



Siegel
Rare Neuroimmune
Association

Membership Packet



advocating for those with ADEM, AFM, MOGAD, NMOSD, ON & TM

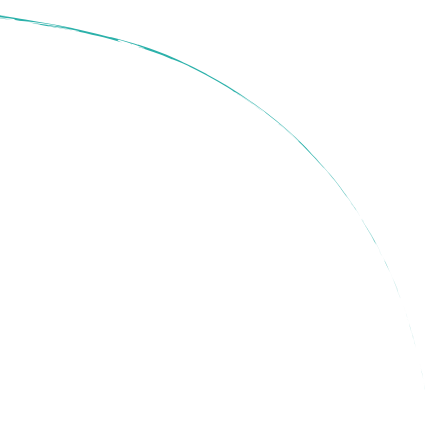


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Welcome

Being diagnosed with a rare neuroimmune disorder is often frightening and isolating. You are fine one day, and then are suddenly unable to move, see, or feel your body. You probably have never heard of your disorder before you were affected. You may be lucky enough to have support from friends and family members, but something seems to be missing; you know no one else with a rare neuroimmune disorder. No one knows the searing pain, the fatigue, the sense of anxiety, and confusion. **We are here to help.**





We know firsthand how difficult being diagnosed with a rare neuroimmune disorder can be. We know how isolating it can be to live with a condition so rare and life-changing, but please know that we are here for you. **You are not alone.**

Please read through this packet carefully to learn more about SRNA, the benefits of membership and being part of the community, and specific information about rare neuroimmune disorders.



Our Mission

The Siegel Rare Neuroimmune Association (SRNA) **advocates** for, **supports** and **educates** individuals and their families diagnosed with acute disseminated encephalomyelitis, acute flaccid myelitis, MOG antibody disease, neuromyelitis optica spectrum disorder, optic neuritis, and transverse myelitis, and **accelerates** and **invests** in scientific research, therapy development, and training of clinician-scientists dedicated to these disorders. Our end goal is to improve the quality of life of individuals with rare neuroimmune disorders and redouble our commitment to finding a cure. **Together.**



Founded in
1994



We are a team of
11 people



Supporting
15,351 members



From
121 countries



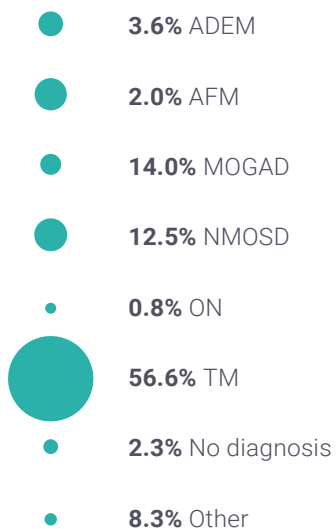
Frankie Reich, diagnosed with vascular myelopathy at less than 12 months old.

Our Impact

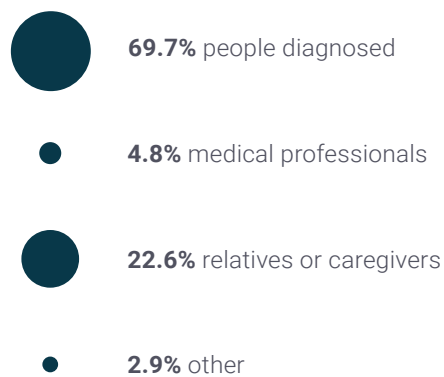
In 2021, we supported and advocated for **15,351** members worldwide



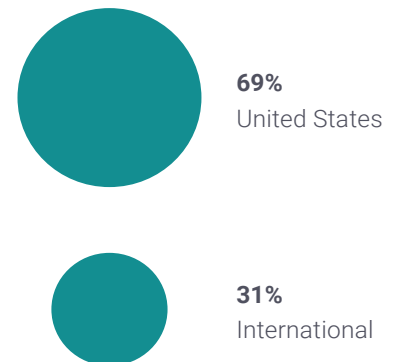
Diagnoses



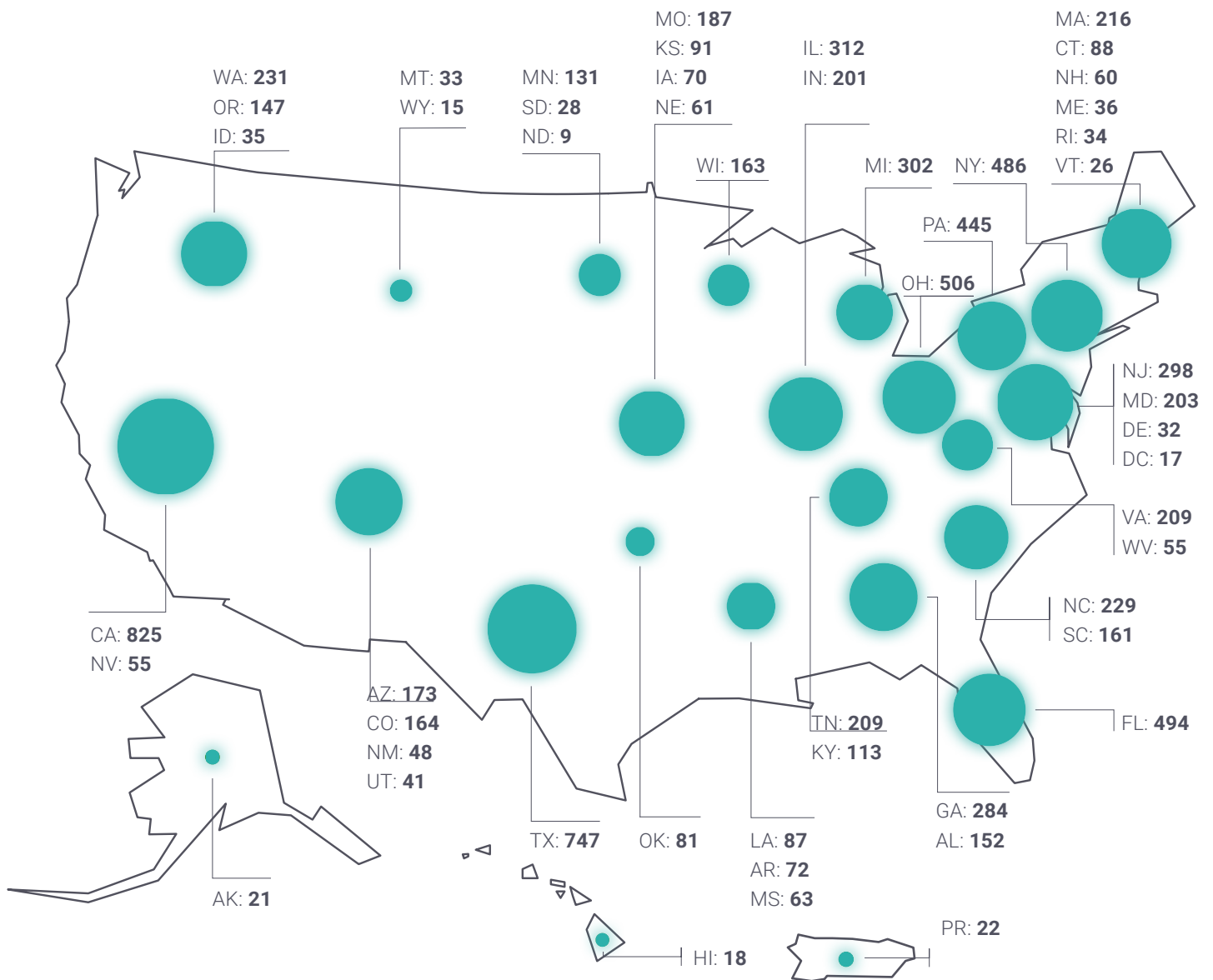
Type of membership



Location



Membership Breakdown



> 3,800

emails and calls answered offering support

20

national and international support groups

207

medical professionals in our network

643

individuals supported through the SRNA Helpline

632

resources published in our resource library

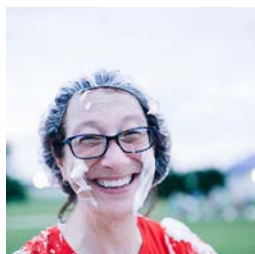
179

participants at the 2021 virtual RNDs

Our Community

Our community is made up of individuals with rare disorders, their family members and caregivers, and the medical professionals who treat individuals with these disorders. They are a **community of heroes** for a common cause – to advance diagnosis, treatment, research, and awareness of **ADEM, AFM, NMOSD, MOGAD, ON, and TM**, and share their stories with others. SRNA currently has more than **15,351 members** from more than **121 different countries**.





Janet, CRNP, KKI



Noah, AFM



Jessica, TM



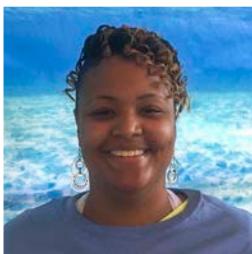
Barbara, NMOSD



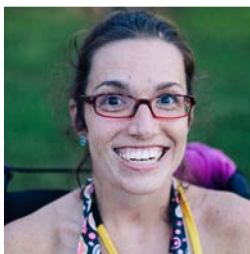
Abhijit, TM



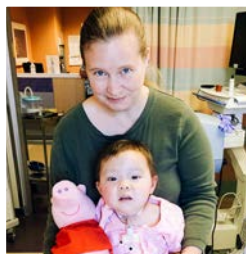
Cynthia, MOGAD



Cicely, TM



Ashley, ADEM



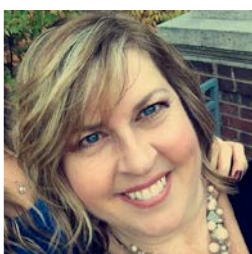
Kayla, AFM



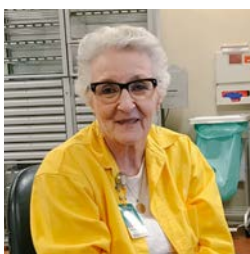
Dennis, NMOSD



Anibal, ADEM



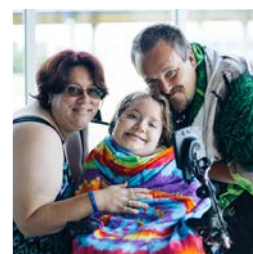
Julia, MOGAD



Sheila, NMOSD



Dr. Pardo, JHMC



Gabby, TM



Anjali, TM



Marcella, AFM



Huy, ADEM



Allen, TM



Samantha, ON



Dr. Wang, UTSW



Andrea, MOGAD



Dr. Greenberg, UTSW



Larry, NMOSD



Nash, ADEM



I became a mom on a mission after Noah was diagnosed. I knew there were many families who were in the same boat as us even though I never met them. I didn't know how many existed, but I knew they were out there. I wanted answers for not only my son, but for all the children who are currently diagnosed with a rare neuroimmune disorder, and those to come. To get those answers we need research and funding, and we need awareness. I knew I needed to be a part of that movement. I have big dreams and goals for the Massachusetts Walk-Run-N-Roll event and I will continue to dream big.

Elisa Holt, mother of Noah. Noah (right), was diagnosed with AFM at four months old.



After receiving a diagnosis in 2007 of NMOSD, I eventually found Dr. Greenberg at UTSW who encouraged me to contact SRNA and begin a Support Group for the Dallas-Fort Worth (DFW) area. It has been so encouraging to find an organization doing so much to advance the cause of advocacy, education, support for the patient community, and funding many vital projects for advancement of better treatments and knowledge of these demyelinating disorders.

Barbara Nichols, Dallas-Fort Worth Support Group Leader. Barbara was diagnosed with NMOSD at 50 years old.





Our lives were forever changed on April 1, 2013. I dropped my perfectly healthy, nine-month-old daughter, Rilynn, off at daycare that morning before heading to work. At 4:45 pm, I received a phone call from our daycare provider telling me that something was wrong. Rilynn had woken from her nap around 4:00, she drank a bottle and had a snack. And then something changed. Her eyes were glassy, and she couldn't put any weight on her legs. I left work and had no idea as I walked out the door that I wouldn't set foot in the building for another 56 days.

Both Danny and I would do anything to change this for Rilynn – let one of us deal with TM, not her. But Rilynn doesn't let it stop her. There's nothing she can't or won't do. Our family is closer because we know how quickly life can change. We appreciate the little things. We have met some amazing people and experienced some incredible generosity throughout this journey. And while we would do anything to change this for Rilynn, this is our life, this is our hope. And we embrace it.

Niki Stotler, mother of Rilynn. Rilynn was diagnosed with TM at nine months old.



I am lucky, as others are left with bigger scars from this disease. I have to deal with the occasional pain in between my shoulders and while I can see, I have visual issues. Color is dimmer, and I can't pick things out as quickly in a complicated arrangement of objects. I have had my tears, but I had to find the silver lining.

Because of these struggles, my daughter and I decided to start the MOG Project. My good friend, also a newly diagnosed MOG patient, as well as my sister, happily made the commitment to join us to support the community of those who have nowhere to go and are frightened at the prospect of having a rare disease with no cure. SRNA has graciously taken us in and allowed us to help launch their newest disease advocacy. Things are looking up and for once, the road ahead seems hopeful.

Julia Lefelar, originally diagnosed with NMOSD at 51 years old, but correctly diagnosed with MOGAD at 54 years old.





I am blessed. I have been given the humbling opportunity to provide care and guidance to many. I am surrounded by a team of professionals who are dedicated, brilliant, and passionate about our work. I am supported by institutions that are committed to the care of patients, support of families, generation of new knowledge, and the education of future practitioners. I am thankful for these gifts and committed to doing my part in the global effort to heal our patients.

My hope is to make a meaningful contribution to the patients I treat and a meaningful contribution to the patients I will never meet. My hope is that we will one day close our program because there isn't a need. My hope is that all of the amazing ambassadors recognize the incredible gift they give when sharing their story. My hope is that I will teach like Dr. William Osler (known for revolutionizing the way in which medical education was taught), by training my students to listen.

Treatments will come. Outcomes will improve. We will achieve these goals together.

Benjamin M. Greenberg, MD, MHS. Director, Transverse Myelitis, Neuromyelitis Optica Programs, UT Southwestern Medical Center and Childrens Health, Dallas, Texas



I consider myself one of the lucky ones. I grew up near Boston, Massachusetts and acquired my disability at a very young age. I was adopted from Calcutta, India and at four months of age, I became sick and was diagnosed with transverse myelitis, which left me paralyzed from the waist down.

Part of my own mission in life is to show others what is possible and help them reach their fullest potential. To me, there is power in seeing someone like you and to be a resource for many parents of kids with ADEM, AFM, MOGAD, NMOSD, ON, and TM. The researcher in me hopes that research will continue to get more national attention and we will have more dedicated dollars to grow and expand intervention and therapeutic opportunities.

Dr. Anjali Forber-Pratt, Paralympian. Anjali was diagnosed with TM at four months old.



Living with ADEM has been hard because it is a rare disorder and much is still unknown. Many doctors cannot explain the behavior changes or what we should expect. We go to many different specialists and try new therapies and medications for side effects until we find what works for him. It is hard living the unknown. I am hopeful for more research and more awareness, so others will have faster treatment, information, and a better outlook for the future.

SRNA Quality of Life Family Camp is always a special time for our family, it is a time where we get to connect with other families who are having the same struggles that we are. But the most important part of camp is that our kids get to enjoy themselves in a judgement-free zone. We get to have fun as a family, SRNA family.

Jennifer Oberfell, mother of Nash. Nash was diagnosed with ADEM at two years old.



To read their full stories, visit srna.ngo/hope-ambassadors

We are here to help

SRNA was founded in 1994 by individuals with rare neuroimmune disorders and their family members—to bring support, insight, and knowledge to those going through similar journeys. Our goal is to help individuals diagnosed with rare neuroimmune disorders and their loved ones become empowered advocates for their health, and to improve the quality of life for the people in our community.



A focus on research and training

A priority for SRNA is to partner closely with physicians to expand the medical professional network for those with rare neuroimmune disorders. We fund Fellowship training to establish more specialists in these disorders, and support research into causes and potential treatments that will one day help us develop novel therapies.








Talk to us

We invite you to ask questions, share your story, and speak to those who have gone through similar situations. We are here for you if you have just received a diagnosis, or whenever you need to talk to someone who understands. You can reach us via email at info@wearesrna.org or phone at +1 (855) 380-3330

We are also on Facebook, Twitter, Instagram, LinkedIn, and YouTube. Connect with members of our community, reach out to us if you need help and follow us for the latest news and updates.

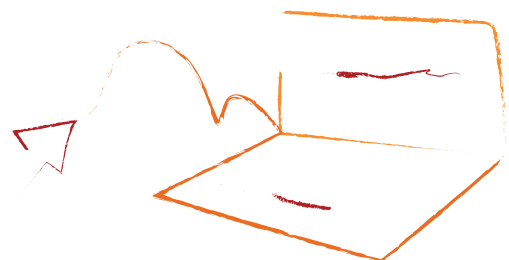


-  facebook.com/wearesrna
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-  twitter.com/wearesrna
-  youtube.com/wearesrna
-  linkedin.com/company/wearesrna

Sharing knowledge and resources


Visit srna.ngo to learn about our programs, disorder-specific information, and the latest research, and to access a wide array of in-depth resources:

- Magazines
- Podcasts
- Weekly Blogs
- Support Group Meetings
- An Extensive Resource Library
- Yearly Medical/Research Symposia



Membership benefits and programs





Now that you are a member of SRNA, you will receive information, updates, and inspiration. You can learn about other people's experiences with rare neuroimmune disorders and share your own story. You are now a member of a community dedicated to:

- ❑ facilitating a **collaborative**, dedicated **network** of patients, researchers, and healthcare professionals focused on providing **exceptional care**
- ❑ advancing our **understanding of the causes** of these disorders
- ❑ developing new acute and **restorative therapies**
- ❑ developing the **most effective management strategies and treatments** for the many challenging symptoms from these disorders

01 Disease Information

srna.ngo/disease-info

Access an up-to-date information network dedicated to rare neuroimmune disorders and find the answers you need at **srna.ngo**. SRNA's website has the most comprehensive, reliable, and accurate sources of information about rare neuroimmune disorders.

02 Medical Professional Network

srna.ngo/mpn

Search by name, country, state, and specialization to find the institutions and experts in rare neuroimmune disorders near you and connect your health care team to our medical experts to ensure you are getting the best care possible. We have over 190 medical professionals in our network, and the list is growing!

03 **Resource Library**

srna.ngo/resource-library

Find the answers you are seeking and learn about the latest research in our comprehensive Resource Library. You can easily filter content specific to your needs, including disorders, acute therapies, symptom management strategies, advocacy, caregiving, quality of life concerns, and scientific research. We have over 550 resources for you to explore.

04 **Myelitis Helpline**

srna.ngo/helpline

This online resource provides knowledge and help to our community, including those who have recently been diagnosed, or who have questions at any point after the onset of a rare neuroimmune disorder. You'll answer a brief survey so the results you receive will be specific to your needs. You'll also have the opportunity to ask detailed questions about your individual situation, and we'll respond if you need more help or information.

05 **Podcasts**

srna.ngo/podcasts

We have moderated podcasts on a wide variety of topics that affect people living with rare neuroimmune disorders. We also have a series of podcasts that focus specifically on each of the rare neuroimmune disorders. During a podcast, you have the opportunity to interact with the moderator and ask questions in real time. All of our past podcasts are available in the Resource Library, on our YouTube page, and via iTunes. Podcasts are transcribed and are also available in the Resource Library.

06 **Magazines**

srna.ngo/magazines

Our Magazines are delivered through email and, if you choose, through regular mail. Magazines feature the latest information and inspiration about SRNA and our community, and highlight events, opportunities, and research updates. Magazines include a list of upcoming events from across the country, articles written by medical professionals and members of our community, as well as a list of currently recruiting clinical studies and trials. You can find an archive of all our Magazines in the Resource Library on srna.ngo.

07 **Weekly Blogs**

srna.ngo/blog

We feature helpful blogs written by SRNA members, as well as clinical experts in rare neuroimmune disorders. The blogs cover a wide variety of topics that affect the lives of people with these disorders. Read powerful personal stories of how individuals and their loved ones have dealt with a diagnosis, adapted to a “new normal,” and handled challenges they never imagined. Our team of healthcare professionals post about the latest research and treatments, and offer practical advice on common, day-to-day issues often faced by members of our community.

08 **Global Support Group Network**

srna.ngo/sgn

Join a support group near you and benefit from the insights and experiences of people whose lives have been affected by a rare neuroimmune disorder. Learn their stories and share yours. Ask questions of those who have been there and understand what you are going through. If you would like to start a support group, you'll find the tools to do so at srna.ngo.

09 **Education Symposia**

srna.ngo/rnds

Our informative symposia are designed for people with rare neuroimmune disorders and their families — everyone is welcome. Attend lectures by leading clinicians, participate in workshops, and get to know people from around the world who have these disorders. All symposium talks are recorded and are available in the Resource Library and on our YouTube page. Transcriptions and closed captions are also available.

10 **Annual Quality of Life Family Camp**

srna.ngo/camp

SRNA is proud to offer a camp for children diagnosed with ADEM, AFM, MOGAD, NMOSD, ON, and TM and their families. The camp helps children with these disorders and their family members experience the joys of summer camp and develop relationships and connect with others who experience the same symptoms and conditions. Medical professionals from our community attend camp and give a three-day education program to parents and older children during camp. Visit srna.ngo to learn more about camp and how to apply.

11

Smart Patients Online Community

srna.ngo/smart-patients

Join an online community of patients and caregivers. Be connected directly to other members via the Smart Patients Online Health Community. Join Smart Patients, ask a question, learn from other patients, and share your voice and your stories to help support others.

12

James T. Lubin Fellowship

srna.ngo/fellowship

Our Fellowship program helps train neurologists to become specialists in rare neuroimmune disorders. The objectives of the program are to provide high quality, state-of-the-art care, advance research and understanding of these disorders, and help develop leaders in the rare neuroimmune disorders clinical community. The goal is also to create centers of excellence across the country to facilitate multicenter research and collaboration.

13

SRNA Registry

srna.ngo/registry

Members of SRNA have the opportunity to participate in the SRNA Registry, which is designed to help advance research about rare neuroimmune disorders and treatment. The participation of individuals with rare neuroimmune disorders in SRNA Registry is important for improving our understanding of these disorders.

14

The Pauline H. Siegel Eclipse Fund for Research

srna.ngo/research

The Eclipse Fund was established in memory of one of our founders, Pauline H. Siegel, who lived her life trying to improve the future for other people diagnosed with rare neuroimmune disorders. Pauline's is a legacy of hope, and in her name, the Eclipse Fund will drive critical research to:

- ☐ Restore function
- ☐ Identify genes and causes
- ☐ Improve diagnosis
- ☐ Investigate novel therapies

The Eclipse Fund will support and accelerate SRNA's research portfolio and fund discoveries that will directly impact the quality of life for members of our community. Visit our website to learn about publications, clinical studies, and trials we have funded, as well as ongoing research.

15

Our Hope Ambassadors

srna.ngo/hope-ambassadors

Our Hope Ambassadors are a community of heroes for a common cause – to advance diagnosis, treatment, research, and awareness of rare neuroimmune disorders, and to share their stories with others. Hope Ambassadors include clinicians and individuals with rare neuroimmune disorders who are making a profound and positive impact on our community and our world.

16

Our Peer Connect Program

srna.ngo/p2p

Our Peer Connect Program connects people with a rare neuroimmune disorder with a peer. Peers are people diagnosed with a rare neuroimmune disorder or care partners of someone diagnosed with a rare neuroimmune disorder. They can provide emotional support and share what they have learned. Whether you are newly diagnosed, have been living with a diagnosis for years, or are a family member or care partner, we have a Peer who can empathize with your situation. Once you are matched, someone will contact you to set up the next steps. Get matched. Get connected. Get support.

17

“This is Me”

srna.ngo/me

“This is Me” is an educational awareness campaign that challenges the social issues and understanding around rare diseases & disabilities and aims to break the silence by supporting people diagnosed with rare neuroimmune disorders to tell their own stories.

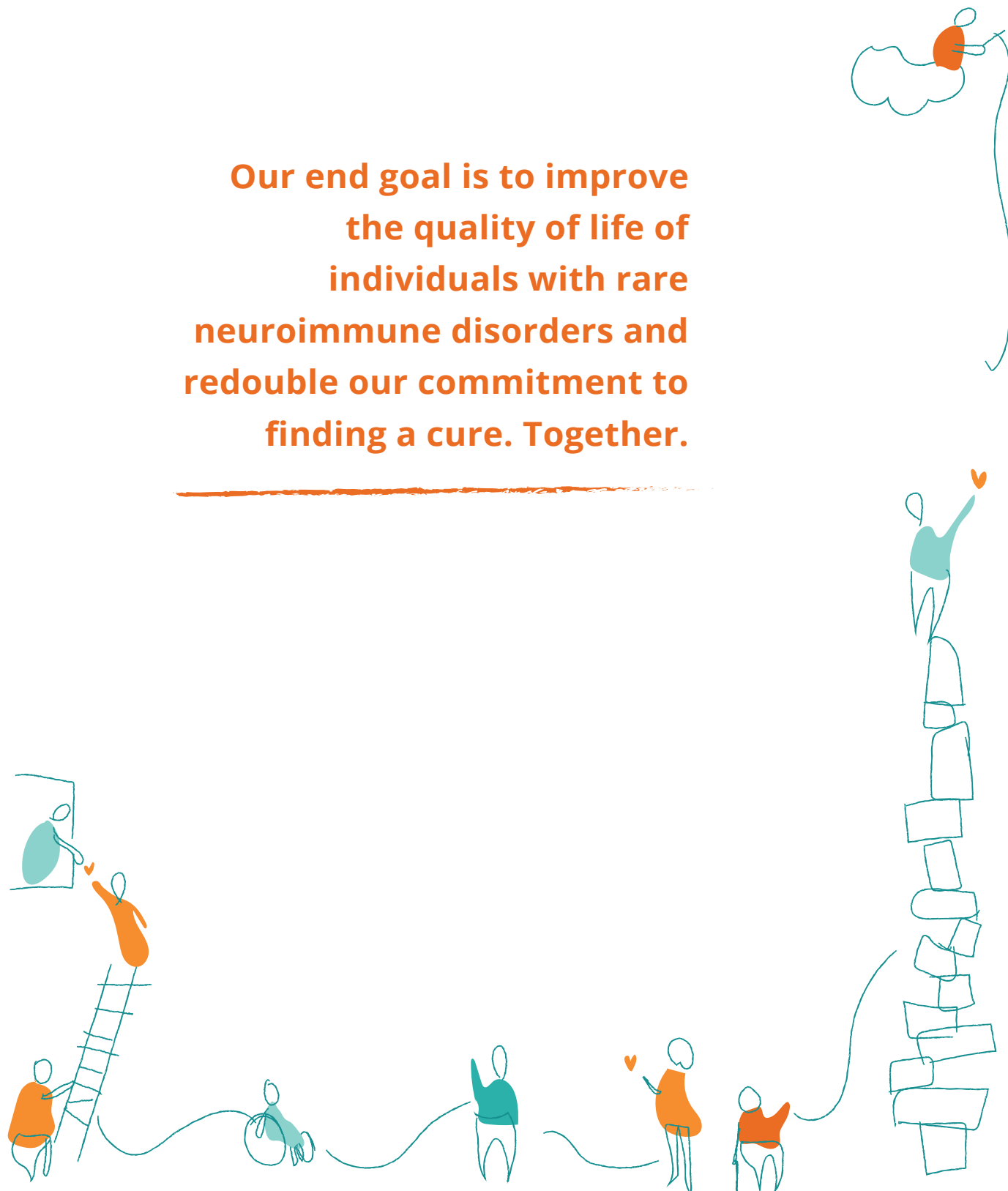
18

Upcoming Events

srna.ngo/events

Emails from SRNA will keep you up-to-date and informed about events, news, and research.

**Our end goal is to improve
the quality of life of
individuals with rare
neuroimmune disorders and
redouble our commitment to
finding a cure. Together.**



Our Officers & Staff



Deborah Capen
Secretary and Board Member



Linda Malecky
Vice President, Treasurer, and Board Member



GG deFiebre
Director of Research and Programs



Roberta Pesce
Director of Strategy | Creative Director



Krissy Dilger
Research and Program Manager



Sandy Siegel
President and Board Member



Chitra Krishnan
Executive Director



Angel Simpelo
Administrative and Creative Assistant



Lydia Dubose
Community Engagement Manager



Rebecca Whitney
Associate Director of Programs and
Community Support



Skye Corken
Community and Engagement Coordinator



Jim Lubin
Board Member

Take Action!

We believe that everyone has a role in improving the quality of life of people with rare neuroimmune disorders. Whether you support us with your time, expertise, or funding, you will be a key player in helping us end rare neuroimmune disorders for good. Join us. **We can't do it without you.**



Use Your Voicesrna.ngo/voice

You are your own most powerful advocate. Your own voice is the most effective in relaying your story and it must be heard! Share your story with your friends, family, and local community. Be powerful and enact change – sign on to legislation or encourage and empower others through sharing your story on our blog. Change begins when we speak up and make our voices heard!

Mobilize an Awareness Daysrna.ngo/awareness-day

Begin locally. Start a Walk-Run-N-Roll in your community to raise awareness of these rare disorders. Join others in your community who share your experience to petition your local and state government to recognize the lives of those living with and caring for those with a rare neuroimmune diagnosis and the importance of awareness days and events.

Start a Support Groupsrna.ngo/start-support-group

Sharing our experiences and learning together with others who truly understand what it is to live with or care for another with a rare neuroimmune disorder can be life-changing. Start a Support Group in your area to connect with others. Our own voices are powerful but just imagine what can be done when we come together as one!

Volunteersrna.ngo/volunteer

Looking for a way to get more involved in a cause you care about? Become a volunteer! We need your leadership, enthusiasm, and support to achieve our goals.

Fundraisesrna.ngo/fundraise

Your fundraising fuels the programs that are improving the quality of life of individuals with rare neuroimmune disorders. From bake sales to dinner, auctions, and birthday fundraisers, they're creative and inventive! You can collectively raise thousands of dollars and be the one responsible for the expansion of our research and education programs. Join us!

Donatesrna.ngo/donate

Our work is made possible through the generous support of our community. By choosing to donate to SRNA, you are actively helping advance research, enhance clinical care, raise awareness, and advocate for those with rare neuroimmune disorders.

Join the SRNA Registrysrna.ngo/registry

Share information about your diagnosis in a patient registry that has been designed to learn more about the natural history of rare neuroimmune disorders, treatments, and outcomes using standardized tools. By sharing your information, you will help advance research about rare neuroimmune disorders.

Want Support?

We are here for you. If you have questions, need inspiration, or just want to chat about different ways to get involved, give us a call: at +1 (855) 380-3330 or send us an email at info@wearesrna.org.

Facts about Rare Neuroimmune Disorders

The 5Ws



Dr. Cynthia Wang, University of Texas Southwestern

Who gets these illnesses?

- › **ADEM** tends to affect young children, typically ages 4-8, without a significant bias for specific gender or ethnic background.
- › **AFM** tends to affect children as well, and increases in cases have occurred every other year since 2012.
- › We are still learning about who is more likely to get **MOGAD**. Some studies have shown that those with MOG antibody disease are on average younger and are likely to be male compared to those with aquaporin-4 (AQP-4) positive NMOSD. Those with MOGAD may be more likely to have bilateral involvement of the optic nerves.
- › **NMOSD** associated with AQP-4 antibodies tends to disproportionately affect non-Caucasian women in their 30-40s.
- › **TM** can affect individuals of all ages, ethnicities, and either gender.
- › **ON** is more common in women and develops in most patients between the ages of 20 and 45. Additionally, ON typically occurs more frequently in Caucasians than African Americans.

Where in the nervous system do these disorders affect?

- › inflammation in optic nerves = optic neuritis (ON)
- › inflammation of spinal cord, primarily the white matter of the spinal cord = transverse myelitis (TM)
- › inflammation of spinal cord, primarily the grey matter of the spinal cord = acute flaccid myelitis (AFM)
- › inflammation of brain = encephalitis
- › inflammation of brain and spinal cord (and sometimes optic nerve) = encephalomyelitis (acute disseminated encephalomyelitis (ADEM) is a subtype

- that may or may not include spinal cord involvement)
- › inflammation of brain, optic nerves, and/or spinal cord = neuromyelitis optica spectrum disorder (NMOSD) or MOG antibody disease (MOGAD)

What does monophasic or relapsing mean?

- › Some of these disorders are monophasic, meaning a one-time confused reaction of the immune system, without any further episodes of inflammation (TM, AFM, ADEM, ON).
- › Other disorders are known as relapsing, in which a persistently confused immune system can continue to cause inflammatory episodes (NMOSD and MOGAD, although ADEM, TM, and ON can be initial presentations of these relapsing diseases)
- › For the disorders that can be relapsing, people are given long-term therapies to diminish the chance of future episodes or to lessen their impact should they occur.
- › Testing for AQP-4 and MOG antibodies can help predict if someone will have a monophasic or relapsing course.
- › If antibody testing is negative, the longer one goes without another attack, the more likely it is that the condition is monophasic.

Which of these conditions tend to be relapsing or recurring?

- › Multiple sclerosis and neuromyelitis optica spectrum disorder associated with aquaporin-4 (AQP-4) antibodies are the two most well recognized forms of relapsing CNS auto-immune disorders.
- › 60-80% of individuals with optic neuritis and longitudinally extensive transverse myelitis (involvement of greater or equal to the length of 3 vertebrae) have antibodies to aquaporin-4 (AQP-4), a water channel in astrocytes, a type of support cell in the central nervous system.
- › A proportion of individuals who test negative for AQP-4 and some of those diagnosed with recurrent ON or ADEM are now known to have antibodies against another target, called myelin oligodendrocyte glycoprotein (MOG). MOG is a protein on myelin and oligodendrocytes, the myelin-producing cells of the central nervous system and are thought to have MOGAD. Individuals who continue to test positive for MOG antibodies 6-12 months after their initial attack are at risk for recurrent disease and should discuss with their provider if chronic immunosuppression is warranted.

Why do people get these disorders?

This is a central question in neuroimmunology and currently we still don't know for sure. It is hypothesized that these disorders result from a specific set of circumstances, namely 1) a person whose immune system may be primed to overreact or get confused, or a genetic predisposition to auto-immunity and environmental triggers, and 2) a life event, perhaps a bodily stressor, such as an infection, to trigger the attack. We do not yet know the genetics or environmental factors that lead to these conditions.

Disorder	Areas of CNS Involvement	Specific Diagnostic Tests	Relapsing or Monophasic	Ongoing Immunosuppression indicated?
ADEM	Brain Spinal Cord Optic Nerve	None if monophasic	If MOG negative 6-12 months after onset, typically monophasic	No
		MOG Antibody	If MOG positive 6-12 months after onset, might be recurrent (MOGAD)	Yes
AFM	Spinal Cord (primarily grey matter)	Enterovirus PCR in CSF (though virus is very difficult to isolate), positive enterovirus/rhinovirus on respiratory specimen is supportive	Monophasic	No
MOGAD	Brain Spinal Cord Optic Nerve	MOG Antibody	Uncertain, persistence of MOG antibodies are associated with relapsing disease	Yes, if relapses occur
MS	Brain Spinal Cord Optic Nerve	None, though CSF oligoclonal bands are supportive	Relapsing	Yes
NMOSD	Brain Spinal Cord (typically lesions more than 3 vertebral segments in length) Optic Nerve	Aquaporin-4 antibody	Relapsing	Yes
ON	Optic Nerve	None	Depends if ON is a part of MS, NMOSD, or MOGAD	Typically yes if relapsing
TM	Spinal Cord (primarily white matter)	None	Monophasic	No
			In very rare cases can be recurrent	Case-by-case

Rare Neuroimmune Disorders

An Overview



Rare neuroimmune disorders are immune-mediated disorders of the central nervous system (brain, spinal cord, and optic nerves). The immune system is the body's defense against foreign invaders, such as viruses and/or bacteria. Normally, the cells that are a part of the immune system have the ability to distinguish an infectious agent from a person's body; however, sometimes some of these cells become 'confused' and mistakenly attack an organ within a person. This is known as autoimmunity. Health care providers sometimes use the term 'inflammation' to describe this occurrence. Inflammation refers to situations when immune cells invade human tissue. For example, if there is inflammation in a spinal cord, then immune cells have invaded the spinal cord. Inflammation can be normal, such as during an infection, or abnormal, such as during autoimmune attacks. The neuroimmune disorders that are supported by SRNA occur when a person experiences an inflammatory attack at some location in their central nervous system. When the spinal cord is affected it is called Transverse Myelitis (TM), and when the optic nerve is affected it is called Optic Neuritis (ON). In Acute Disseminated Encephalomyelitis (ADEM), MOG antibody disease (MOGAD), and Neuromyelitis Optica Spectrum Disorder (NMOSD) there are various patterns of organ involvement, and in some disorders there is the potential for recurrent events. When the central nervous system is affected, there are multiple kinds of damage that can occur. The connections between the brain and body are like insulated electrical wires. During an immune mediated attack on the central nervous system, the insulation around the wire (myelin) or the wire itself (axon) can be damaged. When an inflammatory attack damages the insulation, the damage is referred to as demyelination. When the myelin or axon of a neuron is damaged, it is unable to conduct a signal. The symptoms are dependent on which axons are affected. For example, if the wire that carries visual information from the eye to the brain (optic nerve) develops demyelination, then signals are not carried to the brain efficiently resulting in a person having blurred or lost vision (ON). If the demyelination occurs in the wires sending motor signals to a person's legs, then the person has weakness and difficulty walking.



Mechanism of Disease

Very little is understood about the disease mechanisms for these disorders. It is believed that a person who develops one of these rare neuroimmune disorders likely has a genetic predisposition to autoimmunity, and that there are environmental factors that interact with these genetics to trigger the disease. The specific genetics in each of these disorders is not completely understood and environmental factors have not been clearly identified. In the case of Multiple Sclerosis (MS), a relationship to decreased levels of vitamin D and diminished exposure to sunlight are being considered, but no other factors are suspected for these other neuroimmune disorders. It is believed that the immune system response could be to a viral, bacterial, or fungal infection, and in the case of TM, a significant number of people have flu-like symptoms, a respiratory infection, or a child might have an ear infection preceding their attack. This immune response might explain why the immune system was revved up. However, it does not explain why the immune system becomes dysfunctional and attacks 'self.' Additionally, no one understands why some people have a good recovery from an attack, while others have no recovery.

The central nervous system is separated and protected from foreign agents by the blood brain barrier. For the immune system to attack anywhere in the central nervous system, cells from the immune system have to pass through this barrier. Thus, in the case of these disorders, not only does the immune system become confused, it also has to find a way to cross this protective barrier to get to the brain, the spinal cord and/or the optic nerves. These mechanisms are not very well understood.



Differential Diagnoses

Acute Disseminated Encephalomyelitis (ADEM) involves inflammation and demyelination in the brain and often involves inflammation in the spinal cord. In some instances, there can also be optic nerve involvement. ADEM may occur after a bacterial or viral infection (post infectious), or following an immunization (post vaccination). The demyelination in the brain is different than a demyelinating attack from MS; white matter lesions tend to be diffuse. ADEM is most often monophasic, although there are rare recurrent variants of ADEM. It can be characterized by headache or seizures and may involve vision loss. The spinal cord involvement is the same as TM, as are the associated symptoms. ADEM is more common in children than in adults. Antibodies to Myelin Oligodendrocyte Glycoprotein or anti-MOG have been found in individuals diagnosed with ADEM and those with persistent detection of anti-MOG may be more likely to have a relapsing rather than monophasic disease course. More information about anti-MOG can be found in the MOG antibody disease section.

Multiple Sclerosis (MS) involves an inflammatory attack that can occur anywhere within the central nervous system (i.e., brain, spinal cord and/or optic nerves). Brain lesions at the time of onset or early in the course of the disease are common. The lesions in the brain are ordinarily identified in a specific pattern; however, lesions may be present anywhere in the white matter. MS involves more than one episode (i.e., recurrent attacks), and the multiple episodes occur in different locations in the central nervous system.

... Differential Diagnoses

MOG antibody disease (MOGAD) is a neuro-inflammatory condition that preferentially causes inflammation in the optic nerve but can also cause inflammation in the spinal cord and brain. Myelin oligodendrocyte glycoprotein (MOG) is a protein that is located on the surface of myelin sheaths in the central nervous system. While the function of this glycoprotein is not exactly known, MOG is a target of the immune system in this disease. The diagnosis is confirmed when MOG antibodies in the blood are found in patients who have repeated inflammatory attacks of the central nervous system. Those with MOG antibody disease may previously have been diagnosed with Neuromyelitis Optica Spectrum Disorder (NMOSD), Transverse Myelitis (TM), Acute Disseminated Encephalomyelitis (ADEM), Optic Neuritis (ON), or Multiple Sclerosis (MS) because of the pattern of inflammation it causes including brain, spinal cord, and optic nerve damage. Patients with persistently positive antibodies are at risk for recurrent events. Those with MOG antibody disease do not test positive for the NMO antibody called aquaporin 4 (AQP-4). MOG antibody disease and AQP-4 positive NMOSD are thought to have distinct immunological mechanisms.

Neuromyelitis Optica Spectrum Disorder (NMOSD) involves immune-mediated inflammatory attacks in the spinal cord and/or the optic nerve. A person with NMOSD is at risk for multiple attacks of spinal cord inflammation or ON, or both. There is ordinarily no brain involvement, but this is not always the case. It is typically characterized by longitudinally extensive transverse myelitis (LETM, myelitis which is 3 vertebral segments in length or greater), which can leave one quite debilitated at presentation, and unilateral or bilateral optic neuritis. There is a blood test for NMOSD called NMO-IgG that is clinically available. It is highly specific (>99%) and its sensitivity ranges from 48-72%, depending on the assay used. Antibodies to Myelin Oligodendrocyte Glycoprotein or anti-MOG have been found in individuals diagnosed with NMOSD. Those with MOG antibody disease do not test positive for the NMO antibody called aquaporin 4 (AQP-4). MOG antibody disease and AQP-4 positive NMOSD are thought to have distinct immunological mechanisms.

Optic Neuritis (ON) involves a demyelinating attack of the optic nerve. In isolated ON, there is no brain or spinal cord involvement. An episode of ON may be a first attack of MOGAD, NMOSD or a first attack of MS. Working through a differential diagnosis is important. A person may have ON or Recurrent ON and never have an attack in the spinal cord or brain.

Transverse Myelitis (TM) is an immune-mediated inflammatory attack of a person's spinal cord. Sometimes the inflammation has no clear cause and is referred to as Idiopathic TM. The majority of these cases are probably post infectious events, but this can be difficult to prove. In general, individuals with Idiopathic TM do not have recurrences or future inflammatory events. At other times, TM is part of a larger autoimmune process, such as MOGAD, NMOSD, MS, Sarcoidosis, Sjogren's Syndrome, Lupus, or ADEM. When presenting with TM, clinical care should focus on reducing inflammation acutely and trying to determine if there is an underlying cause. In rare cases, a person can have more than one inflammatory attack in their spinal cord; this is called Recurrent Transverse Myelitis (RTM). In each unique episode, the inflammatory attack occurs only in the spinal cord. There is no brain or optic nerve

... Differential Diagnoses

involvement in any of the episodes. It is important in these cases that the inflammatory attack in the spinal cord be identified; the diagnosis cannot be based solely on clinical symptoms, as there can be a worsening of symptoms apart from a new attack in the spinal cord. It is also important that the attack be identified as a unique attack and not associated with an unresolved initial attack. For example, if a person experiences an inflammatory attack and then two weeks later, the inflammation worsens; this cannot be considered a second attack. The first attack must completely resolve over time and the next attack must occur after this resolution to be considered a subsequent attack. Everyone with recurrent TM must have MOGAD and NMOSD ruled out. There should also be a rule out of an underlying rheumatic disorder.

Acute Flaccid Myelitis (AFM) is inflammation of the spinal cord and generally presents with unique clinical and MRI features that are not typical of classical transverse myelitis. AFM abnormalities noted on MRI are predominantly found in the gray matter of the spinal cord.



Diagnosis

Each of these neuroimmune disorders remain a challenge to diagnose. Only MOGAD and NMOSD have distinct and defined markers. The diagnostic criteria for the other disorders are neither entirely clear-cut nor universally accepted in medicine (i.e., there appear to be numerous exceptions to every rule). The relationships between each of these disorders are also not well understood (i.e., is each of these disorders a unique disease, or are some of them variants of the same disease?) To arrive at a diagnosis for any one of these disorders, an MRI will need to be done, with and without contrast agent, a spinal tap (lumbar puncture) should be performed, and brain scans will need to be done to rule out MS. If NMOSD is suspected (recurrent TM, ON, recurrent ON, or LETM), the NMO-IgG should be done, and a test for anti-MOG should be done.



Acute Treatments

Treatment for these disorders in their acute or early stages involves quieting down the immune system as quickly as possible, before damage is done. These treatments need to be considered in the context of the correct diagnosis and administered as quickly as possible. Time is critical. Unfortunately, there is very little research and almost no scientific evidence available as to the most effective treatments for any one of these disorders. It is important to be working with a physician who has good experience with these disorders, because acute treatment is going to involve primarily or exclusively clinical judgment. If your physician does not have this experience, it is important to ask your physician to consult with a physician who does. There are very few clinical centers with physicians who specialize in TM or NMOSD (e.g., University of Texas Southwestern, Johns Hopkins University, Mayo Clinic, University of California San Francisco, Walton Centre – Liverpool, England), but there are numerous

... Acute Treatments

Multiple Sclerosis Centers associated with prominent medical centers and medical schools. A specialist from one of these centers should be considered, as they have experience in demyelinating disorders of the central nervous system. The acute therapies most frequently used to treat an inflammatory attack include: high dose intravenous steroids (methylprednisolone), Plasmapheresis (Plasma Exchange or PLEX), Immunoglobulin Therapy (IVIG), and cyclophosphamide.

After the inflammation has begun to resolve and the person is medically stable, the next course of treatment for a person who has an inflammatory attack in their spinal cord (ADEM, MOGAD, NMOSD, MS or TM) involves intensive rehabilitation therapy. Centers devoted to spinal cord injury and disease or stroke offer comprehensive rehabilitation programs for people who have suffered significant spinal cord deficits from the inflammatory attack. Children and adults who have experienced significant muscle weakness or paralysis should be admitted to a specialized rehabilitation hospital, and the program should include an aggressive physical and rehabilitative therapy regimen (as opposed to an exclusive emphasis on independence training).

Most cases of ADEM and TM are considered monophasic. It is important to have regular appointments with a neurologist to monitor the progress of the disease, if any. Over time and depending on symptoms, a yearly exam might be sufficient for many people. The symptoms from these disorders can be quite challenging to manage and can change over time. Other specialists should be considered in consultation with a neurologist and general practice physician or pediatrician (e.g., urology, psychiatry, orthopedics, and physiatry).

People with MOGAD, NMOSD, Recurrent TM, or recurrent ADEM are at risk for multiple attacks and should be monitored more closely. People with these disorders will likely receive medication to either diminish the chance of another attack, or lessen its severity should it occur. It is important that a definitive differential diagnosis from MS be made by a physician. The MS treatments (i.e., Avonex, Betaseron, Copaxone, Gilenya, Rebif, and Tysabri) have not proven to be effective in the treatment of people with MOGAD, NMOSD or Recurrent TM and in some cases may cause more harm than good. Most often, people with Recurrent TM, MOGAD or NMOSD are considered for immune suppressant therapies. Which therapies a person is placed on is based entirely on the clinical judgment (experience) of the physician, combined with individual needs.

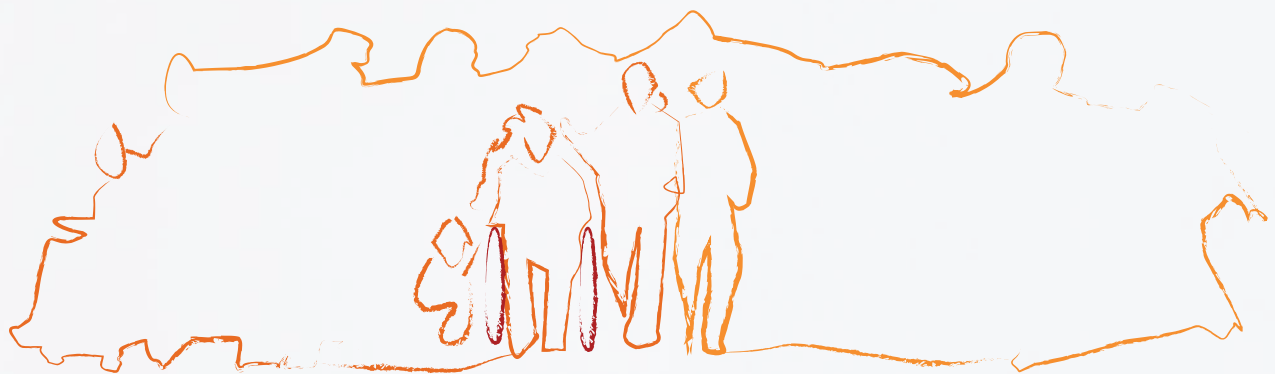
Additional Resources

Myelitis Helpline *srna.ngo/helpline*

For questions about our organization and rare neuroimmune disorders, visit the Myelitis Helpline, an online tool developed by SRNA.

Resource Library *srna.ngo/resources*

To access up-to-date resources on rare neuroimmune disorders, which include symposium videos, magazines, podcast recordings, published research summaries, information sheets and relevant external resources, visit our Resource Library.



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