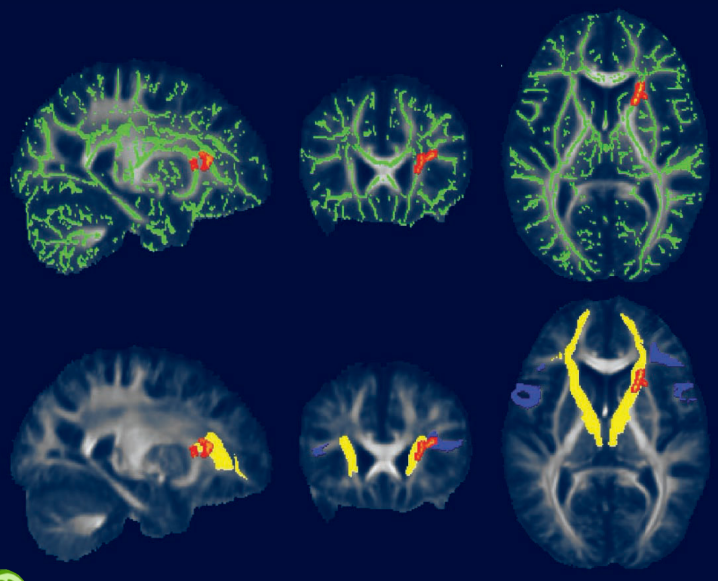
JOHNS HOPKINS MEDICINE

Lyme Disease Research Center



ADVANCING LYME DISEASE RESEARCH

IMPACT REPORT 2022

SLICE STUDIES

www.HopkinsLyme.org

OUR MISSION
is to bridge the gaps in Lyme disease knowledge and translate our research findings into improved patient care.

RESEARCH IS KNOWLEDGE

KNOWLEDGE IS HOPE

Patient Care
Research
Education

Letter from Director, John Aucott, MD

The Johns Hopkins Medicine Lyme Disease Research Center is committed to bridging patient care to research. Our 2022 Impact Report provides exciting highlights of our research advances in Lyme Disease.

Nothing has caused more confusion and controversy than what to name the condition that has long been called chronic Lyme disease. In our report you will see the research term, Post Treatment Lyme Disease (PTLD), used when discussing research results. In this context, PTLD is a narrow definition designed specifically to facilitate research and discovery. Research results can be extrapolated and generalized when appropriate to the much broader group of patients with chronic or persistent Lyme disease.

In the clinical context there is an ongoing debate about renaming chronic Lyme disease to another name such as Long-haul Lyme, persistent Lyme disease, or Lyme disease associated chronic illness. However, the clinical name should not limit research into underlying causes and biomarkers for this persistent illness. The patient's illness is real and the care of the patient remains paramount as we pursue multifactorial causes and a cure.

We thank our donors for supporting our clinical research program including our groundbreaking new fellowship program. Progress would not be possible without you, and we are grateful for your continued support.

Together we are working to improve Lyme disease knowledge and patient care.

May you and yours be well.

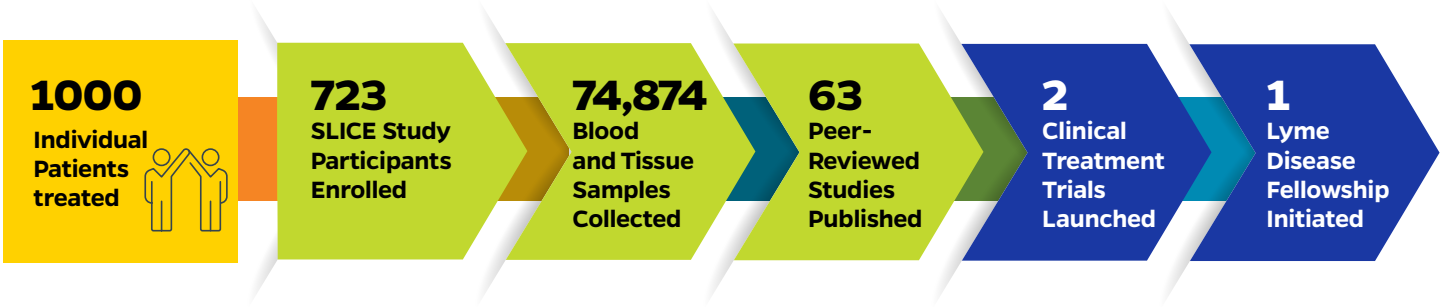
Warm regards,

John Aucott

John Aucott, MD
Associate Professor of Medicine
Johns Hopkins University School of Medicine
Director, Lyme Disease Research Center

RESEARCH CENTER MILESTONES

2022 MILESTONES



PATIENT CARE

Since our Center opened in the Division of Rheumatology at Johns Hopkins University School of Medicine in the spring of 2015, we have provided patient care to over 1000 individual patients in addition to 723 enrolled study participants. For the past 5 years, we have averaged over 1200 clinical and research appointments per year.

WE LISTEN CAREFULLY TO OUR PATIENTS to better understand their symptoms, concerns, and priorities. We work to provide illness validation, hope, and a path forward to renewed health.

OUR CLINICAL EXPERIENCE INFORMS OUR RESEARCH PROGRAM. Our rigorous translational research program aims to bridge the gaps in patient care through robust scientific research and discovery.

We strive to bridge the gaps in Lyme disease knowledge and translate our research findings into improved patient care.

OUR PATIENT-BASED CLINICAL RESEARCH PROGRAM ADVANCES LYME DISEASE UNDERSTANDING

SLICE Studies · Biorepository · Collaborations · Advanced Neurologic and Joint Imaging Early Diagnosis Research · Data · Insights · Publications · Education · Patient Care

SLICE STUDIES

- **S**tudies of
- **L**yme disease
- **I**mmunology &
- **C**linical
- **E**vents

We pay attention to and meticulously characterize the symptoms illness experience of our study participants.

723	2290	84%
Participants Enrolled in SLICE Studies	Research Visits	1 Year Retention Rate among study participants

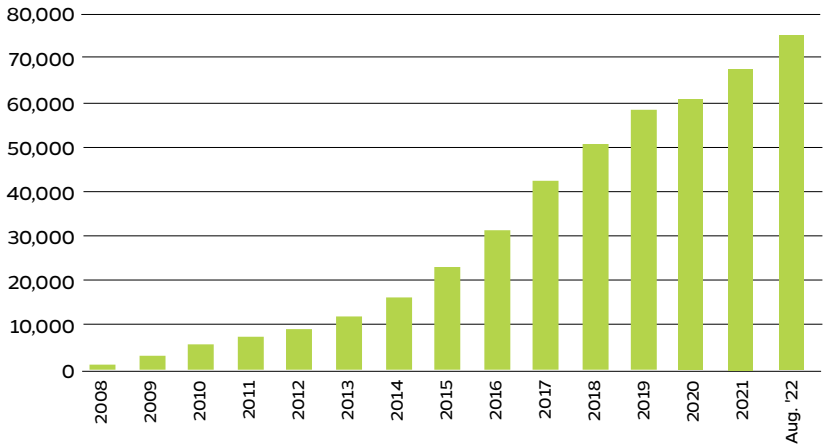
As of August 31, 2022

We are grateful to our patients and our study participants.
Our dedicated team is urgently working on your behalf towards solutions.

SLICE BIOREPOSITORY

Our SLICE biorepository is comprised of blood and tissue samples from people with validated acute and chronic Lyme disease along with their well-characterized clinical and epidemiologic data. This treasure-trove of gold-standard samples are valuable cornerstones to advancing leading-edge research collaborations and scientific discoveries that expand the understanding of Lyme disease.

Cumulative Numbers of Blood and Tissue Samples



RESEARCH COLLABORATIONS

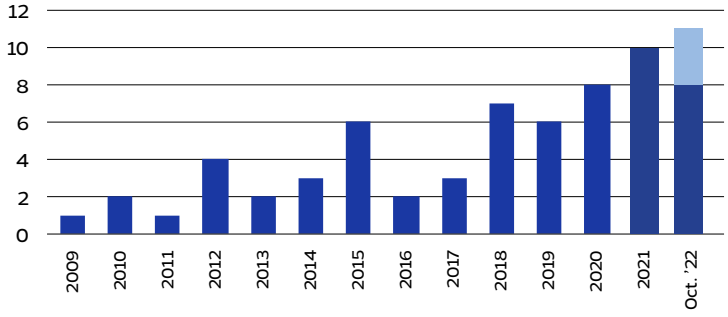
Over 8,585 samples from our SLICE biorepository have been utilized by 37 different academic, scientific, and medical collaborators at 26 different institutions. Our multidisciplinary SLICE collaborators use multiple advanced scientific approaches including immune profiling, transcriptomics, proteomics, metabolomics, microbiomics, and direct detection methods to generate novel insights into the complex biologic drivers and mechanisms of Lyme disease. Our research, published in peer-reviewed studies, enables the discovery of diagnostic biomarkers and potential treatments to improve patient care, education, and health outcomes for Lyme disease patients.

Our human-based clinical research program is helping to identify complex biology, validate persistent symptoms, reveal multi-organ impact, and detect immune system biomarkers.

RESEARCH PUBLICATIONS

The productivity of our Center's research pipeline continues to be strong, with 39 publications in the past 5 years, including 10 in 2021 and 8 year to date through October 2022, with an additional 3 publications under review.

Peer-Reviewed Publications by Year

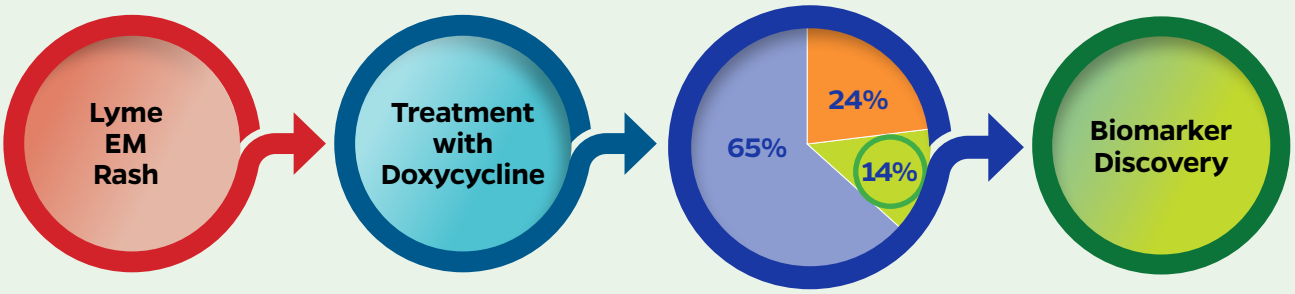


RESEARCH

SLICE STUDIES VALIDATE PERSISTENT ILLNESS AND ELUCIDATE UNDERLYING BIOLOGY OF SYMPTOMS

A 2022 SLICE Studies publication finds that 14% of early diagnosed and promptly treated Lyme disease patients develop Post Treatment Lyme Disease (PTLD). The PTLD patients have persistent functionally impairing symptoms 6 months following the end of treatment, including severe fatigue, body pain, and cognitive challenges. The results confirm that Lyme disease can trigger PTLD despite early treatment with 21 days of the antibiotic doxycycline. This rigorously designed prospective controlled study validates that Lyme disease associated chronic illness is real and significant. The study's PTLD incidence of 14% compares with 4% in a healthy control group. Importantly, the risk of functionally impairing persistent illness would likely be greater than 14% in community (non-study) settings due to the complexity of real-world disease, which includes misdiagnoses and treatment delays. There are already an estimated 2 million patients in the US living with persistent or post treatment Lyme disease. With 500,000 new U.S. cases of Lyme disease per year, the number of people experiencing chronic symptoms is a growing public health concern. Notably, many persisting Lyme disease symptoms overlap with other infection-associated chronic illnesses such as Long COVID and ME/CFS, and additional studies are needed to determine if they may share some common biologic pathways.

SLICE STUDIES REVEAL A RANGE OF CLINICAL OUTCOMES AFTER PROMPT TREATMENT OF EARLY LYME DISEASE: *14% HAVE PERSISTENT SYMPTOMS AND IMPAIRED QUALITY OF LIFE*



SLICE STUDY (n=255)

Returned to pre-Lyme health status | Persistent symptoms with normal functioning | Post Treatment Lyme Disease

Aucott JN, Yang T, Yoon I, Powell D, Geller SA, Rebman AW. Risk of post-treatment Lyme disease in patients with ideally-treated early Lyme disease: A prospective cohort study. Int J Infect Dis. 2022 Mar;116:230-237. doi: 10.1016/j.ijid.2022.01.033.

SLICE STUDIES PROMOTE BIOMARKER DISCOVERY

By evaluating the biologic distinctions of different stages and manifestations of Lyme disease, our well-characterized SLICE biorepository samples are enabling biomarker discovery. In 2022, we published two biomarker studies that could help advance future diagnostics.

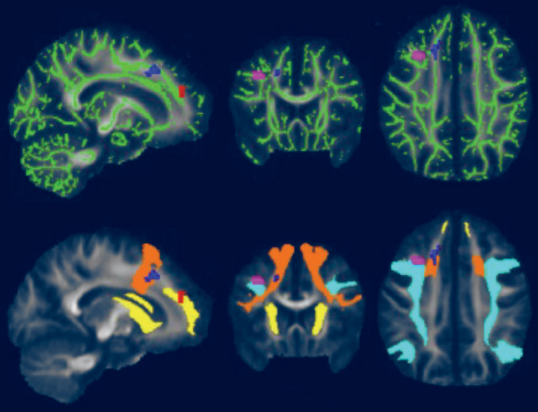
A study published in collaboration with Charles Chiu, MD, PhD, and colleagues at UCSF, et al, found a gene expression signature for early Lyme disease using next generation RNA-Sequencing data of the human host response. This signature could potentially be used to diagnose patients earlier and more accurately, including those testing negative by current conventional serologic tests.

Servellita V, Bouquet J, Rebman A, Yang T, Samayoa E, Miller S, Stone M, Lanteri M, Busch M, Tang P, Morshed M, Soloski MJ, Aucott J, Chiu CY. A diagnostic classifier for gene expression-based identification of early Lyme disease. Commun Med (Lond). 2022 Jul 22;2:92. doi: 10.1038/s43856-022-00127-2.

Another study, published in collaboration with Avi Ma'Ayan, PhD, and Daniel Clarke, et al, at Mount Sinai Center for Bioinformatics and Icahn School of Medicine, discovered distinct gene expression RNA-Seq signatures for acute Lyme disease and Post Treatment Lyme Disease. The mRNA-based signatures can potentially be utilized in a diagnostic biomarker panel to confirm a clinical diagnosis of acute Lyme disease or PTLD.

Daniel J.B. Clarke, Alison W. Rebman, Jinshui Fan, Mark J. Soloski, John N. Aucott, Avi Ma'ayan, Gene set predictor for post-treatment Lyme disease, Cell Reports Medicine, Volume 3, Issue 11, 2022, 100816, ISSN 2666-3791. doi.org/10.1016/j.xcrm.2022.100816

NEUROIMAGING STUDY SHOWS FUNCTIONAL & STRUCTURAL BRAIN ABNORMALITIES IN LYME DISEASE PATIENTS



Brain fMRI images (above and on cover) show white matter changes associated with post treatment Lyme disease.

Functional abnormalities as well as distinct structural changes in the white brain matter of Lyme disease patients were discovered in a specialized brain imaging study conducted by our Center in collaboration with Cherie Marvel, PhD, and her colleagues at Johns Hopkins Medicine departments of neurology and psychiatry and behavioral sciences. Utilizing functional MRI (fMRI) brain scans in conjunction with diffusion tensor imaging (DTI) the study identified marked functional and structural physical brain abnormalities in post treatment Lyme disease (PTLD) patients versus healthy controls. The cause of PTLD symptoms typically cannot be identified with regular MRIs, CT scans, or blood tests. However, fMRI is an objective quantitative test that measures brain function during cognitive tasks, and fMRI results show that the brains of PTLD patients work harder than normal, unexpectedly by activating white matter in the frontal lobe to try to maintain normal function. In addition, using DTI to measure structural brain integrity researchers found abnormalities in the same white matter regions as the fMRI scans. These neuroimaging results provide new objective validation of a biologic basis for working memory impairment, slower processing speed, and other cognitive problems experienced by PTLD patients. More research is needed to better understand the diagnostic and therapeutic implications of these remarkable findings.

Marvel CL, Alm KH, Bhattacharya D, Rebman AW, Bakker A, Morgan OP, et al. (2022) A multimodal neuroimaging study of brain abnormalities and clinical correlates in post treatment Lyme disease. PLoS ONE 17(10): e0271425. https://doi.org/10.1371/journal.pone.0271425

TWO TREATMENT TRIALS INITIATED

New treatment approaches are needed to address the long-term symptoms associated with Lyme disease which can be debilitating to patients and costly to society. In 2022, our Center began its first two treatment trials for patients with Lyme disease infection associated chronic illness. These pilot clinical trials are made possible thanks to the generous support of the Steven and Alexandra Cohen Foundation.

Psilocybin treatment trial for Post Treatment Lyme Disease

Johns Hopkins University School of Medicine researchers in psychiatry, psychedelic science, and neuroscience are joining forces with the Lyme Disease Research Center to study psilocybin, a psychoactive substance found in certain mushrooms, in the treatment of post treatment Lyme disease. The pilot study that commenced in 2022 is being led by Albert Garcia- Romeu, PhD, Assistant Professor of Psychiatry and Behavioral Sciences, in collaboration with John Aucott, MD, Director of the Lyme Disease Research Center. The clinical trial is investigating the therapeutic potential of psilocybin in people with well-documented current post treatment Lyme disease (e.g. functionally impairing symptoms >6 months following standard of care antibiotic therapy). Multi-symptom burden and changes in functional health and well-being are being evaluated, including changes in fatigue, pain, mood and quality of life. The pilot study will determine the feasibility of studying psilocybin as a potential new therapy for Lyme disease.

TETRACYCLINE TREATMENT TOLERABILITY TRIAL FOR POST TREATMENT LYME DISEASE

A pilot tetracycline study began in 2022 at our Center in conjunction with the Clinical Trials Network for Lyme and Tick-Borne Diseases sponsored by the Steven & Alexandra Cohen Foundation. This clinical trial is investigating tetracycline treatment tolerability in people with post treatment Lyme disease. The study is randomized, double-blind, and placebo-controlled and involves 3 months of treatment.

Tetracycline is an FDA approved antibiotic with both antimicrobial and anti-inflammatory properties.

Tetracyclines have been used as anti-inflammatories in chronic illnesses including dermatologic and rheumatologic illnesses. However, no clinical trials have yet examined the benefit of longer (>4 weeks) tetracycline therapy in post treatment Lyme disease.

Extended duration tetracycline could be a potentially beneficial and accessible addition to a clinician's therapeutic toolbox. Results of the pilot tetracycline study will determine the feasibility of conducting a larger controlled treatment trial.

To stay abreast of our pilot studies and other research news please sign up for our newsletter.

Subscribe

EDUCATION

NEW FELLOWSHIP PROGRAM LAUNCHED

In 2022, our Center launched the Johns Hopkins Lyme and Tickborne Disease Fellowship Program, the first tickborne fellowship program housed within a department of internal medicine in the nation. The program emphasizes multidisciplinary clinical and translational research and provides education and training in tickborne diseases to the next generation of physician scientists. The program is integrated in the Division of Rheumatology, consistently ranked the number one Division of Rheumatology in the United States.

MEET OUR FIRST LYME DISEASE FELLOW

Marzieh Keshtkarjahromi, MD, The Center's First Lyme and Tickborne Disease Fellow

Marzieh Keshtkarjahromi, MD, is the first fellow of the newly launched Johns Hopkins Lyme and Tickborne Disease Fellowship Program. Marzieh is Board Certified in Internal Medicine and has completed her internal medicine residency training at MedStar Health Baltimore. In her first year, under the tutelage of Center Director, John Aucott, MD, and his multidisciplinary clinical research team, Marzieh is learning all aspects of Lyme disease clinical care. In her second year, in conjunction with the Johns Hopkins Bloomberg School of Public Health, Marzieh will conduct a Lyme disease research project while pursuing a fully funded Masters degree or certificate in Epidemiology and Clinical Research. Marzieh is excited about being the Center's first fellow. "I am immensely grateful for this outstanding fellowship opportunity and eager to make a difference to the Lyme disease patient community."

Graduates of an Internal Medicine Residency Program are Invited to Apply to Our Fellowship Program.

Apply

WHY WE GIVE

Beth and Greg McCrickard of Towson, Maryland, have helped support Dr. John Aucott's SLICE study since the very beginning. Beth is a member of the Advisory Board of the Lyme Disease Research Center, serving since 2015 when the Center was established at Johns Hopkins University School of Medicine. Greg is retired from his position as a vice president of T. Rowe Price Group, Inc. Although their family has not been directly impacted by Lyme disease the McCrickards know they are at risk for tick bites given their love of spending time gardening, hiking, and enjoying the outdoors in the Baltimore area as well as on their farm in Virginia. They have many friends who have become sick with Lyme disease and are aware of the urgent need for better diagnostic and treatment options.

> **Beth explains "We have long-standing respect for Dr. Aucott as a physician-scientist and believe in his capabilities and vision. Lyme disease needs improved solutions, and his research program is transformative." Greg adds, "Dr. Aucott had incredible foresight to design the SLICE study 15 years ago. He knew the value of data. It seems obvious now, but it wasn't back then. It's exciting to see his early vision coming to fruition with even more impact than we could have imagined."**

With a long history of supporting education initiatives, the McCrickards have also been leading supporters of the newly launched Lyme and Tickborne Disease Fellowship Program. Beth emphasizes, **"We know this first of its kind fellowship program will have a huge impact on medical education. We are proud to be contributing to this program and hope others will, too."**

RESEARCH CENTER TEAM

CLINICAL RESEARCH TEAM

John Aucott, MD
Associate Professor of Medicine
Director, Lyme Disease Research Center

Alison Rebman, MPH
Instructor in Medicine
Director for Clinical and Epidemiological Research

John Miller, MD
Assistant Professor of Medicine
Lyme Arthritis Program

Pegah Touradji, PhD
Assistant Professor of Physical Medicine & Rehabilitation
Lyme Disease Rehabilitation Neuropsychology Program

Ting Yang, PhD
Senior Biostatistician

Erica Kozero, BS, CCRP
Senior Research Program Coordinator

Cheryl Novak, MSN, CRNP
Certified Registered Family Nurse Practitioner

Susan Joseph, BSN, RN
Senior Research Nurse

Cindi Crews
Senior Medical Office Coordinator

Verna Scheeler, BSHA, MA
Clinical Research Program Manager

Isabella Brothers, BS
Research Program Coordinator

LABORATORY RESEARCH TEAM

Erika Darrah, PhD
Associate Professor of Medicine
Director for the Basic Science Laboratory

Mark Soloski, PhD
Professor of Medicine
Senior Advisor

Daniela Villegas de Flores, MEd
Senior Research Specialist

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Isaac Yoon, MD
Tanya Bentley Young

EDUCATION AND COMMUNICATIONS LIAISON

Nancy Dougherty
NVantage Consulting, LLC

Philanthropic Support Makes A Difference.

Philanthropy enables the Johns Hopkins Medicine Lyme Disease Research Center to pursue groundbreaking research that is critical to improving diagnostics, treatments, and health outcomes for Lyme disease patients. By bridging the gaps in Lyme disease knowledge, we strive to improve education and patient care. As we launch our first Fellowship Program and our first clinical trials for Lyme disease, we are especially grateful for our philanthropic partners who continue to support and believe in our mission.

Our Research Center is grateful for the support of:

- **Steven & Alexandra Cohen Foundation**
- **Brennan Family**
- **Global Lyme Alliance**
- **Bay Area Lyme Foundation**
- **Department of Defense**
- **Individual donors, family foundations and collaborators**
- **Our Advisory Board**

SUPPORT OUR LYME DISEASE FELLOWSHIP PROGRAM

YOUR GIFT ADVANCES KNOWLEDGE TOWARDS A CURE

If you would like to contribute to this important work, please contact:
Department of Medicine Development Office

Phone: 410-550-3417
Email: departmentofmedicine@jhmi.edu

If making a gift by check, please make payable to: JHU, with "The Lyme Disease Research Center" noted.

Mailing address:
Johns Hopkins University and Medicine
Attn: Department of Medicine/Lyme Disease Research Center
PO Box 49143
Baltimore, MD 21297-9143

You may also make a donation by visiting our website at HopkinsLymeDonate.

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Provider Office: 410-616-7596
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JOHNS HOPKINS MEDICINE

www.HopkinsLyme.org

We appreciate your support which is vital to our program.