January 2020 Newsletter

Accelerated Cure project for multiple sclerosis

Accelerating research towards a cure for multiple sclerosis

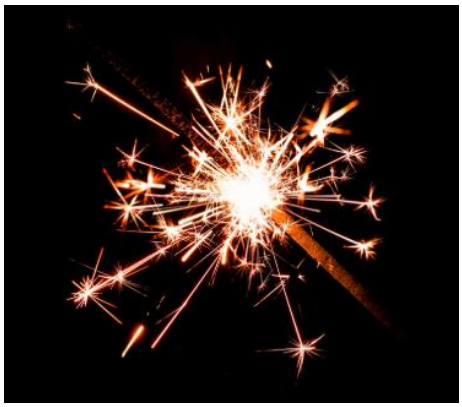
iConquerMS™

ACP Repository™

New Year's Resolutions – In One Year and Out the Other?

Are you interested in being as fit as possible with MS? Would you like to tell others affected by the disease how they can be, too? Check out and share five quick tips for people with MS to stay as healthy as possible!

Making resolutions for the New Year is as traditional as making a champagne toast at midnight. The first of January each year millions of people make pacts and turn over new leaves as another year stretches ahead of them. Some pledge to lose weight or exercise more. Others want to quit smoking or make better financial decisions. While New Year's resolutions are popular, few people actually succeed at keeping them. According to US News and World Report, eighty percent of those who set New Year's resolutions have fallen off the bandwagon and given up by the second week of February. Keeping resolutions can be especially challenging for people with MS. The disease puts many obstacles in the way of a person's resolve to make healthy lifestyle choices. For some, looking ahead may be uncertain and scary. In other cases, motivation may collapse when symptoms flare. However, some of the smallest positive changes in behavior can be the biggest spark leading to significant benefit. Read more about why it's so important for people with MS to "muscle through" and work toward a "new you."



It's a well-established fact that smoking increases the risk of lung cancer and heart disease. Several studies link smoking to MS and other autoimmune diseases. In fact, research shows the risk of MS in smokers is 1.5 times higher compared to nonsmokers and the more cigarettes an individual smokes the higher the risk. A link between smoking and other MS risk factors has also been established. In addition, there is evidence that individuals with MS who smoke appear to have a much greater chance of experiencing a more rapid progression of their disease. Data suggest the risk of progressing from relapsing remitting to secondary progressive MS is 3.6 times higher for current and past smokers compared to people who never smoked. Researchers are working to understand why smoking has this effect in the MS population. Learn more about what they're discovering.

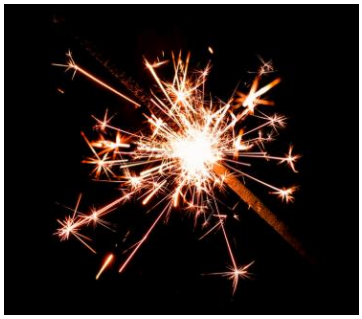
Our Research Spotlight contains opportunities to participate in studies, MS events, as well as recent research results. This month we feature a study on the practice of telemedicine, two exercise studies (one on exercise behavior, and one looking at an at-home exercise program for people with MS), and a study 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. May your New Year start off bright and continue to shine throughout the year!

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

The Best Project You'll Ever Work On Is You

Making resolutions for the New Year is as traditional as making a champagne toast at midnight. The first of January each year millions of people make pacts and turn over new leaves as another year stretches ahead of them. Some pledge to lose weight or exercise more. Others want to quit smoking or make better financial decisions. While New Year's resolutions are popular, few people actually succeed at keeping them. According to US News and World Report, eighty percent of those who set New Year's resolutions have fallen off the bandwagon and given up by the second week of February. Keeping resolutions can be especially challenging for people with MS. For many, looking ahead may be uncertain and scary. Motivation may collapse when symptoms flare. As difficult as it may be, it's important for those living with MS to be proactive about making healthy lifestyle choices, and to keep in mind some of the smallest positive changes in behavior can be the biggest sparks leading to significant benefit.



One of the most popular resolutions is to eat healthier. A recent study shows that diet can influence the course of inflammatory diseases in two ways. What you eat can change the mix of "good" and "bad" bacteria in the digestive tract (the gut microbiome). A healthy digestive tract is populated by a great number of microorganisms living in balance. A

disruption of this balance can have a significant impact on one's health, specifically the chronic, systemic inflammation that occurs in diseases such as MS. In our September 2017 newsletter, Dr. Farren Briggs covers the influence of the diet on the gut microbiome and how this plays a strong role in MS. Research also shows diet affects metabolic and inflammatory pathways. Inflammation is increased by high-calorie diets, which include foods that are low in fiber, and high in salt, sugar, fried food, red meat and animal fat. On the other hand, low-calorie diets that include vegetables, fruit, legumes, fish, and grains reduce inflammation and restore or maintain a healthy gut microbiome.

As we discussed in our August 2019 newsletter, there is no specific diet that will prevent or cure MS. However there is evidence to support that eating certain foods and nutrients, and avoiding others, may help a person's MS symptoms and disease activity. In our December 2017 newsletter, Dr. Briggs highlighted a study looking at the relationship between diet and disease severity in people with MS. Results show individuals with MS eating a healthy diet have better outcomes (are less likely to have severe disability and have lower rates of depression). In our January 2018 newsletter Dr. Briggs focused on the possible benefits of probiotic supplementation and eating grapefruit. Other studies suggest vitamin D is a key diet-related factor in the possible prevention of MS. The most natural way to get vitamin D is through exposure to sunlight. Vitamin D is also naturally present in fatty fish and is added to milk, some cereal products, and a few other foods. A Swedish study recently found that a high consumption of coffee is associated with a lower risk of developing MS. In addition, researchers have determined resveratrol (a compound in red wine) may exhibit anti-inflammatory effects in the brain and may also promote restoration of the myelin coating that surrounds nerve cells in mouse models. Finally, another study showed that periodic cycles of a fasting-mimicking diet had beneficial effects in both mice and human participants with relapsing-remitting MS. Human subjects in this study reported improvements in their health and quality of life. It's important to note, however, that more research is needed to determine the role of fasting in humans with MS.

According to a recent survey, exercising more has been one of the top three resolutions for three years running. For people with MS, physical activity can be very beneficial to overall health and may even help ease MS symptoms. One of the pioneering studies on the benefits of exercise in people with MS (done in 1996) found that 15 weeks of aerobic training helped to improve bowel and bladder function in people living with the disease. However, exercise doesn't have to be a rigorous cardiovascular workout to provide benefits. Physical activity in general is beneficial and can include a variety of things most people can do in the comfort of their home or community. A small pilot study by researchers at Rutgers University found that a specially designed yoga program also yielded better bladder control among people with MS. Fatigue is a common complaint among those living with MS, but a variety of types of exercise can help combat this. A 2014 review found that yoga is as good as other forms of exercise at reducing fatigue in people with MS. Another study showed that eight weeks of water exercise helped to improve quality of life and decrease the perception of fatigue in women with MS. Many people with MS struggle with depression at some point. Exercise has been shown to improve mood in people who are depressed. A 2015 study found that benefit also applies to adults with neurological disorders, including MS.

Exercise can help head off some complications that are commonly associated with MS. Many people with MS are at risk of developing osteoporosis, a bone-thinning disease that raises the risk of fracturing bones. Physical activity strengthens bones and protects against osteoporosis. In addition, exercise is extremely helpful with regards to weight management. If MS symptoms lead to reduced physical activity, one of the results can be putting on a few more pounds. Use of corticosteroids can also cause weight gain. This can make it even harder for an individual to get around. Exercise can help to slow or stop unwanted weight gain. It also holds benefit for those who are underweight by increasing appetite. It's important for those living with MS to work with their healthcare team to find the activities that suit them best and any assistive devices that may help keep them mobile.

While resolutions often center on developing new habits that will get us into better physical shape, getting into better mental and emotional shape can also provide huge rewards. Stress can have a significant detrimental effect on people with MS. It can worsen MS symptoms and research suggests that stress can also increase the likelihood of developing MS. While it's impossible to go through life without some tension (and living with MS is inherently stressful), it's important to try and avoid triggers as much as possible and to develop good lifestyle habits that can help manage and reduce stress. This might include getting plenty of rest, taking the time to do something enjoyable or practicing relaxation techniques, such as meditation or yoga.

As discussed in our March 2019 newsletter, making sleep a priority in the New Year is a universally good idea. Studies show more than half of people with MS have difficulty sleeping. This could be for a variety of reasons. Some may have to get up to use the bathroom frequently at night, while leg spasms or pain may awaken others. Some may be taking medications that cause insomnia. No matter what the cause, sleep deprivation can not only aggravate physical MS symptoms, such as balance and spasticity, but it can also worsen things like cognition and fatigue, which are harder to see, but equally disabling. People with MS are prone to a number of sleep disorders, such as insomnia, obstructive sleep apnea and restless legs syndrome. Awareness and treatment of these conditions is vital for improving the health and quality of life for individuals with MS. Fortunately, there are many options to help in this regard, including both behavioral and pharmaceutical remedies. It is very important for those living with MS to discuss any concerns about the amount or quality of sleep they are getting with their healthcare team and work with them toward the best solution.

According to writer Carl Bard, "though no one can go back and make a brand-new start, anyone can start from now and make a brand-new ending." Healthy lifestyle choices can greatly improve an individual's happiness and quality of life, whether they have MS or not. When MS enters the picture, the disease puts many obstacles in the way of a person's resolve to keep resolutions like these. However, it's very important to "muscle through" and work toward a "new you." The upside may far outweigh the downside.

Who Says Being a Quitter is a Bad Thing?

It's a well-established fact that smoking increases the risk of lung cancer and heart disease. Several studies link smoking to MS and other autoimmune diseases, such as rheumatoid arthritis, Graves' disease and inflammatory bowel disease. In fact, research shows the risk of MS in smokers is 1.5 times higher compared to nonsmokers and the more cigarettes an individual smokes the higher the risk. A link between smoking and other MS risk factors has also been established. For example, a study from Denmark found that smoking is associated with the Epstein-Barr virus. Investigators at Harvard found individuals with MS who smoke also appear to have a much greater chance of experiencing a more rapid progression of their disease. Data suggest the risk of progressing from relapsing remitting to secondary progressive MS (SPMS) is 3.6 times higher for current and past smokers compared to people who never smoked.

While these findings suggest a correlation between cigarette smoking and MS disease progression, the underlying mechanism for this effect isn't clear. Researchers are studying several different hypotheses. Most cigarettes have a glass fiber filter through which the smoke is inhaled. Tobacco smoke consists of two phases: a particulate phase (the particles captured by the filter) and a gaseous phase (the portion of smoke that passes through the filter). A Swedish study compared the effects of tobacco smoking and smokeless tobacco on MS risk. Interestingly, their results showed smokeless tobacco was not associated with an elevated risk for MS. This suggests that the predisposition to MS may be caused by irritation in the lungs from the gaseous phase of tobacco smoke.

Cigarette smoke contains over 4,500 potentially toxic components, including tars, nicotine, carbon monoxide and other particles. Some components of cigarette smoke may have direct toxic effects on the central nervous system. Both the particulate and gaseous phases of tobacco smoke contain high concentrations of free radicals, which may cause nerve degeneration. Free radicals are molecules that are highly

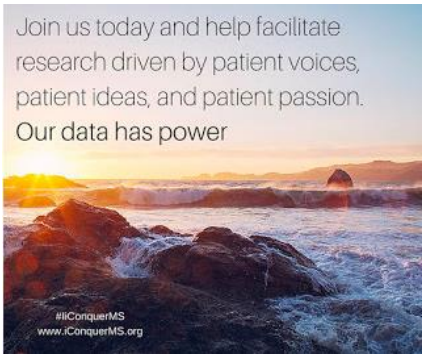
reactive with other cells because they contain unpaired electrons. They can cause damage to parts of other cells by stealing their electrons through a process called oxidation. When free radicals oxidize important components of other cells, those components lose their ability to function normally, and the accumulation of such damage may cause the cells to die. Numerous studies indicate that increased exposure to free radicals causes or accelerates nerve cell injury and leads to neurodegenerative diseases (such as MS). Research shows serum concentrations of cyanide, a component of cigarette smoke, and its main metabolite thiocyanate causes demyelination in the brain and spinal cord in animal models. Smokers are exposed to high levels of nitrous oxide (NO), also known as "laughing gas," from two sources: first high amounts of inhaled NO in smoke and, second, endogenously released NO after uptake of nicotine in the brain. Exposure to NO has been shown to cause nerve degeneration or to block nerve conduction, especially in demyelinated axons. This suggests that NO may play a role MS disease activity and progression.

MS is considered to be an immune-mediated disease in which the body's immune system attacks the central nervous system, which causes nerve damage. Immune system activity results in the inflammation responsible for many MS symptoms. An inflammatory mediator is a messenger that acts to promote an inflammatory response. Studies show cigarette smoke stimulates the influx and activation of a several inflammatory mediators, such as neutrophils, monocytes and macrophages. Various inflammatory markers are used to assess systemic inflammation. Acute phase reactants (APRs) are inflammation markers that increase or decrease in an individual's serum during times of acute tissue injury or inflammation. Fibrinogen is an APR, which means fibrinogen levels may rise sharply in any condition that causes inflammation or tissue damage (like MS). Results from the Framingham Heart Study indicate current and past smokers have higher fibrinogen levels than non-smokers, and these levels correlate with the number of cigarettes smoked per day. Peripheral blood leukocyte counts are routinely measured in clinical practice and are the only cellular marker of systemic inflammation. Research suggests cigarette smoke elevates peripheral blood leukocyte counts and is associated with other important markers of inflammation like the C-reactive protein and interleukin-6 (IL-6).

Another hypothesis involves a direct effect of smoke components on the blood–brain barrier (BBB) which separates the brain from the circulatory system and protects the central nervous system from potentially harmful chemicals. In order for the immune system to launch an attack on the myelin sheath surrounding nerves in the brain and spinal cord, T-cells (a type of white blood cell) from the immune system must first cross the BBB. Leakage of this barrier has been suggested as a factor in initiating the development of MS. Nicotine, a major component of cigarettes, has been shown to affect the integrity and function of the BBB. A 2010 study also suggests the compounds contained in tobacco smoke may affect the viability of cells in the BBB and trigger an inflammatory response that, in turn, may further lead to the loss of its integrity.

As discussed in our May 2018 newsletter, there is mounting evidence that estrogen (a female hormone), not only affects the reproductive system, but also impacts the nervous and immune systems. Many women find that their MS symptoms worsen just before and during their menstrual period. The decrease in estrogen levels leading up to menstruation may be a contributing factor. MS symptoms may also slightly worsen as women go through menopause. One possible reason for this is the decline in estrogen that occurs around this time of life. Research shows that women who smoke cigarettes are estrogen deficient. Women who are smokers undergo menopause earlier than non-smokers. This may play a role in the worsening of disease.

There is growing scientific evidence that smoking not only increases the risk of developing MS but also influences disease progression. The suggestion that components of smoke play a role in this is supported by a recent finding that even passive smoke exposure (second hand smoke) increases the MS risk. Further investigation with well-designed prospective studies is necessary in order to better understand the underlying mechanisms behind these effects. Understanding the role of smoking in the MS disease process may enable us to one day slow disease onset and, perhaps, also control disease progression in high risk individuals by stopping exposure. It may also facilitate the development of more effective



MS treatments by identifying new therapeutic targets. ACP and iConquerMS are committed to facilitating research efforts like these, which have the potential to significantly improve the health and quality of life for those living with MS.

January 2020 Research Spotlight

RESEARCH OPPORTUNITIES

A Study to Understand the Use of Telemedicine in MS Care

Study Purpose:
We're conducting this study with researchers from the Veterans Administration. They are interested in knowing how telemedicine (healthcare delivered over the phone or Internet instead of in person) is being used in MS. The results will be used to advocate for healthcare options that are the most helpful for people with MS.

This study involves:
The study involves completing an on-line survey on the iConquerMS web site. It will take around 15 minutes to complete. Study participants will be entered into a drawing for an Amazon Gift Card. We will be awarding two $100 gift cards and thirty $10 gift cards. Just log into your account at www.iConquerMS.org and look for the My Research Surveys list. You'll see a survey named "Use of Telemedicine in Multiple Sclerosis." Click on the survey name to get started.

Researcher:
Mitchell Wallin, M.D., M.P.H.

Recruiting:
This study is open to all iConquerMS members who have MS. Anyone who has been diagnosed with MS can participate, whether or not you've ever heard of or used telemedicine.

Study contact information:
If you have any questions, please email us at info@iConquerMS.org.

STEP
SUPERVISED VS TELEREHAB EXERCISE PROGRAM FOR PEOPLE WITH MULTIPLE SCLEROSIS

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**

EXERCISE
NEUROSCIENCE
RESEARCH
LABORATORY

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.

A Study to Understand the Needs of Patients with RRMS

Study Title: UBIMS: Understanding the barriers and informational needs of patients with relapsing-remitting MS (RRMS)

Study Purpose:
The purpose of this research is to explore the needs of individuals with RRMS. Results from this study will be used to create better education and information about RRMS for doctors, patients, and caregivers.

This study involves:
Participants will be asked to complete an on-line survey. The survey will ask a series of questions exploring experiences as an individual with MS. Subjects will be asked a few questions about themselves. The online survey is expected to take about 20 minutes or less. Participants should plan to complete the entire process at one sitting. Subjects completing the survey will be offered a $20 Amazon.com gift card which will be sent within 2 weeks using the contact information that they provide. Contact information will only be used to send the gift card and will not be used for any other purpose.

Researcher:
Gregory D. Salinas, PhD

Recruiting:
To be eligible for this study you must be 21 years of age or older, a resident of the United States and be diagnosed with RRMS. Participants must be able to read and speak English.

Contact:

For more information, contact Greg Salinas at (205) 259-1500 or email at greg.salinas@ceoutcomes.com.

Anyone interested in participating in this study should follow this link: http://bitly.com/MS284

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