In Focus

Dear Readers

This “In Focus” report is the third in a series of MDA comprehensive reports about the latest in neuromuscular disease research and management.

This report focuses on the periodic paralyses, a group of disorders that result from malfunctions in so-called ion channels, microscopic tunnels that make possible high-speed movement of electrically charged particles across barriers inside cells and between cells and their surroundings.

When ion channels fail to open or close according to an exquisitely fine-tuned program, episodes of paralysis of the skeletal muscles and even temporary irregularities in the heartbeat can occur.

Throughout history, and unfortunately down to the present day, people who experience episodes of paralysis or weakness, interspersed with periods of normal functioning, have been met with suspicion by their peers and even their doctors. Individuals have been accused of faking their attacks to gain attention or shirk their responsibilities, and parents have been suspected of child abuse when their children displayed these mysterious symptoms.

Today, molecular biology has pinpointed the precise mechanisms that underlie the periodic paralyses, and drug trials to treat them are under way. There is much work to be done, but awareness of the diagnosis can provide significant reassurance and help in managing these conditions.

This special section includes:
• “Fast Facts” about periodic paralysis
• An update on state-of-the-art research and disease management, with first-person stories from families affected by periodic paralysis
• Information about genetic testing

To learn more about periodic paralysis, visit www.mda.org or call your local MDA office at (800) 572-1717.

Fast Facts

MDA’s three-year commitment for all periodic paralysis research as of March 2009 is $1,938,367. The Association’s allocation for research on hyperkalemic and hypokalemic periodic paralysis research since 1950 is $8,125,341. MDA’s allocation for the recently identified Andersen-Tawil syndrome is $515,430 since 2001. MDA is currently funding 11 grants in the periodic paralyses.

The periodic paralyses are generally divided into hyperkalemic periodic paralysis, hypokalemic periodic paralysis and Andersen-Tawil syndrome. The first two are caused by genetic defects in high-speed tunnels in skeletal muscle fibers known as ion channels. The last is due to such defects in both skeletal and cardiac muscle.

All forms of periodic paralysis affect both sexes equally and are inherited in a dominant manner, meaning only one genetic flaw (mutation) from one parent can cause the disease.

Hyperkalemic periodic paralysis

Hyperkalemic PP usually begins early in childhood, with episodes of muscle weakness or paralysis lasting from 15 minutes to hours or even days. With time, some people develop permanent mild or moderate weakness that persists between bouts of severe weakness. Some patients also experience episodes of myotonia, the inability to relax muscles completely.

The underlying cause is any of several genetic mutations in a gene on chromosome 1 that carries instructions for a calcium channel protein in skeletal muscle fibers. When this channel fails to transmit a signal to a calcium storage area inside the cell, the muscle fiber can’t contract. A minority of people have sodium channel mutations, but not the same ones that cause hyperkalemic periodic paralysis.

Andersen-Tawil syndrome

This syndrome usually begins in childhood or adolescence and is characterized by episodes of weakness of the skeletal muscles and irregular heartbeat in the cardiac muscle. Occasionally people may develop permanent weakness between episodes. Heartbeat irregularities can be serious enough to warrant treatment with medication or electronic devices. Widely spaced eyes, low-set ears and a small chin also are characteristic of this disorder.

The underlying cause of Andersen-Tawil syndrome is any of a number of genetic mutations in a chromosome 17 gene for a potassium ion channel present in both skeletal and cardiac muscle tissue. When these channels fail to open, the exit of potassium from muscle cells after they contract is impaired, and the cells can’t “reset” to receive further contraction signals.

Hypokalemic periodic paralysis

Hypokalemic PP can begin anywhere from early childhood to the 30s, with periodic attacks of severe weakness lasting hours to days. The frequency of attacks generally lessens in the 40s or 50s. Permanent weakness may persist between attacks, usually beginning in middle age and progressing slowly over years.

The most common underlying cause is any of several genetic mutations in a gene on chromosome 1 that carries instructions for a calcium channel protein in skeletal muscle fibers. When this channel fails to transmit a signal to a calcium storage area inside the cell, the muscle fiber can’t contract. A minority of people have sodium channel mutations, but not the same ones that cause hyperkalemic periodic paralysis.

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In Focus: It’s All in the Muscles, Not the Head

Individuals and families struggle to manage the periodic paralyses, a group of diseases that’s too often misunderstood by teachers, employers and even health professionals

by Margaret Wahl

People who know me know I lead an extremely active life," says Linda Feld of Longwood, Fla. “People don’t see me as somebody on a scooter. I’m Linda, and I do all these things every day, and they know me for me. I tell people that periodic paralysis has become my friend. It’s along for the ride, but it’s not going to rule my life.”

Feld, now 59 and a hospice volunteer, says her experience with the genetic disease she now knows as hypokalemic (“low potassium”) periodic paralysis goes back to her earliest memories, at age 3 or 4.

“I would develop a limp [periodically],” she recalls. “We’re talking the early 1950s, and not much was known about periodic paralysis. Even though my father was disabled, he didn’t have a diagnosis.”

An orthopedic specialist suspected her legs were of unequal length and prescribed a lift for her shoe and supportive footwear. “It was always very important to my parents that I wore really sturdy shoes. I wanted to be like the other kids and wear sneakers,” Feld says.

“I was never good at gym in school. There was teasing by fellow classmates. I couldn’t run fast. When I reached my teen years, I started having terrible muscle cramps. There was nothing that would alleviate the pain. The muscles became rock hard. It was not my whole body, always just a limb. Those cramps lasted 24 to 48 hours. Then they would start to subside, but the weakness took weeks to come back from. I missed big segments of school.”

Feld finished high school and went on to college. When she was about 20, she visited the MDA clinic at Yale University in New Haven, Conn., where a doctor suggested her condition might be periodic paralysis but wasn’t sure.

She tried to work, but soon “it became more and more difficult to hold down a job. The weakness episodes would come on, and I couldn’t get out of my desk chair at work. I’d be sitting there working and couldn’t get up to go to the copy machine. It became impossible to hold a job.”

As she aged, the paralysis episodes ceased, but were replaced by progressive and ultimately permanent weakness. (The lack of episodes and the permanent weakness made diagnosis even more elusive.) She tried breeding dogs, but the work of maintaining a kennel eventually proved too taxing.

Feld’s sister, Sally, nine years younger, began following a similar pattern. “When she reached her teenage years, she started with terrible episodes of muscle cramping,” Feld recalls. Sally was given an erroneous diagnosis of limb-girdle muscular dystrophy.

Their father retired at age 55 because of continued weakness, including weakness of his respiratory muscles. A bad chest infection when he was 72 caused his doctor to recommend a tracheostomy, a surgical opening in the trachea, through which mucus would be suctioned out.

The family was unaware at the time that certain anesthetics, both gas and local, and muscle relaxants called “depolarizing” agents, frequently used during surgery, can cause long-lasting and severe weakness in people with periodic paralysis. Epinephrine, often added to local anesthetics, also can cause problems. If the respiratory muscles are affected, respiratory insufficiency can result.

Feld’s father became completely paralyzed after the anesthesia he was given for the tracheostomy procedure and succumbed to a respiratory arrest a few days later.

Feld finally got a definitive diagnosis when she was 56 years old, through the laboratory of Frank Lehmann-Horn at Ulm University in Germany.

Lehmann-Horn, who received several MDA grants in the 1990s to study the periodic paralyses, was originally trained as an engineer, later becoming a medical doctor. He’s widely regarded as an outstanding contributor to the study of ion channel physiology, having done more to describe its behavior in health and disease and to apply his findings to patient care than perhaps any other professional.

Feld says the disease has forced many compromises in her life. “I had to learn I could not be everything that everybody else was. I couldn’t be the athlete, couldn’t follow the crowd and do what they did. I couldn’t go out and go drinking with them. Alcohol was a big trigger. I wish I had known earlier in life some of the things that work for people.”

Today, she manages her disease with a medication called eplerenone (Inspra),
which keeps her serum potassium levels up; potassium supplements as needed; and avoidance of certain activities, foods and medications.

Carbohydrates and salt bother her, as does repetitive muscle activity, like peeling potatoes. “I work with computers, and that doesn’t bother me,” she says. “But if I were to hold a potato and use a peeler to keep peeling that potato, my hand would become paralyzed.”

Being cold can trigger an attack, as can corticosteroid medications (such as prednisone).

She’s undergone a hip fracture repair and a hysterectomy with spinal instead of general anesthesia. “That was a piece of the puzzle that was extremely important to get,” she says. “We have a very strict anesthesia protocol.”

“I’m happy to be the vehicle to tell the story to as many people as possible, so that the children growing up today with this disease do not have to follow the same frustrating path I did,” Feld says. She welcomes inquiries about periodic paralysis, especially the diagnosis odyssey, and can be reached at lfeld@cfl.rr.com.

Channel problems can cause myotonia, weakness or paralysis

There are three major periodic paralyses: hyperkalemic (high potassium) periodic paralysis, hypokalemic (low potassium) periodic paralysis, and Andersen-Tawil syndrome, explains Louis Ptacek, a neurologist who specializes in the study and treatment of ion channel diseases at the University of California at San Francisco.

The first two affect only the channels in skeletal muscles. The last affects ion channels in both skeletal and cardiac muscles.

During the 1990s, when he was an MDA research grantee at the University of Utah, Ptacek played a major role in the identification of the genes underlying hyper- and hypokalemic periodic paralysis. More recently, he’s received MDA support to study Andersen-Tawil syndrome at the University of California. Although the first two periodic paralyses are named for their relationship to serum potassium levels (kalium is Latin for potassium), this can be misleading, Ptacek says.

People with periodic paralysis often have normal serum potassium levels when tested between attacks, and even often during an attack, contributing to the difficulty of diagnosing their disease. “The term ‘kalemic’ has to do with the ability to precipitate attacks,” Ptacek says. “It does not have to do with whether serum potassium is high or low during an attack.”

In general, people with hyperkalemic PP are more likely to experience an attack of paralysis when their serum potassium is temporarily high, and those with hypokalemic PP are more likely to experience one when their serum potassium is temporarily low. (Normally, serum potassium levels are 3.5 to 5.0, measured in units called “milliequivalents” per liter.)

Most people have ion channels that work so effectively that they can quickly readjust for a transiently high or low blood potassium level, so that muscles stay poised to receive nerve signals that allow them to contract or relax. But in periodic paralysis, these ion channels, because of a genetic mutation, don’t work the way they should. They may open or close too easily, or with difficulty; or they may stay open or closed too long. Or they may fail to transmit a signal to another part of the cell.

When serum potassium levels change in response to dietary intake, medications, cold temperatures, exercise, rest or anesthesia, the channels can’t quickly adjust to compensate for the change. Patients then become temporarily paralyzed, although not necessarily throughout the body. A more localized attack may affect just part of the body, such as a leg or arm.

In some cases people also experience a tingling sensation. Pain or prolonged contraction (myotonia), sometimes with severe cramping and hardening of the muscles, is most likely to occur in hyperkalemic PP. Permanent weakness between attacks sometimes develops.

‘Interesting and different’

Andersen-Tawil syndrome is a more dangerous condition than the other two forms of PP because of its potential to induce serious abnormalities in heart rhythm. Ellen Andersen at the University Hospital of Copenhagen (Denmark) is credited with the first description of this disorder back in 1971.
In the early 2000s, Rabi Tawil at the University of Rochester (N.Y.) led an effort to collect a large cohort of patients and refine the diagnostic criteria. Tawil is co-director of the MDA clinic at the University of Rochester Medical Center, where he conducted MDA-supported research on what would later become known as Andersen-Tawil syndrome. Ptacek and colleagues identified the underlying genetic and biochemical mechanisms.

"Andersen-Tawil syndrome is interesting and different," Ptacek says. "It’s a complicated, multisystem disease. Like other periodic paralyses, it’s highly penetrant, which means that if you have the genetic mutation, you get the disease. But in many cases, the person with periodic paralysis knows of no family history of the condition. In these cases, it’s believed to be caused by a new genetic mutation, not one that’s been seen before in the family. (From that point on, however, it can be inherited by future generations.)

A long and winding road led to hyperkalemic periodic paralysis diagnosis

Hyperkalemic PP stems from mutations in the sodium channels that sit on the surface of muscle fiber membranes. These channels normally respond to a signal from a nerve cell by opening briefly and allowing sodium ions to flow into the fiber.

Sodium ions carry a positive electrical charge, and when they enter a cell, they make it more positive, a phenomenon referred to as "depolarization."

But mutations in the sodium channel gene cause these channels to malfunction when they’re in a high-potassium environment, such as when foods high in potassium are ingested or when a person rests after exercising. Under these circumstances, the sodium channels fail to close right away, allowing sodium to continue leaking into the muscle fiber and keeping the muscle fiber (muscle cell) membrane depolarized.

This depolarization may cause prolonged muscle contraction temporarily. However, weakness or paralysis soon occur, because a depolarized muscle fiber can’t receive new signals from a nerve cell.

"Too much potassium narrows the
safety margin, and people with hyperkalemic periodic paralysis have less of a safety margin to begin with," Ptacek says. "When you increase the extracellular potassium, it pushes them over a threshold where the cell remains depolarized."

That's what began happening to Faith Couture of Dayton, Ohio, when she was 2 years old. She's now 9.

"It looked like she would play possum when anybody would get her out of the car," says her mother, Enola. "But we started thinking, 'she's too young to do that.' We watched how she reacted when we set her on the ground. She was like a blob of Jello. She would just collapse and start crying."

Soon after the car episodes, Faith began waking up from naps unable to move, sweating and screaming. There was no family history of anything like what Faith was experiencing.

The pediatrician suggested the problem was "growing pains," later revising his diagnoses to juvenile arthritis or multiple sclerosis. A referral to one neurologist resulted in a diagnosis of learning disability and speech impairment, while another neurologist told the Coutures, "It's in your daughter's head. Get over it."

Faith's father was in the Air Force at the time, and the frequent moves around the country added complications to the diagnostic process.

"We've had so many misdiagnoses that if we hadn't taken the initiative and been guided by two or three doctors, we probably would have gone with whatever we heard. We were told 19 times this was seizures."

When Faith was 7, the family received orders to go to Ohio and ended up at Children's Hospital in Dayton. There, a geneticist who had worked with Robert Griggs, a longtime MDA grantee at the University of Rochester, thought he knew what the problem was and recommended DNA testing.

"They took her blood two days before her eighth birthday," Enola recalls. "When it came back a month later, it was like Christmas." The diagnosis — hyperkalemic periodic paralysis — "wasn't something we were extremely excited about," Enola says, "but we were excited to know that we weren't crazy."

Faith's episodes still aren't well controlled, but her mother says they're "still testing everything."

Faith is in the extremely unusual situation of being steered away from most fruits and vegetables, which are high in potassium, and toward sugar, which can ward off an attack of paralysis. "For now we try to manage her diet and watch how much she has in fruits and vegetables," her mother says. "The only problem we have with her is tomatoes. She's a Southern child and loves tomatoes."

Because some kidney diseases require a potassium-restricted diet, a good reference for the potassium content of foods, and a method to reduce the potassium in vegetables, is the National Kidney Foundation Web site at www.kidney.org. (There are, however, marked differences between the management of kidney disease and periodic paralysis, even if they overlap in one area.) The potassium fact sheet can be found at www.kidney.org/news/newsroom/fs_new/potassiumCKD.cfm; or you can contact the Foundation at (800) 622-9010.

Giving Faith some sugar to take to school has helped somewhat as well, says Enola. A Coke around 11 a.m. seems to have helped a little bit. "She's not having [attacks] as frequently. We keep an eye on her."

How Ion Channels Regulate Muscle Contraction

Depolarization of the muscle fiber is sensed by calcium channels and triggers the release of calcium ions from internal storage areas. This flood of released internal calcium is the chemical signal that causes the thick and thin filaments of the muscle fiber to slide past each other (contract).

The sodium channels spontaneously close, potassium channels open, and positively charged potassium ions exit the fiber. Chloride channels also stay open, and negatively charged chloride ions enter the fiber. All these actions cause the inside of the fiber to become more negative ("repolarized"). The muscle fiber returns to its resting state, calcium is pumped back into the internal storage vesicles, and the fiber is now ready to accept another surge of positively charged ions in response to stimulation from a nerve fiber. (When several muscle fibers are at rest, a muscle can relax.)
Father, son and daughter struggle with hypokalemic PP

Carl Parker, 43, of Enon, Ohio, who has hypokalemic periodic paralysis, says his life has never been easy. But finding out his children also are affected has been even harder than having the disease himself.

Parker’s parents knew something was wrong fairly early, but they didn’t know what. As in Faith Couture’s family, no one else was affected.

“As a kid, I was very clumsy, but we didn’t really know why,” he recalls. In 1972, when he was 6 years old, he underwent a muscle biopsy at Children’s Hospital in Columbus, Ohio (now Nationwide Children’s). Neurologist Jerry Mendell, then a young physician

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### The Periodic Paralyses

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Hyperkalemic Periodic Paralysis</th>
<th>Hypokalemic Periodic Paralysis</th>
<th>Andersen-Tawil Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of problem</td>
<td>sodium channel</td>
<td>calcium channel (most common)</td>
<td>potassium channel</td>
</tr>
<tr>
<td>Location of gene</td>
<td>chromosome 17</td>
<td>chromosome 1</td>
<td>chromosome 17</td>
</tr>
<tr>
<td>Inheritance pattern</td>
<td>dominant</td>
<td>dominant</td>
<td>dominant</td>
</tr>
<tr>
<td>Functional defect</td>
<td>channel does not close properly; prolonged sodium leak into cell</td>
<td>calcium channel on cell surface does not transmit signal for interior calcium release</td>
<td>channel does not open properly; potassium can’t leave cell</td>
</tr>
<tr>
<td>Average age of onset</td>
<td>before age 10</td>
<td>age 5 to 35</td>
<td>age 2 to 18</td>
</tr>
<tr>
<td>Average duration of episodes</td>
<td>30 minutes to 4 hours</td>
<td>2 to 24 hours</td>
<td>1 to 36 hours</td>
</tr>
<tr>
<td>Maximum weakness</td>
<td>mild to severe</td>
<td>severe</td>
<td>moderate</td>
</tr>
<tr>
<td>Development of permanent weakness</td>
<td>may occur; increases with age</td>
<td>may occur; increases with age</td>
<td>may occur; increases with age</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>may occur in exercised muscles</td>
<td>may occur in exercised muscles</td>
<td>may occur in exercised muscles</td>
</tr>
<tr>
<td>Episode triggers</td>
<td>high blood potassium; high potassium intake; fasting; cold temperatures; certain anesthetics; depolarizing muscle relaxants</td>
<td>low blood potassium; high carbohydrate intake; rest after exercise; cold temperatures; certain anesthetics; depolarizing muscle relaxants</td>
<td>high or low blood potassium, depending on exact genetic mutation; certain anesthetics; depolarizing muscle relaxants; other triggers consistent with either hyper- or hypokalemic PP</td>
</tr>
<tr>
<td>Treatment</td>
<td>• hydrochlorothiazide, furosemide, acetazolamide or dichlorphenamide; glucose-insulin solution; inhaled albuterol; drugs that bind potassium • carbohydrate intake, low-potassium diet • frequent meals, warmth, keep moving • avoid certain anesthetics and depolarizing muscle relaxants</td>
<td>• potassium supplements, acetazolamide (can harm some patients), dichlorphenamide, spironolactone or eplerenone • high-potassium, low-carbohydrate, low-sodium diet; warmth; keep moving • avoid certain anesthetics and depolarizing muscle relaxants</td>
<td>• cardiac medications such as beta blockers and anti-arrhythmics, implanted pacemaker-defibrillator • acetazolamide or dichlorphenamide can help or harm • high- or low-potassium diet, depending on mutation • avoid certain anesthetics and depolarizing muscle relaxants</td>
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and now a longtime MDA research grantee at Ohio State University and Nationwide Children’s, arranged for a muscle biopsy. The diagnosis came back “unknown,” Parker says, but the tissue appeared to have bubbles called vacuoles. “They said it looked like a Milky Way candy bar,” he says.

As his childhood progressed, Parker continued to be clumsy. “Some days I didn’t function well. I had trouble getting up and down, couldn’t run well and would fall down for no apparent reason. They tried high-top shoes. We went to different doctors, but they didn’t understand the problem.”

Then, at age 12, Parker experienced his first true attack of periodic paralysis. “My parents were out for the evening,” he remembers. “I was sitting on the couch, eating popcorn and drinking a pop. I went to get up and I couldn’t.”

Parker’s parents arrived home, and his father tried unsuccessfully to get him up and walking. “My legs didn’t work, and my arms were weak. I could still move them a little bit. I could wrap my arms around my dad’s neck,” he remembers.

At Children’s Hospital, Parker’s serum potassium level was 1.8, which is very low, and he was started on potassium supplements. “That started a whole process of doctoring. We went through a whole gamut of potassium [types] to find the one that worked for me.” Although Parker still didn’t have a diagnosis, at least he had something that seemed treatable, if imperfectly.

Then, at 15, he experienced a major attack of paralysis. He was already in the local hospital undergoing intravenous treatment for an extremely low serum potassium level. Unfortunately, in addition to potassium, the IV contained glucose (sugar), which drives potassium from the bloodstream into cells.

When treating potassium deficiency in other conditions, that would be the goal. But in hypokalemic periodic paralysis, which Parker would soon learn was his diagnosis, it triggers a paralysis attack by lowering serum potassium.

“Potassium travels into muscle cells when glucose goes in,” Ptacek says. “If you drop a hypokalemic periodic paralysis patient’s serum potassium level, you can precipitate an attack.”

“It was the worst spell I ever had,” Parker says. “They had pulled the door shut on my room that night. I was trying to yell, but I couldn’t, and I couldn’t reach the buzzer.”

Parker was finally taken to Ohio State by ambulance, where they started treating him with oral potassium. Several hours later, his serum potassium level was back up, and the diagnosis became clear.

“They did a lot of tests. They finally got me medicated and got me going.”

Parker began taking oral potassium and acetazolamide.

Ptacek admits that the mechanism by which acetazolamide and other diuretics in the “carbonic anhydrase inhibitor” family actually work in periodic paralysis remains uncertain. Some experts believe they interact directly with ion channels, he says, while others believe their effects on the acidity of the serum are involved.

“The teenage years were very rough for me,” Parker says. He had paralysis attacks every few days, often requiring a hospital stay.

Like other periodic paralysis patients, he soon learned that high-carbohydrate meals (such as the popcorn and soda he ingested the night of his first full-blown episode) trigger attacks. (Like intravenous glucose, these carbohydrates cause potassium to migrate from the serum into the cells, lowering serum potassium levels.) But the paralysis was still unpredictable.

“I could eat almost anything and not have an attack and then three days later have an attack,” he says. He also found attacks could be triggered by excess sodium and by cold temperatures.

“Until about 25, it was very rough. I had a lot of attacks. I always had a rough time holding jobs. It’s hard to explain to people. I’m 6 feet 2, 290 pounds. I could tear the barn doors off a barn, but some days I can’t get out of bed.”

Parker has the type of hypokalemic PP caused by a mutation in a cell-surface calcium channel gene. (A minority of patients have hypokalemic PP caused by sodium channel mutations that are different from those that cause hyperkalemic PP.)

The surface calcium channels, unlike the other ion channels, don’t play an important role in the movement of calcium into and out of the muscle fiber. Instead, their role is to sense changes in the electrical state (voltage) in the fiber and transmit signals to storage areas inside the fiber, from which calcium ions are then released, causing contraction of the fiber.

When the surface calcium channels malfunction in hypokalemic PP, this signaling doesn’t happen, and the muscle fiber doesn’t contract.

In 2002, Parker’s DNA was tested at Lehmann-Horn’s laboratory in Germany, the same lab that would later pinpoint Linda Feld’s genetic abnormality, and he learned the precise mutation that affects his calcium channel gene.

Although his own attacks of paralysis have become less frequent, he now has a son and a daughter with the disease.

“From what we were told [in the 1980s], we thought it couldn’t be geneti-
Genetic testing can bring relief, assist with management

Many laboratories in the United States and Europe now conduct genetic testing for the periodic paralyses. See www.genetests.org for a list. (Click on Laboratory Directory and search by disease name.)

Frank Lehmann-Horn and Karin Jurkat-Rott conduct extensive genetic testing for all three types of PP (including Andersen-Tawil syndrome). Their laboratory is at Ulm University in Germany, but they also help U.S. patients. The Web address, with all pertinent information, is http://physiologie.uni-ulm.de/angewandte-physiologie. Contact Lehmann-Horn at frank.lehmann-horn@uni-ulm.de.

“I traveled throughout the United States trying to find a diagnosis,” says Linda Feld. “I feel the [doctors] in the United States try to put people with periodic paralysis into too tiny a box. They have a very definite diagnosis in their mind. They describe the disease in very narrow terms, so it’s hard to fit the box they’re trying to put you into. Dr. Lehmann-Horn goes to the nth degree. He makes a box for the patient. If he doesn’t find your mutation, he does linkage analysis on the whole family.”

Linkage analysis is a technique in which the DNA of family members with and without a genetic disorder is compared in an effort to find the disease-associated difference.

A study of Feld’s family revealed they had a previously unknown mutation in the gene for the voltage-sensing calcium channel.

“I could never get a firm diagnosis from any physician until I was genetically identified by Dr. Lehmann-Horn in the fall of 2006 at age 56,” Feld says. “It was my new birthday. My diagnosis up to that point had included and excluded periodic paralysis several times, as well as many other diseases.

“Finding the mutation has made a huge difference in my life, because they were able to tell me what kind of drugs I could use to better manage the disease.” Feld now takes eplerenone (Inspra), a so-called potassium-sparing diuretic, a drug that increases water loss through the kidneys but maintains or raises serum potassium levels. She also takes acetazolamide, although she’s reduced her dosage of that drug, and potassium supplements.

“I also learned that potassium is a really good friend of mine,” Feld says, “and that taking a lot of potassium is not a dangerous thing for somebody with hypokalemia. If I feel an arm muscle getting stiff, I take potassium and get rid of it.”

MDA supports basic and clinical research

Today, MDA is allocating about $2 million for studies related to periodic paralysis. Of immediate relevance to patients and families is a multicenter clinical trial comparing acetazolamide with another carbonic anhydrase inhibitor called dichlorphenamide for people with hyper- or hypokalemic periodic paralysis.

For more about this study, which is being funded by the National Institutes of Health with additional support from MDA, contact project coordinator Patty Smith at the University of Rochester (N.Y.) Medical Center, (585) 275-4339 or patty_smith@urmc.rochester.edu.

Other MDA-supported researchers are studying how mutations in genes for ion channels affect channel function and muscle contraction; creating mouse models of the periodic paralyses; and identifying the characteristics of Andersen-Tawil syndrome.

For updated information about clinical trials and studies in the periodic paralysis, see the clinical trials section of the MDA Web site at www.mda.org/research/clinicaltrials.aspx and the National Institutes of Health clinical trials site at www.clinicaltrials.gov.

Editor’s note: As this article went to press, we learned that Carl Parker died abruptly following an appendectomy. The cause of death has not yet been determined.