

February 2020 Newsletter



Have you ever wondered if MS is different when it occurs in children and teenagers? Did you know the first therapy for pediatric MS was recently approved by the U.S. Food and Drug Administration (FDA)? Take a look at some interesting [facts](#) about MS in kids!

According to the National MS Society, approximately 3 to 5 percent of individuals with MS are diagnosed before the age of 16. The causes of MS are not well understood but are likely to be the same for adults and children. MS is not inherited however genetics appear to play a role in an individual's risk of developing the disease. A number of environmental triggers are thought to increase the risk of developing the disease during childhood in those who are genetically susceptible. Most symptoms of MS in children are the same as in adults. As with adults, the symptoms a child experiences depends on which nerves have been damaged. Since demyelination can affect any part of the central nervous system, the symptoms of MS are unpredictable and vary from person to person. Pediatric MS can cause emotional and social challenges for the whole family. Coping with living with MS may negatively affect a child's self-image, confidence, academic performance, social life, family relationships, and behavior as well as how they view the future. [Read more](#) about the causes and symptoms of pediatric MS, including ACP's plan for 2020 to learn more about the needs and priorities of children and adolescents diagnosed with the disease, their parents and family members.

MS in children and teenagers can be difficult to diagnose. In order to determine a diagnosis, a child must experience at least two separate and distinct MS flares (just like an adult). These attacks must occur at least one month apart and be in different parts of the central nervous system. In May 2018, the U.S. Food and Drug Administration (FDA) approved the first disease modifying therapy (DMT) for the treatment of children and adolescents 10 years of age or older with relapsing-remitting MS (RRMS). Even though the remaining DMTs are not FDA approved to treat pediatric MS, they are still used in children, but at lower doses. Researchers are evaluating their effectiveness, tolerability and safety in this population. [Learn more](#) about how MS is diagnosed and treated in youth.

Our Research Spotlight contains opportunities to participate in studies, MS events, as well as recent research results. This month we feature a **new study** to provide patient opinions and preferences regarding clinical trial participation to the pharmaceutical companies that plan and carry out these trials. Other opportunities include two exercise studies and research to help improve MS clinical trials. Click [here](#) to learn more!

We hope you enjoy this newsletter and encourage you to share it with anyone you think may be interested in learning more about MS research.

Jan and Lindsey, on behalf of the Accelerated Cure Project Team

[Pediatric Versus Adult MS, the Same or Different?](#)

According to the National MS Society, approximately 3 to 5 percent of individuals with MS are diagnosed before the age of 16. MS is different for each person, whatever their age. Children almost always have relapsing remitting MS and tend to have multiple symptoms at disease onset. This means the disease alternates between relapses in which symptoms flare up and remissions in which there are only mild or no symptoms. Flares can last days to weeks, and remission can last months or years. [Research](#) shows children tend to have more frequent flares than adults during the first few years after diagnosis. However, they also recover from them and go into remission more quickly than people diagnosed as adults.



The causes of MS are not well understood but are likely to be the same for adults and children. MS is not inherited however genetics appear to play a role in an individual's risk of developing the disease. Children with a first degree relative with MS (a parent or sibling) are 2 to 4 percent more likely to develop MS than the general population. Though no single gene has been identified to cause MS, many [single nucleotide polymorphisms](#) (SNPs) have been associated with increased risk in children and adults. For example, a [2013 study](#) found 57 SNPs associated with both adult and pediatric onset MS. [Researchers](#) in Canada concluded one SNP ([HLA-DRB1](#)) is associated with increased risk of MS in children.

Having these alterations in the [genetic sequence](#) is not enough to cause MS on its own. Instead, a combination of genetic susceptibility and a number of environmental triggers are

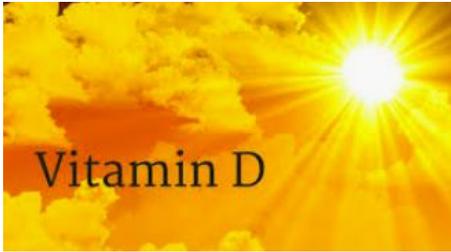


generally thought to increase the risk of developing the disease. The onset of puberty increases the risk for developing MS in girls. [Research](#) shows equal numbers of boys and girls are diagnosed with MS before puberty. After puberty, 2 to 3 times more girls are diagnosed than boys which suggests that the hormonal changes that happen at puberty may affect susceptibility.

Exposure to the Epstein-Barr virus (EBV) may act as a trigger for MS in children who are susceptible to it. [Investigators](#) at the Harvard School of Public Health found the chances of developing MS is approximately 15 times higher in individuals infected with EBV in

childhood and about 30 times higher among those infected with EBV in adolescence or later in life. Although the underlying mechanisms are unclear, these results provide strong evidence of an association between EBV infection and MS risk. It's important to note that many children are exposed to EBV and don't develop MS.

Low vitamin D levels may not only be a [risk factor](#) for pediatric MS, but are also linked to increased [disease activity](#). The sun is one of the best sources of vitamin D. When [UVB](#)



[light](#) from the sun strikes the skin, the body synthesizes vitamin D3 (the most natural form). MS is found more often in people from Northern climates where there's less sunshine than near the sunny equator. People in Northern climates tend to have lower vitamin D levels. This implies a link between

MS and low vitamin D. The possibility of disease prevention with vitamin D supplementation or increased sun exposure in childhood is an emerging concept that is currently under study.

A number of other environmental factors may contribute to a diagnosis of MS in children. Cigarette smoke, both first-hand use and second-hand exposure, has been [shown](#) to increase the risk of developing the disease. [Research](#) suggests changes in the gut microbiome may affect the chances of an individual developing MS at a young age. There is also [evidence](#) of a significant association between obesity and MS risk in adolescents with genetic susceptibility to the disease.

Most symptoms of MS in children are the same as in adults, including weakness, tingling and numbness, vision problems, difficulty with balance and walking, tremors, spasticity, or slurred speech. Symptoms often seen in children but not adults include seizures and lethargy. As with adults, the symptoms a child experiences depends on which nerves have been damaged.



Since demyelination can affect any part of the central nervous system, the symptoms of MS are unpredictable and vary from person to person. It is unusual for children to have significant physical impairment when they are first diagnosed. There is [evidence](#) that physical symptoms usually increase more slowly in children than in adults but, as

symptoms begin at an early age, higher levels of disability are generally reached at a younger age than for people whose symptoms began in adulthood.

Mood disorders occur frequently in children with MS. Depression is the most common, occurring in about [27 percent](#). Other common conditions include anxiety, panic disorder, or bipolar depression. Approximately [30 percent](#) of children with MS have cognitive impairment or trouble with their thinking. The most frequently affected activities include memory, attention span, information processing, as well as executive functions like



planning, organization, and decision-making. [Studies](#) show these symptoms often progress over time in children and may affect their performance at school. However, a small number of subjects showed improvement in their cognitive symptoms over time, suggesting early intervention may be of benefit to address any cognitive difficulties a youth with MS may have.

A [study](#) from the University of California at San Francisco found pediatric MS subjects have more T2 and enhancing lesions than adults. Both have been associated with disability progression in adults. [Researchers](#) in Germany did a post-mortem comparison of brain tissue in pediatric and adult MS subjects. They found more extensive nerve damage in inflammatory demyelinating lesions in the pediatric brains. These data suggest that MS in children may be more inflammatory in nature.

Pediatric MS can cause emotional and social challenges for the whole family. Coping with MS may negatively affect a child's self-image, confidence, academic performance, social life, family relationships, and behavior as well as how they view the future. Watching their child endure a chronic disease like MS can leave a parent feeling helpless and frustrated. While support from caring individuals in daily life can provide some comfort (teachers, friends, family or clergy), the challenges of living with pediatric MS may still feel overwhelming at times. The National MS Society offers a number of helpful resources for all members of the household, including [brochures](#), [support groups](#) and [counseling services](#). The Society's [MS Navigator Program](#) may also provide the information, resources and support families may be looking for.

One of ACP's areas of focus in 2020 will be learning more about the needs and priorities of children and adolescents diagnosed with MS, their parents and family members. There is a robust [pediatric research network](#) in MS, funded by the National MS Society. ACP plans to engage with this existing network of pediatric centers and learn from them in the coming year. We also plan to document the unmet needs of children and adolescents living with MS through literature review, facilitated interviews and two broadly distributed surveys, one to pediatric patients and their families, and the other to health care providers. Ultimately, we plan to inform the iConquerMS program with this information and open the initiative up to pediatric patients. Integrating patient-centered data into the existing knowledge base about pediatric MS will open doors to exciting new possibilities for children living with MS and their loved ones. This is one of the many ways iConquerMS is enriching research on matters of importance to the MS community.



How is MS Treated in Children?

MS in children and teenagers is uncommon and can be difficult to diagnose for several reasons. Because the disease is relatively rare, doctors may not be looking for it. Other conditions, such as Lyme Disease or migraines can have similar symptoms and are often hard to differentiate.

Diagnostic tests for MS in children often don't show the changes typically seen in adults with the disease. In addition, there may not be much evidence of MS if the evaluation is done when a child is in remission.



In order to determine a diagnosis of MS, a child must experience at least two separate and distinct MS flares (just like an adult). These attacks must occur at least one month apart and be in different parts of the central nervous system. A doctor uses information from a child's history (including the type and frequency of symptoms), neurological exam, and the same diagnostic tests as in adults. An MRI is used to see if there are lesions or

inflammation in any parts of the central nervous system. A doctor may perform a spinal tap, in which a sample of the fluid around the brain and spinal cord is taken and evaluated for signs of MS. A pediatric MS evaluation may also include evoked potentials. This test measures how fast signals are transmitted across nerves (demyelinated nerves are typically slower).



More than a dozen [disease modifying therapies](#) (DMTs) are approved by the U.S. Food and Drug Administration (FDA) to treat adults with relapsing remitting MS (RRMS). In May 2018, the FDA [approved](#) the use of an oral medication, [Gilenya](#) (fingolimod), for the treatment of children and adolescents 10 years of age or older with RRMS. Even though the remaining DMTs are not FDA approved to treat pediatric MS, they are still used in children, but at lower doses. Researchers are evaluating their effectiveness, tolerability and safety in this population.

Other oral therapies for MS, including [Tecfidera](#) (dimethyl fumarate) and [Aubagio](#) (teriflunomide), are being studied in clinical trials as potential treatments for pediatric MS. The [FOCUS study](#) looked at dimethyl fumarate treatment in subjects with RRMS age 10 to 17. Subjects taking this medication had less disease activity on MRI. Data suggest the side effects and safety profile are the same in children and adults. There were no serious adverse events associated with dimethyl fumarate. The [TERIKIDS study](#) is underway to evaluate the safety and efficacy of teriflunomide in this same demographic.

[Canadian researchers](#) evaluated [Betaseron](#) treatment (interferon beta-1b) in a cohort of 43 children and adolescents with MS. Data suggest Betaseron is safe and well tolerated, however further study is necessary to determine its long-term effects in organ systems that have not reached maturity. [Investigators](#) at UCSF looked at the tolerability of [Avonex](#) (interferon beta-1a), in children with RRMS. Data from 9 children were collected via a standardized questionnaire, completed by their treating neurologist. While none of the subjects stopped Avonex because of adverse effects (suggesting it was tolerable), the number of subjects in the study was very small and data were collected retrospectively by chart review (which may not be the most accurate account of what each subject experienced). [Austrian researchers](#) followed 7



pediatric MS subjects treated with [Copaxone](#) (glatiramer acetate) for 24 months and found this treatment to also be safe and well tolerated. However, as above, larger studies are necessary to confirm these results.

A recent [study](#) found [Tysabri](#) (natalizumab) to be safe, well tolerated and effective in children with MS where first-line therapies have failed. There was a significant reduction in EDSS scores (a standardized method of quantifying disability in MS) and the number of relapses during treatment with Tysabri and no evidence of disease activity in over half (58%) of subjects. [Rituxan](#) (rituximab), which is used off-label to treat MS, has been evaluated in one small [pediatric trial](#). While results show it is safe and effective it's important to keep in mind that data was collected from only one subject. However, there is [evidence](#) that Rituxan has been widely used in other pediatric autoimmune disorders and has a favorable safety profile.

[Steroids](#) can reduce inflammation and lessen the length and severity of flares in children. [Plasma exchange](#) can be used to treat a flare if steroids don't work or aren't tolerated. Specific symptoms can be treated with [other medications](#) to improve quality of life. Physical, occupational, and speech therapy can also be helpful for children with MS.



Adherence to MS therapy can pose a problem for children and adolescents. In a [2009 study](#), 17 adolescents with RRMS on DMT were interviewed to explore their experiences with MS and the impact of peer relationships on adherence to treatment. Investigators found discontinuation rates were high (47%) and side effects common (which may at least partially explain why so many stopped). Results suggest peer support plays a significant role in helping teenagers adjust to living with the disease. In addition, data indicate many struggle with having to take injections on a regular basis. A [2014 study](#) found the most common reason for non-adherence among adolescents with MS is forgetting to take their medication.

MS is an unpredictable, chronic and progressive disease no matter how old a person is when it starts. The disease usually progresses more slowly in children and teens, however because the disease starts at a younger age, they typically experience significant disability about 10 years earlier in life than those with adult-onset MS. Children tend to have more

frequent flares than adults during the first few years after diagnosis. But they also recover from them and go into remission more quickly than those diagnosed as adults. Pediatric MS can't be cured or prevented, but by treating the symptoms, addressing emotional and social challenges, and maintaining a healthy lifestyle, young individuals with MS can still have an excellent quality of life.



February 2020 Research Spotlight

RESEARCH OPPORTUNITIES



Are you interested in a new way to participate in MS research? [iConquerMS](#) empowers all people living with the disease to be a part of the process of finding new treatments and, ultimately, a cure. Joining the initiative opens up many opportunities to drive MS research forward, including participating in [REAL MS](#) (our collection of information from people affected by MS over time) and other adhoc surveys, engaging with MS researchers, and contributing ideas for future studies. [Join](#) iConquerMS today. Every person who contributes their data and ideas, advances MS research forward more rapidly!



Patient Satisfaction Questionnaire: Clinical Research

Study Purpose:

The Accelerated Cure Project, along with two other patient advocacy groups, is helping with a survey led by Firma Clinical, a company that provides clinical research services including in-home visits. The goal of the survey is to provide patient opinions and preferences regarding clinical trial participation to the pharmaceutical companies that plan and carry out these trials. The results may help to enhance the patient experience and involvement in drug development in the future.

This study involves:

This study involves completing a short, anonymous survey about participating in clinical trials. Study results and summary will be provided to ACP for sharing with members of the ACP and iConquerMS communities. This research is not sponsored by any pharmaceutical company and they will not have access to any raw data.

Participating locations:

This survey is being conducted under approval by the Institutional Review Board at the University of North Carolina – Wilmington.

Researcher: Firma Clinical

Recruiting: All people with MS, including those who have participated in clinical trials in the past and those who have not.

Contact information/Study website:

To participate in this study, please click the following link. Thanks in advance for your input! <https://www.surveymonkey.com/r/7QRZGT8>



New Year, New You

Study Title: Step for MS (Supervised versus Telerehab Exercise Program for People with Multiple Sclerosis)

Study Purpose:

New research shows that exercise is good for people with MS and may decrease symptoms and improve health and walking ability. An exercise study called *STEP for MS* will compare the outcomes of a 16-week exercise program conducted at home to a program conducted in a gym. The researchers conducting the study hope that the findings will make exercise and its benefits more available to people with MS who have problems walking.

This Study Involves:

Participants will exercise two times per week for about one hour each session for 16 weeks. A trained “coach” will help participants learn how to exercise and will provide encouragement throughout the program. Participants will take assessments before starting the program, two months into the program, at 16-weeks when the program ends, and at 6 and 12 months after starting the program.

Eligibility:

If you are between the ages of 18 and 65 years and you have Multiple Sclerosis you may qualify if you:

- Can **walk** but you have **some difficulty**, with or without a device
- **Do not exercise** regularly
- Have not had a **relapse** in the past month
- Can commit to **train 2 times a week for 16 weeks**
- Can **drive to study site** for assessments and potentially for exercise training
- Have reliable **internet access**

Participating Locations:

- Massachusetts General Hospital, Boston, MA (new site for the New Year!)
Contact: Dr. Plumer 617-724-3103/ PPlummer@MGHIHP.EDU
- Shepherd Center, Atlanta, GA
Contact: Erica Sutton at 404-367-1305
- Cleveland Clinic, Mellen Center, Cleveland, OH
Contact: Darlene Stough at 216-445-5877/ stoughd@ccf.org
- University of Colorado, Denver
Contact: Alexa Vareldzis: neurologyresearchpartners@cuanschutz.edu / 303-724-4644
- University of Alabama, Birmingham
Contact: Petra Silic at 205-975-1306/ petra09@uab.edu
- University of Georgia, Athens
Contact: Megan Ware at 423-260-5045/ megan.ware20@uga.edu
- Marquette University, Milwaukee, WI
Contact: Heidi Feuling at 414-288-6209/ Heidi.feuling@marquette.edu
- University of North Carolina, Chapel Hill
Contact: Rachel Keen at 704-877-5636/ rayray@live.unc.edu

For more information, please visit our

website: <https://www.iconquerms.org/welcome-step-ms>



A Study to Understand Exercise Behavior in People with MS

Study Title: Social Cognitive Correlates of Physical Activity in Adults with Multiple Sclerosis in the United States.

Study Purpose:

Social cognition focuses on the role that thought processes play in our social interactions. Previous research suggests cognitive processes like social support, self-regulation and motivation significantly impact physical activity in adults in the general population. This study will evaluate various social cognitive factors that may be associated with exercise behavior in people with MS.

This study involves:

This study involves completing a questionnaire about your physical activity and health habits. The survey will take 25-40 minutes to finish. If you begin and want to finish later, you are able to save your progress and come back to answer the questions for up to one week. The valuable feedback that you provide will be used to help inform future exercise interventions for people with MS.

Participating locations:

The University of Alabama at Birmingham

Researcher:

Robert Motl, Ph.D.

Recruiting:

Anyone that is 18 years of age or older and has been diagnosed with MS is welcome to participate in this study. We hope that 1000 people across the United States will complete these questionnaires. Participation in this study is completely voluntary.

Study website:

If you are interested in participating in this study, please click [here](#), or e-mail Stephanie Silveira at enrl@uabmc.edu.



A Study to Help Improve MS Clinical Trials

Study Purpose:

A pharmaceutical company (Sponsor) is conducting patient interviews with MS pediatric patients (10 - 17 years old) and their caregivers. The Sponsor will use the information collected during these interviews to improve the overall experience in clinical trials for MS pediatric patients and their caregivers.

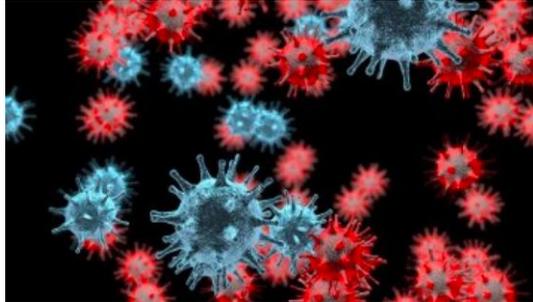
This Study Involves:

These interviews will last at most 1 hour and will be conducted by an independent healthcare communications company, AXON Clinical Trial Services (AXON), on behalf of the Sponsor. AXON will share the information provided during the interviews with the Sponsor in an anonymized manner. This means that it will not include the name or any other personal information that could be used to identify the participants. The information provided will be used to write a report. During the interviews, MS patients and caregivers will be asked about what it is like to live with MS and about their perceptions of clinical trials. Participants will be compensated.

Study Contact Information:

If you're interested in participating in this study, please email MSPeds@axon-com.com, or call (416) 848-1464.

NEW RESEARCH RESULTS



[Human Herpesvirus 6](#) is a set of two closely related herpes viruses known as HHV-6A and HHV-6B. HHV-6B is very common, contracted by most children before the age of three and often results in fever, diarrhea, sometimes with a rash known as roseola. Little is known about the prevalence of HHV-6A or how it is acquired. [New research](#) suggests HHV-6A could be one of the possible causes of MS. Results show people with MS have greater numbers of antibodies to HHV 6A viruses than healthy people, reflecting greater exposure to this type of infection and suggesting a link to this disease. Data also suggest the younger the age at which one tests positive for the HHV 6A virus, the higher the risk of MS.

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