March 2022 Newsletter

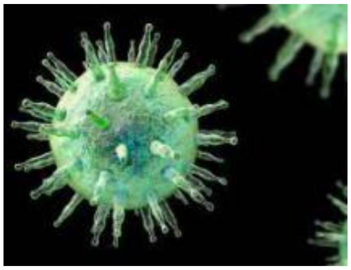
Accelerated Cure project for multiple sclerosis

iConquer MS™

ACP Repository™

MS Minority Research Engagement PARTNERSHIP NETWORK

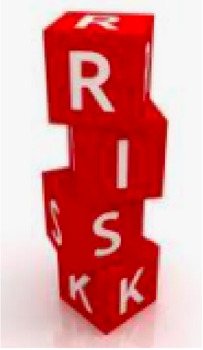
Does Epstein Barr Virus Cause MS?



MS is thought to be caused by a combination of factors, including an individual's genetic background, gender, environment, and lifestyle. Epstein-Barr virus (EBV) has long been suspected to be one of these causal factors. Researchers at Harvard and their collaborators recently published a study that provides the strongest evidence yet that EBV is, indeed, one of the triggers of MS.

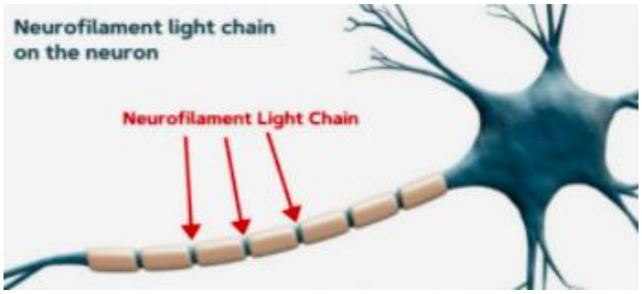
EBV (also known as human herpesvirus 4) is one of the most common human viruses. Most people are infected by it at some point in their lifetime. It is spread primarily through contact with infected saliva. EBV infections in children usually do not cause symptoms, or the symptoms are the same as other mild, brief childhood illnesses. In adolescence and adulthood, it can cause infectious mononucleosis (also called mono). Symptoms of mono include fatigue, fever, inflamed throat, swollen lymph nodes in the neck, enlarged spleen, swollen liver and a rash. After a person is infected with EBV, the virus becomes latent (inactive) and stays in their body throughout their lifetime. In some cases, the virus may reactivate. This does not always cause symptoms, however people with weakened immune systems are more likely to develop symptoms if EBV reactivates.

The Harvard study team used blood samples collected to test for HIV (human immunodeficiency virus) among more than 10 million active-duty United States military personnel between 1993 and 2013. Samples from 801 people who developed MS and 1,566 controls without MS were analyzed. Investigators determined each participant's EBV status at the time the first sample was taken by looking for specific antibodies that signal past infection, and then analyzed additional samples from the same people to determine the relation between EBV infection and MS onset during their period of active duty.



This pivotal research study demonstrates that EBV infection precedes both the symptoms of MS and nervous system damage, and that becoming infected significantly increases the risk for developing MS in susceptible individuals. Of the 801 people with MS and 1,566 without, 35 and 107, respectively were negative for EBV infection in the first blood samples taken. By analyzing additional samples from these same individuals over time, the research team was able to determine that the risk of developing MS increased 32 times in those who became positive for EBV infection. All EBV infections occurred before MS onset.

In order to rule out other possible causes, the Harvard study team also tested for an immune response to cytomegalovirus (which, like EBV, is also transmitted through contact with infected saliva), but this virus was not linked to an increase in MS risk. Using a novel tool called VirScan, which screens for evidence of an immune response to approximately 200 viruses, they also found no links between other viruses and MS risk.



To test whether EBV infection predated MS-related nervous system damage, the research team looked at levels of a molecule called neurofilament light chain (NfL), which is a substance released into the spinal fluid and blood when nerves are damaged. Studies have linked it to MS relapses and disease progression. For the participants who were EBV negative at the time of their first blood sample and who later went on to be diagnosed with MS, the study results showed that there was no indication of elevated NfL prior to EBV infection. After EBV infection, however, elevated levels were detected prior to MS diagnosis.

There is currently no way to avoid infection with EBV. The virus is easily transmitted and most people have been exposed. There is no specific treatment for EBV and there is no medication that will remove the virus from a person's system once they are infected. However, some things can be done to help relieve EBV symptoms, including drinking fluids to stay hydrated, getting plenty of rest and taking over-the-counter medications for pain and fever. Individuals can help protect themselves from EBV infection by not kissing or sharing drinks, food, or personal items (like toothbrushes) with people who have an active EBV infection.

According to the National MS Society, "We don't know yet if the Epstein-Barr virus causes relapses or influences the MS disease course. However, having an anti-viral medicine that combats the virus may help answer that important question. At least one study is testing an experimental anti-EBV medication in people with MS, and there are several experimental EBV vaccines in development, including this recent one announced by Moderna testing its safety in healthy volunteers… It is possible in the future an EBV vaccine could prevent MS. We know that this virus does not act alone, but rather in combination with other risk factors such as a person's genes and environment. In addition to the possibility of an EBV vaccine, researchers are working on ways to calibrate any individual's personal risk for developing MS to provide a possible rationale for intervening before it takes hold."

The ACP Repository was an important resource that helped lay the groundwork for the Harvard study (samples and data were used in one of the author's early studies on EBV). Accelerating research efforts such as these is the heart of ACP's mission. We are grateful for all who have participated in the ACP Repository and iConquerMS. Your contributions make advances in research like this possible! We would also like to express our heartfelt thanks for the many ways that our partners, donors and volunteers have given of their time, talents and resources. Together we are accelerating research for all affected by MS, bringing us closer to a cure. Thank you for your partnership, support and collaboration!

Understanding Factors Affecting MS Onset

While MS is not an inherited disease, there are genetic factors that predispose people to it. One of the strongest genetic risk factors for MS is a mutation in the HLA-DRB1 gene called HLA-DRB1*15:01. The HLA-DRB1 gene provides instructions for making a protein that plays a critical role in the immune system. It is part of a family of genes called the human leukocyte antigen (HLA) complex. The HLA complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders such as viruses and bacteria. About 200 genetic variations outside the HLA complex have also been associated with MS.

A recent study conducted by Drs. Elina Misicka and Farren Briggs at Case Western Reserve University and their collaborators found that people with a higher genetic risk of MS (those that have more genetic variations) are likely to develop the disease at an earlier age. Participants' first MS symptom appeared at a mean age of 32. Investigators looked at data from 3,495 adults with MS, most of whom (71%) were women. Data for 1,268 participants came from the ACP Repository. The remaining 2,227 participants were from Biogen-sponsored clinical trials, including the ADVANCE trial, the ASCEND trial, and the DECIDE trial. About 45% of all participants were positive for the HLA-DRB1*15:01 genetic variant. Genes are usually found in two copies (called alleles). Each copy is inherited from one parent. Results showed that people with the highest genetic risk (HLA-DRB1*15:01 in both gene copies plus other high-risk gene variants) were on average five years younger at disease onset than those with the lowest genetic risk (some disease-associated genetic variants but no copies of HLA-DRB1*15:01).

This is the first time that the genetic variants related to developing MS have been associated with an earlier age of onset. This finding is key to achieving better outcomes for people with MS. Those diagnosed with the disease earlier in life tend to experience more extreme symptoms over the course of the disease. If a person knows they are at a higher risk for early onset, they and their healthcare team can be more aggressive with treatment (for example, make the decision to start MS disease modifying therapy (DMT) at a younger age).

Facilitating research such as this is central to ACP's mission. In 2018, ACP announced a collaboration with the Regeneron Genetics Center that sequenced the entire exome region of all DNA samples in the ACP Repository. The exome is the protein-coding region of the human genome, which represents under 2 percent of the genome, but contains a majority of the known inherited genetic variants associated with all diseases. According to ACP's data return policy, this information was added to the ACP Repository database for the benefit of future research. These data were instrumental in the Case Western study findings. Drs. Misicka, Briggs and their collaborators are taking a deeper dive into these data as their work toward better understanding the genetic factors related to MS onset continues.

March 2022 iConquerMS Spotlight

COVER-MS PROJECT

The COVID-19 VaccinE Response in MS Project

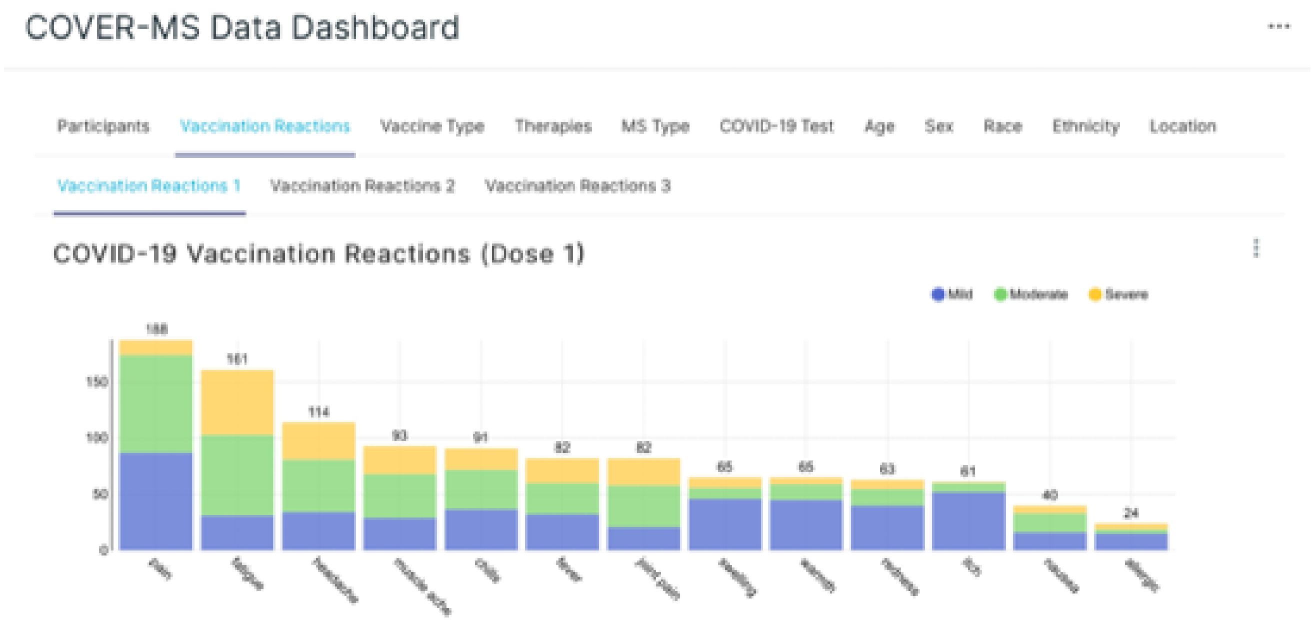
iConquerMS

Participate at iConquerMS.org

COVER-MS Update: New dashboard, 4th dose reporting and more!

We hope that you are navigating all of the changes that COVID-19 keeps sending our way. It's clear by now that vaccines are helping reduce its impact. However, there is still much to learn about COVID-19 and vaccines in people with MS. So, we're planning some new activities for the COVER-MS study. **What questions do you have that COVER-MS could help to answer?** Send us an email and let us know.

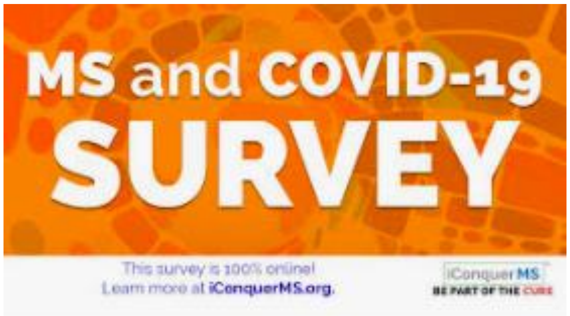
New Data dashboard: Our technical team has created a real-time data display for the COVER-MS study, showing key characteristics of our participants and their vaccination experiences. Please take a look and let us know what you think!



Have you received any vaccine doses that you haven't reported yet? If so, please log in to your iConquerMS account and share the details. We're hoping to have all of our participants' vaccinations reflected in the dashboard and the database.

Received a 4th dose? Some countries are advising people who are immunocompromised to receive 4 vaccine doses. If you've received a 4th dose, you can now provide the details in COVER-MS by completing "Vaccination Details Survey – 4." We'll begin displaying the details for dose #4 on the dashboard once we have more data.

Please let friends and family members who are interested in MS research know about COVER-MS. The study is open to anyone who has received a COVID-19 vaccine or plans to receive one. Our website has more information about COVER-MS and we always welcome questions and feedback at info@iConquerMS.org.



Thanks for your help conquering COVID-19!

March 2022 Research Spotlight

EVENTS

The next Chat with Chat webinar is coming soon!

The Next Steps Committee of iConquerMS has launched a webinar series called “Chat with Chat” and you’re invited! Hosted by our research collaborator Chat Ngorsuraches, these conversations provide a glimpse at the researchers working with iConquerMS, what they study, and how their work will benefit people with MS.

The next webinar, entitled “COVID-19 vaccine safety: A study from iConquerMS data,” is scheduled for April 12, 2022 at 4 pm EDT. Dr. Farren Briggs will be the guest speaker. Anyone interested in attending, please register here.

A heartfelt thank you to Chat and his colleagues for making this educational resource possible. Stay tuned for future episodes!

In case you missed previous episodes of Chat with Chat:

In Episode 1, Chat spoke about his own research into the aspects of MS drugs that people value the most.

In Episode 2, Chat spoke with Nina Bozinov, MD MS, about "Measuring the Quality of Life of People With MS: Findings From the REAL MS Study."

In Episode 3, Chat spoke with Farrah Mateen, MD PhD, about what we've learned from iConquerMS about COVID-19 and MS. If you’ve participated in REAL MS, this is a great chance to learn what your data is telling us about life with MS. P.S. The **next round** of REAL MS surveys is now available through the iConquerMS portal! If you are a member of iConquerMS, why not complete yours today?

RESEARCH OPPORTUNITIES

W UNIVERSITY of WASHINGTON

A new study looking at language usage among people with disabilities – all adults with disabilities are welcome to participate!

What is the study about?

This research attempts to gather evidence on the preference between identity-first and person-first language by and for people with disabilities. The lead researcher is a graduate student in the University of Washington's department of Computer Science and Engineering as a member of multiple labs focused on accessibility in computing.

Why participate?

The topic of language preference has been discussed often, but often while excluding community and individual perspectives.

The research data gathered will help to work towards more consistent respectful language usage in future projects.

Participants will contribute to a public website that features a visualization that explores the ways different backgrounds (age, country, gender) may or may not affect language preference.

Who can participate?

All people with disabilities over the age of 18 who have access to and can use a computer and access to the internet are welcome to participate.

How to participate:

Follow this link: https://bit.ly/disability-language-survey to access our participant survey. It should take around 5 minutes to complete.

Complete your REAL MS surveys!

In the summer of 2016, the iConquerMS initiative launched REAL MS (Research Engagement About Life with MS), a longitudinal study of MS. Participants complete questionnaires online twice each year on a variety of subjects, including health history, diet, exercise and their experience with MS. The **next round** of REAL MS surveys is available now through the iConquerMS portal. Completing these surveys is one of the simplest ways you can accelerate MS research. The information collected will play a pivotal role in helping scientists and clinicians gain a better understanding of the health and quality of life over time for people with MS. REAL MS is just one of the many ways iConquerMS is facilitating research on topics of importance to people affected by the disease. If you are not already a member, please consider joining iConquerMS, the only people-powered research network for MS!

DELIVER-MS

Early Intensive versus Escalation Approaches for the Treatment of Relapsing Remitting MS – Which is More Effective?

A study based at the Cleveland Clinic and the University of Nottingham (United Kingdom) is comparing two treatment strategies in 800 people with relapsing-remitting MS who have never taken a disease-modifying therapy. The study is recruiting at 30 centers in the United States and United Kingdom. One strategy is an “escalation” approach, in which individuals start taking a less-powerful therapy with the option of switching to a more potent one if disease activity continues. The other strategy involves starting with a strong therapy that is potentially more effective, but also carries greater risk for significant adverse effects. The DELIVER-MS Trial (Determining the Effectiveness of Early Intensive versus Escalation Approaches for the Treatment of Relapsing-Remitting Multiple Sclerosis) is funded by the Patient-Centered Outcomes Research Institute (PCORI).

Eligibility and Details

Investigators are seeking participants diagnosed with relapsing-remitting MS who are between the ages of 18 and 60 years. Participants are eligible if they have had MS for five years or less and have never been treated with an MS disease-modifying therapy. Further enrollment criteria are available from the contact section below.

Eligible participants will be randomly assigned into one of two groups and will choose along with their neurology provider among options in either a first-line or higher-efficacy therapy group. Participants and their neurology specialist will choose the therapy within the category that is most appropriate for them.

During the three years that they are enrolled in the study, participants will have regular check-ups and MRI scans with their MS team, to look at the effects of treatment. They will be free to change treatment, in discussion with their neurologist, for any reason at any time.

The primary outcome being measured is the effect of treatment on brain tissue loss. Investigators will also monitor treatment effects on disability progression as measured by the EDSS scale, quality of life, other imaging measures, and safety.

Contact

To learn more about the enrollment criteria for this study, and to find out if you are eligible to participate, please visit the study website and you will be connected with a participating site in your area.

Site Locations

Cleveland Clinic, Cleveland, OH
Cleveland Clinic-Las Vegas, NV
Ohio Health, Columbus, OH
University of Colorado, Anschutz Medical Campus, Aurora, CO
University of Rochester, Rochester, NY
University of Texas, Houston, TX
University of Virginia, Charlottesville, VA
Baylor College of Medicine, Houston, TX
University of Wisconsin, Madison, WI
University of Cincinnati, Cincinnati, OH
University of Minnesota, Minneapolis, MN
Mayo Clinic, Rochester, MN
University of Texas, Austin, TX
University of Buffalo, Buffalo, NY
Virginia Commonwealth University, Richmond, VA

The DELIVER-MS Trial is one of two studies funded by PCORI that will help inform treatment decisions around whether, and which, people with MS would most benefit from early, possibly more risky aggressive therapy. The other study is TREAT-MS

(TRaditional versus Early Aggressive Therapy for Multiple Sclerosis). Both studies are recruiting participants.

iConquerMS™

Your health data has power!

A new topic for the Our Questions Have Power program!

When it comes to MS symptoms and how to manage them, what questions are most important to you? What symptom-related topics do you wish researchers were studying? **Your questions are valuable** and we invite you to share them through the **Our Questions Have Power** program on the iConquerMS website.

The Our Questions Have Power program was launched in March 2021 with an initial focus on COVID-19. Questions submitted by iConquerMS members have helped shape the COVER-MS vaccination study and are being shared with the research community to guide other efforts.

We're now extending Our Questions Have Power to include a second topic: **MS symptoms and their management and treatment**. As before, you're invited to share questions on this topic that you think should be studied and to vote on questions submitted by other iConquerMS members.

We'll share these questions with people affected by MS, researchers, healthcare professionals, advocates, and funders – and, together, we'll work to launch research studies to answer those questions.

It's easy to share your ideas and input in Our Questions Have Power!

- Log into iConquerMS to start (create an account first if you don't already have one).
- Have a research question to submit? Click **PROPOSE an MS Research Question** to submit a question you'd like to see studied.

- Want to weigh in on other people’s ideas? Click **VOTE and COMMENT on MS Research Questions** to review, comment, and vote on questions submitted by other iConquerMS members.