MPG.0000000000002180.

Authors: Bar Aluma BE, Norcliffe-Kaufmann L, Sarouk I, Dagan A, Ashkenazi M, Bezalel Y, Vilozni D, Lahad A, Efrati O.

ABSTRACT

Respiratory care in familial dysautonomia: Systematic review and expert consensus recommendations.

BY MIKHAIL KAZACHKOV, ALBERTO PALMA et al.,
August 2018, Respir Med. 141, p 37

BACKGROUND: Familial dysautonomia (Riley-Day syndrome, hereditary sensory autonomic neuropathy type-III) is a rare genetic disease caused by impaired development of sensory and afferent autonomic nerves. As a consequence, patients develop neurogenic dysphagia with frequent aspiration, chronic lung disease, and chemoreflex failure leading to severe sleep disordered breathing. The purpose of these guidelines is to provide recommendations for the diagnosis and treatment of respiratory disorders in familial dysautonomia.

METHODS: We performed a systematic review to summarize the evidence related to our questions. When evidence was not sufficient, we used data from the New York University Familial Dysautonomia Patient Registry, a database containing ongoing prospective comprehensive clinical data from 670 cases. The evidence was summarized and discussed by a multidisciplinary panel of experts. Evidence-based and expert recommendations were then formulated, written, and graded using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system.

RESULTS: Recommendations were formulated for or against specific diagnostic tests and clinical interventions. Diagnostic tests reviewed included radiological evaluation, dysphagia evaluation, gastroesophageal evaluation, bronchoscopy and bronchoalveolar lavage, pulmonary function tests, laryngoscopy and polysomnography. Clinical interventions and therapies reviewed included prevention and management of aspiration, airway mucus clearance and chest physical therapy, viral respiratory infections, precautions during high altitude or air-flight travel, non-invasive ventilation during sleep, antibiotic therapy, steroid therapy, oxygen therapy, gastrostomy tube placement, Nissen fundoplication surgery, scoliosis surgery, tracheostomy and lung lobectomy.

CONCLUSIONS: Expert recommendations for the diagnosis and management of respiratory disease in patients with familial dysautonomia are provided. Frequent reassessment and updating will be needed.

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PMCID: PMC6084453
DOI: 10.1016/j.rmed.2018.06.017

Authors: Kazachkov M, Palma JA, Norcliffe-Kaufmann L, Bar-Aluma BE, Spalink CL, Barnes EP, Amoroso NE, Balou SM, Bess S, Chopra A, Condos R, Efrati O, Fitzgerald K, Fridman D, Goldenberg RM, Goldhaber A, Kaufman DA, Kothare SV, Levine J, Levy J, Lubinsky AS, Maayan C, Moy LC, Rivera PJ, Rodriguez AJ, Sokol G, Sloane MF,, Tan T, Kaufmann H.

ABSTRACT

Quantitative MRI evaluation of the trigeminal nerve in familial dysautonomia

BY YVONNE LUI, ALBERTO PALMA, HORACIO KAUFMANN et al.,
Feb 2019, Clin Auton Res.

PURPOSE: Familial dysautonomia (FD) is a rare autosomal recessive disease that affects the development of sensory and autonomic neurons, including those in the cranial nerves. We aimed to determine whether conventional brain magnetic resonance imaging (MRI) could detect morphologic changes in the trigeminal nerves of these patients.

METHODS: Cross-sectional analysis of brain MRI of patients with genetically confirmed FD and age- and sex-matched controls. High-resolution 3D gradient-echo T1-weighted sequences were used to obtain measurements of the cisternal segment of the trigeminalnerves. Measurements were obtained using a two-reader consensus.

RESULTS: Twenty pairs of trigeminal nerves were assessed in ten patients with FD and ten matched controls. The median (interquartile range) cross-sectional area of the trigeminal nerves in patients with FD was 3.5 (2.1) mm^2, compared to 5.9 (2.0) mm^2 in controls ($P<0.001$). No association between trigeminal nerve area and age was found in patients or controls.

CONCLUSIONS: Using conventional MRI, the caliber of the trigeminal nerves was significantly reduced bilaterally in patients with FD compared to controls, a finding that appears to be highly characteristic of this disorder. The lack of correlation between age and trigeminal nerve size supports arrested neuronal development rather than progressive atrophy.

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DOI: 10.1007/s10286-019-00593-0

Authors: Won E, Palma JA, Kaufmann H, Milla SS, Cohen B, Norcliffe-Kaufmann L, Babb JS, Lui YW.

LETTER

Improvement of daytime hypercapnia with nocturnal non-invasive ventilation in familial dysautonomia

BY HORACIO KAUFMANN et al.,
April 2019, Clin Auton Res. 29 (2), p 255

DEAR EDITORS,

Chemoreceptor failure is a dramatic feature of familial dysautonomia (FD), a rare genetic disease caused by a founder mutation in the IκB kinase-associated protein gene (IKBKAP) [1–3]. As a consequence, ventilatory responses to hypercapnia are reduced, and those to hypoxia are almost absent. In response to hypoxia, patients can develop paradoxical hypoventilation, hypotension, bradycardia, and potentially death [4–7]. Chemoreflex failure can be devastating during sleep when conscious control of respiration withdraws. Virtually all patients with FD have some degree of sleep-disordered breathing [3, 7], which is a risk factor for sudden unexpected death during sleep [2].

Nocturnal non-invasive ventilation with bi-level positive pressure (BiPAP) reduces daytime hypercapnia in patients with neuromuscular disease, such as Duchenne muscular dystrophy [8, 9], suggesting that nocturnal non-invasive ventilation improves daytime respiratory drive by resetting peripheral and/or central chemoreceptor function [10]. We hypothesized that a similar chemoreceptor reflex resetting occurred in patients with FD after nocturnal non-invasive ventilation. To test this hypothesis, we obtained daytime arterial blood gases in 18 consecutive patients [10 women, 8 men, aged 28 ± 11.7 (mean ± standard deviation) years old] with genetically confirmed FD that were not being treated with non-invasive ventilation, despite having some degree of sleep-disordered breathing. Daytime arterial blood gases were measured at baseline before patients began treatment with nocturnal non-invasive ventilation [BiPAP in all cases except one using continuous positive airway pressure (CPAP)] and arterial blood gases were again obtained at variable follow-up times (ranging from 6 weeks to 6 months) after initiation of noctural non-invasive ventilation. Day-time blood gases after receiving non-invasive ventilation showed that their pCO2 decreased from 45.9 ± 5.1 to 41.4 ± 4.7 mmHg (paired T test, $P < 0.0001$); and their pO2 remained stable (from 84.2 ± 14.7 to 91 ± 16 mmHg; paired T test, $P = 0.1167$), as did their pH (7.4 ± 0.04 before and after non-invasive ventilation)

As nocturnal non-invasive ventilation virtually eliminated diurnal CO2 retention in patients with FD, it is possible that the procedure, by normalizing pCO2 during the night, resets the chemoreflexes to operate at lower CO2 values, a mechanism postulated in patients with neuromuscular disorders. If confirmed in larger studies, our findings may have clinical implications, as diurnal hypercapnia has been associated with poor prognosis in patients with sleep-disordered breathing [11].

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NIHMSID: NIHMS1013774
PMID: 30637592

Authors: Kaufmann H, Norcliffe-Kaufmann L, Palma JA.

REVIEW

Chemoreflex failure and sleep-disordered breathing in familial dysautonomia: Implications for sudden death during sleep

BY ALBERTO PALMA, ALEX GILELES-HILLEL et al.,
August 2018, Respir Med. 141, p 37

Familial dysautonomia (Riley-Day syndrome, hereditary sensory and autonomic neuropathy type III) is a rare autosomal recessive disease characterized by impaired development of primary sensory and autonomic neurons resulting in a severe neurological phenotype, which includes arterial baroreflex and chemoreflex failure with high frequency of sleep-disordered breathing and sudden death during sleep. Although a rare disease, familial dysautonomia represents a unique template to study the interactions between sleep-disordered breathing and abnormal chemo- and baroreflex function.

In patients with familial dysautonomia, ventilatory responses to hypercapnia are reduced, and to hypoxia are almost absent. In response to hypoxia, these patients develop paradoxical hypoventilation, hypotension, bradycardia, and potentially, death. Impaired ventilatory control due to chemoreflex failure acquires special relevance during sleep when conscious control of respiration withdraws. Overall, almost all adult (85%) and pediatric (95%) patients have some degree of sleep-disordered breathing. Obstructive apnea events are more frequent in adults, whereas central apnea events are more severe and frequent in children. The annual incidence rate of sudden death during sleep in patients with familial dysautonomiais 3.4 per 1000 person-year, compared to 0.5-1 per 1000 person-year of sudden unexpected death in epilepsy.

This review summarizes recent developments in the understanding of sleep-disordered breathing in patients with familial dysautonomia, the risk factors for sudden death during sleep, and the specific interventions that could prevent it.

PMID: 30890343
PMC6428199
DOI: 10.1016/j.autneu.2019.02.003

Authors: Palma JA, Gileles-Hillel A, Norcliffe-Kaufmann L, Kaufmann H.

OPPORTUNITIES

Current research studies open for patients with familial dysautonomia

OPEN and ENROLLING

THE NATURAL HISTORY OF FAMILIAL DYSAUTONOMIA
IRB#: S16-01774
ELIGIBILITY: Patients with FD of any age
PURPOSE: To use the clinical information collected during routine medical visits to define the clinical features of FD and how they evolve overtime. The goal of the project is to find biological signals that we can use to track the features of FD to use in clinical trials to test new drug treatments. The study will also measure IKAP protein levels to see how well they correlate with symptoms of FD.
SPONSOR: Familial Dysautonomia Foundation, Inc. and PTC Therapeutics, Inc.

ENROLLING

A STUDY OF GUT FLORA IN FAMILIAL DYSAUTONOMIA (MIBIOM)
IRB#: s16-00718
ELIGIBILITY: Patients with FD age 4 and older and their family members
PURPOSE: Maintaining a healthy weight is a problem for a number of patients with FD. The aim of this study is to better understand the microorganisms that live in the gut of patients with FD and whether these play an important role in digestive function. In this project, we want to understand if differences in the microorganisms in the gut of patients with FD affect the energy derived from food. We will compare differences between tube and oral fed subjects to better understand the differences and also we will compare it with healthy controls. Better understanding of the microbiome in FD might help also to understand whether fungal overgrowth in the GI tract of FD patients is associated with persistent diarrhea in the absence of known pathogens.
SPONSOR: Familial Dysautonomia Foundation, Inc.

ENROLLING

RESEARCH AND TREATMENT IN FAMILIAL DYSAUTONOMIA (HSAN III)
IRB#: R07-938
ELIGIBILITY: Patients with FD of any age.
PURPOSE: Our goal to bring the best clinical care to patients with FD with focus on quality of life. We strive to provide the treatments that are safe and effective, through evidence based-medicine. Research on FD is constantly on going at the Center. We focus on understanding the mechanisms that cause the symptoms of FD and implementing clinical interventions that improve this condition. The medical information collected during each comprehensive evaluation is also used follow the clinical evolution of FD and define treatments have the best outcomes. Information from the FD evaluation is used to understanding cardiovascular, renal, respiratory and neurological function.
SPONSOR: Familial Dysautonomia Foundation, Inc.

OPEN

UNDERSTANDING THE MUSCLE IN FAMILIAL DYSAUTONOMIA
IRB#: S14-01192
ELIGIBILITY: People with familial dysautonomia of any age.
Purpose: Patients with FD frequently develop muscle atrophy. Moreover, the incidence of rhabdomyolysis (episodes of muscle destruction) is increased in people with FD. To investigate this we aim to examine muscle

function in patients with FD and other hereditary sensory neuropathies by studying muscle samples. Small pieces of muscle are obtained during programmed surgery (scoliosis, hip replacement, etc) and studied.
SPONSOR: Familial Dysautonomia Foundation, Inc.

OPEN

PROPRIOCEPTION AND SENSORIMOTOR CONTROL IN HEREDITARY SENSORY AND AUTONOMIC NEUROPATHY
IRB#: s16-00530:
ELIGIBILITY: Patients with FD 16-40 years old.
PURPOSE: The purpose of this study is to understand disturbances in proprioception (how well we sense the positions of our limbs without seeing them) in patients with FD. Our ultimate goal is the help patients with FD walk better. We want to find new and better ways to enhance signals from the skin to help guide the movement of the limbs.
SPONSOR: National Health and Medical Research Council of Australia

OPEN

RENAL INJURY MARKERS IN FAMILIAL DYSAUTONOMIA
IRB#: 13-00279
ELIGIBILITY: People with familial dysautonomia of any age.
PURPOSE: Our ultimate goal is to be able to detect the early onset and stop the progression of chronic kidney disease in patients with familial dysautonomia. The first purpose of this pilot project is to identify early, non-invasive biomarkers of renal injury. The second purpose of this project is to establish a panel of renal injury biomarkers to monitor the progression of renal disease. This study in being carried out in collaboration with Dr. Howard Trachtman (Professor of Pediatric Nephrology at NYU Langone Health).
SPONSOR: Familial Dysautonomia Foundation, Inc.

ENROLLING

BRAINSTEM REFLEXES IN FAMILIAL DYSAUTONOMIA
IRB#: R07-938
ELIGIBILITY: People with familial dysautonomia of any age.
PURPOSE: To understand if dysphagia and dysarthria in FD are due to a reduction in number and/or excitability of afferent trigeminal nerve fibers. In order to achieve this, we are studying brainstem reflexes in familial dysautonomia using electrophysiological techniques.
SPONSOR: Familial Dysautonomia Foundation, Inc.

Recently completed research studies in familial dysautonomia

COMPLETED

THE EFFECTS OF BRONCHODILATOR THERAPY ON RESPIRATORY AND AUTONOMIC FUNCTION IN PATIENTS WITH FAMILIAL DYSAUTONOMIA
IRB#: S13-00004
ELIGIBILITY: Patients with FD age of 12 and older
PURPOSE: Assess the effects of ipratropium and albuterol, which are commonly used in FD patients, on respiratory and autonomic function in patients with FD
SPONSOR: Familial Dysautonomia Foundation, Inc.

COMPLETED

THE USE OF CARBIDOPA IN FAMILIAL DYSAUTONOMIA
IRB#: R09-0011
ELIGIBILITY: Patients with FD age of 12 and older
PURPOSE: The study objective was to determine if carbidopa reduces the spillover of dopamine into the circulation and decreases the frequency of nausea in FD patients
SPONSOR: Familial Dysautonomia Foundation, Inc.

COMPLETED

PHOSPHATIDYLSERINE (PS) IN FAMILIAL DYSAUTONOMIA – DOSE TITRATION STUDY
IRB #: 11-02100
ELIGIBILITY: Patients with FD age 12 years and older
PURPOSE: We propose to conduct a safety, tolerability and early proof of concept efficacy study of phosphatidylserine in patients with FD. Phosphatidylserine is a dietary supplement. We aim to evaluate the potential of Phosphatidylserine to correct the genetic abnormality and restore IKAP protein levels in FD patients. Researchers have shown that Phosphatidylserine can increase IKAP in cell lines derived from patients with FD and in a mouse model of FD.
Sponsor: Familial Dysautonomia Foundation, Inc. and Country Life LLC (which donated PS for the clinical trials).

COMPLETED

KINETIN IN FAMILIAL DYSAUTONOMIA
IRB #: 09-0762
ELIGIBILITY: Patients above the age of 15 years are eligible to participate in this trial
PURPOSE: During the first part of the trial we will evaluate the safety and tolerability of kinetin, a nutritional supplement that corrects the splicing defect, in patients with familial Dysautonomia. In the second part of this trial we will evaluate if kinetin enhances the ability of neuronal tissue to correctly splice IKAP mRNA.
SPONSOR: Familial Dysautonomia Foundation, Inc.

COMPLETED

PHOSPHATIDYLSERINE (PS) IN FAMILIAL DYSAUTONOMIA – LONG-TERM STUDY
IRB #: 11-02100
ELIGIBILITY: Patients with FD of any age
PURPOSE: In this study we will follow, on a yearly basis, patients with FD of all ages who opt to take phosphatidylserine. In this study, we will evaluate the long-term safety of phosphatidylserine in patients with FD and hope to determine whether phosphatidylserine has any impact on the clinical evolution of the disorder.
SPONSOR: Familial Dysautonomia Foundation, Inc.

COMPLETED

CARBIDOPA IN FAMILIAL DYSAUTONOMIA
IRB#: S13-00065
ELIGIBILITY: Patients with FD over the age of 10.
PURPOSE: Researchers at our Center showed that, a drug called carbidopa might dampen the production of norepinephrine during hypertensive crisis in FD, and therefore decrease high BP surges. The goal of this study is to use carbidopa and evaluate the effect in blood pressure peaks and variability, norepinephrine levels and crisis in FD. The drug is currently used to treat other conditions and it is safe. Amendments to the protocol now allow for local monitoring and tele-medicine visits
SPONSOR: Food & Drug Administration Office of Orphan Product Development

COMPLETED

AN OPEN-LABEL PILOT TRIAL OF COGNITIVE BEHAVIORAL THERAPY IN FAMILIAL DYSAUTONOMIA
IRB#: S16-01823
ELIGIBILITY: Patients with FD over the age of 18.
PURPOSE: To evaluate the effect of cognitive behavioral therapy in the severity of anxiety and depression in adults with familial dysautonomia. To ascertain the levels of self-esteem in adults with familial dysautonomia at baseline and after the last session of cognitive behavioral therapy.
SPONSOR: Familial Dysautonomia Foundation, Inc.

NATURAL HISTORY INFO

We need you. The closer we can follow you, the sooner we can understand your issues and the closer it brings us to finding a treatment. Our Natural History Study is currently open and recruiting patients with FD.

There are several ways be involved:

- Patients with FD being evaluated at the NYU Dysautonomia Center in New York or at the Sheba Medical Center in Israel will have the option to be enrolled in the Natural History Study. Both centers share the same database regardless of the different locations.
- If, for whatever reason, you are unable to visit New York or Israel, you can still send medical records from your local doctors. In addition to receiving medical recommendations by the FD doctors, your information will be included in the database.

What type of clinical information should you send?

- Your most recent sleep study report
- Your most recent swallow study report
- Your most recent office visit notes from your neurologist or other specialist
- Your most recent chest-CT or Chest x-ray report. Ideally you should also send a CD/DVD with the images.
- Your most recent eye evaluation, ideally including retinal optical coherence tomography (OCT) and other visual function tests
- Your most recent pulmonary function tests
- 24-hour blood pressure recordings
- Results from regular blood or urine tests
- Notes from hospital admissions or surgical admissions
- A current medication list

These tests are routinely recommended for patients with FD as part of their standard medical care. They help screen for potential problems and determine when treatments are necessary. If you are still unsure of what to send, send us any your information from any visit to a doctor.

The FD Questionnaire: The FD Questionnaire has been developed over several years to provide doctors with the information they need in clinical practice. It is a series of questions that cover all the body systems, how they function, and identify common complications at different stages of the disease. The questionnaire is specifically designed for patients with FD, to be filled on a yearly basis. Filling it out will help families prepare for their visits with doctors. The FD Center will send you a copy of the questionnaire as soon as you schedule your appointment (212-263-7225).

What will happen with my information? The information received will be stored in specially designed databases, an idea originally implemented by Dr. Felicia Axelrod. It will be used by the research team to answer pressing clinical research questions. It allows us to look at trends overtime and examine which treatments are truly effective for treating FD. It allows us to look for patterns to provide guidelines that will shape clinical practice. The study is designed to support clinical trial readiness to speed up drug development to improve the lives of patients with FD. The goal is to help other researchers working and collaborating on FD to use this information to support their scientific work.

Official sites for the Natural History Study of FD: In the United States - NYU Dysautonomia Center, 530 First Avenue, Suite 9Q, New York, NY, 10016. In Israel - Sheba Medical Center, Tel Hashomer, Derech Sheba 2, Ramat Gan, Israel.

How is my information protected? The information collected in the natural history study is stored in a secure encrypted server supported by NYU Langone Health MCIT. Access to identifying information is restricted to NYU Langone Health administered terminals. Patients should transmit their medical records through data-protected safe channels, including MyChart and NYU Langone Safe-Email Portal. Information and support for this can be provided. Data shared for research is de-identified, entered into a secure online data collection platform (RedCap), with controlled access.

Staff

Horacio Kaufmann, MD
Director

Lucy Norcliffe-Kaufmann, PhD
Associate Director

Jose Martinez, MS
Clinical Trials Manager

Bhumika Balgobin, MD
Neurology Fellow

Miguel Perez
Data Manager

Maria Cotrina, PhD
Research Scientist

Jose-Alberto Palma, MD, PhD
Assistant Director

Lee-Ann Lugg, BS
Administrative Assistant

Isabella Schneider
Project Assistant

Vivian Cao, BS
Project Assistant

Amelia Lim Qiu Ru
Project Assistant

Collaborators

Susan Slaughenhaupt, PhD
Frances Lefcort, PhD
Howard Trachtman, MD
Bat-el Bar, MD
Joseph Levy, MD
Amal Dakka, PhD
Monica Salani, PhD
Leela Raju, MD
Carlos Mendoza, MD
Vaughan Macefield, PhD
Mikhail Kazachkov, MD
Alex Gileles-Hillel, MD, PhD
Joel Gutierrez, MD
Elisabetta Morini, PhD
Yvonne Lui, MD, PhD

Support for the Program

Familial Dysautonomia Foundation, Inc.
Food and Drug Administration
MSA Coalition
National Institutes of Health
Michael J. Fox Foundation
PTC Therapeutics

2019 HIGHLIGHTS

Dr. Alberto Palma was recognized by the American Autonomic Society as the first recipient of the Felicia Axelrod Investigator Award.

Expert guidelines published outlining best practices for the treatment of lung disease in familial dysautonomia

Dr. Norcliffe-Kaufmann and Dr. Alberto Palma both promoted to the academic rank of Associate Professor based on their contributions to FD research

Research work shows how to reverse daytime hypercapnia in familial dysautonomia

Dr. Joel Gutierrez recognized by the Cuban Academy of Sciences for his work in mapping nerve reflexes in patients with familial dysautonomia

Dr. Norcliffe-Kaufmann selected for the Rare Disease Scholars Program supported by NIH

Dr. Kaufmann visits Hadassah and Tel Hashomer hospitals to map out a plan for future collaboration

The Natural History Study opens at sites the US and in Israel

Frances Lefcort is awarded an NIH grant to study the microbiome and enteric nervous system in familial dysautonomia

The natural history study expands to capture patients with familial dysautonomia that are cannot visit a clinic

Scientists at PTC Therapeutics declare a candidate compound to develop as a disease-modifying treatment that targets the production of the faulty protein

The first industry-sponsored Clinical Advisory Board Meeting is held in New York City

Familial Dysautonomia Foundation commits to continued support of the center and research program

Montreal Chapter of the Dysautonomia Foundation provides a grant to support a mental health counseling program at the Center

Montreal Chapter of the Dysautonomia Foundation provides a grant to upgrade the research laboratory equipment

The Michael J Fox Foundation, the Familial Dysautonomia Foundation and PTC Therapeutic jointly fund the purchase of a new OCT machine for the eye lab

WAYS TO HELP

Stay up to date: New studies for patients with FD open throughout the year. There are several places where you can learn about new research opportunities: sign up for our blog at DysautonomiaCenter.com; follow the Dysautonomia Center on Facebook; read the Foundation's Dyscourse magazine; and ask the clinicians at your annual evaluation visit.

Give samples: By giving a small sample of blood, we can measure the levels of the IKAP protein. We hope to develop this as a measure to test the outcome of different treatments to preserve neurological function in patients with FD. You can also donate muscle samples when undergoing routine surgeries.

Send your doctors reports: Have you visited your eye, kidney, or lung doctor recently? By sending us your clinical results or reports, we can add the information to our natural history study and help better understand how to treat patients with FD.

Support the Familial Dysautonomia Foundation: No single organization has done more to change the face of treatment of FD. The Foundation's unwavering support over the last 49-years has helped to centralize the care of patients with FD and to bring new treatments to the clinic. The Foundation and its chapters around the world have regular fund-raising events to support the cause. They make it possible for us to make important equipment upgrades, have a mental health program, maintain a dedicated team, and provide 24h emergency care to families at times of need.

Call us: Keep in touch. Periodically calling to find out about new research opportunities is an important way to find out what is new at the Center. Our staff can tell you about new studies and discuss whether our clinical trials may be right for you. Dr. Maria Cotrina is available to answer questions about studies you may be interested in joining and how to enrol.

Tell your friends. Talk to your friends about studies that you participate in. This will hopefully encourage them to be consider participating. Research in rare diseases like FD relies on having a committed community. Each time you give up your time for research the knowledge gained helps pave the way for other potential treatments.

STAY CONNECTED

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https://familialdysautonomia.org/news/newsletter

https://nyulangone.org/locations/dysautonomia-center

NYU Dysautonomia Center
530 First Avenue, Suite 9Q
New York, NY, 10016
www.dysautonomiacenter.com