Mount Sinai South Nassau

Chiari EDS Program

NEWSLETTER | FALL 2022

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News

The latest news from the Chiari EDS Program

On August 28, 2021, The Chiari Neurosurgical Center adopted a new name: **Chiari EDS Center**, with the opening of our clinical offices at *242 Merrick Road, Rockville Centre, NY* in late January 2022. Reflecting the renewed focus of the group, all in close cooperation and with the full support of **Mount Sinai South Nassau**, our multidisciplinary structure emphasizes the comprehensive treatment, prevention, and clinical research of Chiari, Ehlers-Danlos syndrome, and related disorders, including:

- Chiari I Malformation
- Syringomyelia
- Craniocervical Instability
- Idiopathic Intracranial Hypertension
- Intracranial Hypotension
- Tethered Cord
- CSF Leaks
- Styloid Hypertrophy and Eagle Syndrome
- Hydrocephalus
- Postural Orthostatic Tachycardia Syndrome
- Dysautonomia
- Small Fiber Neuropathy
- Post-Treatment Lyme Disease Syndrome
- Long Haul COVID
- Cervical Instability
- Cervical Disc Herniations
- Lumbar Instability and Dislocations

Additionally, our investigation into the role of mast cell activation disease (MCAD) in the Chiari/Ehlers-Danlos syndrome (EDS) complex has led to the establishment of the MCAD Center, led by immunologist Dr. Anne Maitland M.D., Ph.D. – who has now joined Dr. Paolo A. Bolognese, M.D. (Surgical Director, Chiari Neurosurgical Center) and Dr. Ilene S. Ruhoy, M.D., Ph.D. (Administrative Director and Medical Director, Chiari EDS Center at Mount Sinai South Nassau). Dr. Maitland additionally serves as a consultant to the neurosurgical team in the care of those impacted by a debilitating triad of MCAD, EDS, and Autonomic Dysfunction, including overlaps with known co-morbidities as:

- Dysautonomia
- Small Fiber Neuropathy
- Post-Treatment Lyme Disease Syndrome
- Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
- Postural Orthostatic Tachycardia Syndrome
- Immune Dysfunction
- Dysmotility

Of note, we are increasingly seeing patients in the Chiari/EDS/MCAD spectrum struggling with debilitating long term post-viral issues in the wake of the global SARS-CoV-2 pandemic — a condition now widely referred to as **Long Covid**. Recognizing its urgency, we are actively expanding our clinical practices towards including a detailed protocol to monitor and

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The Mount Sinai South Nassau Chiari EDS Center

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treat Long Covid, complete with obtaining tissue samples for genetic analysis of patients. Funding acquisition for this project is underway.

In March 2022, Dr. John Biggins, Ph.D. joined the team as our new Research Director, who has over 25 years of experience in biomedical research. He comes to us after being a founding team member at LifeMine Therapeutics, a biotech start-up launched to leverage genomics and synthetic biology technology towards developing next-generation drugs for targeting the primary cellular drivers of diseases in cancer, immunology, and neuroscience. Dr. Biggins was previously on the faculty of Hofstra University and has past professional affiliations with Rockefeller University, Weill Cornell Medical College, Memorial Sloan-Kettering Cancer Center, University of Wisconsin-Madison, University of Delaware, and Fordham University.

The Mount Sinai South Nassau Chiari EDS Center offers the highest available diagnostic and state-of-the-art treatment options for patients with Chiari/EDS/MCAD-related issues – organized specifically towards integrating all aspects of pre-, post-, and non-surgical outcomes for a reliable new standard of patient care.

Notably, our consortium is the first medical organization in the United States whose mission is designed to specifically address the pressing and unmet needs of the patient population within the Chiari/EDS/MCAD spectrum.

Open Projects

A. Exploration of infectious, immune, and genetic contributors to small fiber polyneuropathy.

Primary Investigator:
Dr. Ruhoy. IRB approved

We seek to better identify and understand biological factors that contribute to the development of small fiber polyneuropathy (SFPN) in patients with disorders as EDS, chronic fatigue syndrome, myalgic encephalomyelitis, post-treatment Lyme disease syndrome, and fibromyalgia. As routine electrodiagnostic study does not detect SFPN, tissue biopsies are required for diagnostic confirmation. Punch biopsy tissue samples are assessed epidermal nerve fiber density and/or sweat gland nerve fiber density, and if the density of epidermal nerve fibers is decreased, as compared to established normative data, a diagnosis of SFPN is supported.

Our goal is to create a tissue bank of research-dedicated biopsies on consenting SFPN patients and control subjects for analysis, concentrating on genetic, immune, or infectious issues or abnormalities among the patient populations. We expect deeper analyses of the tissue biopsy samples will lead to better treatment options for patients with SFPN. A primary study investigating the disease processes, examining both clinical and genetic aspects of SFPN, is underway.

Material transfer agreements between Mount Sinai South Nassau and the **J. Craig Venter** Institute for genetics analyses is in progress. Additionally, a collaborative grant application to the Steven and Alexandra Cohen Foundation has been submitted.

B. Exploration of Nevisense for impedance and tissue oxygenation in mast cell dysregulation

Primary Investigator:
Dr. Maitland. IRB approval, in submission.

Connective tissue is integral to the structure of blood and lymphatic vessels, and therefore, genetic changes may affect vessel compliance resulting in an increase in permeability especially when under increased pressure. As identified via electronic microscopy, the "soft, velvety skin", a marker of a hypermobile Ehlers Danlos hypermobile spectrum disorder (HEDS/HSD) likely reflects abnormal collagen fibers and abnormal glycocalyx barrier function. The abnormal glycocalyx barrier function, from the ability of dermal fibers to separate, may impact capillary diffusion, lead to increased hydrostatic pressure, and predispose the dermis to nonserological inflammation.

Electrical impedance spectroscopy (EIS) has become a useful tool in detecting skin

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barrier dysfunction in a variety of conditions and recently has been used in establishing biomarkers for physiological differences within various dermatological diseases. Using the Nevisense device – an EIS monitor capable of detecting alterations in the electric conductance of skin tissue in a benign, normal clinical setting – we have established a non-invasive tool for improved diagnostics in the monitoring of disorders along the EDS spectrum, correlating the dysfunction of the glycocalyx barrier with tissue perfusion index. As our center sees hundreds of patients per year, we have the capability to assess the extent of skin barrier dysfunction in our patient population to foster the development of this EIS protocol as a standard clinical tool.

C. Autologous Adipose-Derived Stromal Vascular Fraction to Repair Degenerative Neurological Conditions Refractory to Conventional Treatments.

Primary Investigator:
Dr. Ruhoy. IRB approval, submitted.

Adult adipose derived stem cells (ADSCs) are cells that are highly similar to adult mesenchymal stem cells (MSCs). There is significant data demonstrating the benefits that MSC treatment has on inflammatory and degenerative conditions. Whereas MSCs are derived from bone marrow, ADSCs are derived from the stromal vascular fraction (SVF) of human adipose (fat) tissue, which is considerably easier to extract from patients, and compared to MSCs, data supporting ADSC-based treatment is in its infancy. Our intent is to demonstrate the efficacy of using SVF-derived ADSCs for the treatment of degenerative neurological conditions based upon patient evaluation and objective findings.

This protocol investigates the use of autologous mesenchymal stem cells towards treating inflammatory and ischemic processes refractory to conventional treatments and its safety. Relevant medical conditions include myalgic encephalomyelitis, connective tissue disorder, post-viral encephalitis, and autoimmune encephalitis. The primary outcome should demonstrate that administration of autologous SVF as produced by this protocol produces an efficacious response to many of the Neurological conditions treated. Secondarily, we should demonstrate that the treatment is safe.

D. Surgical management of craniocervical instability in patients with connective tissue disorder

Primary Investigator:
Dr. Bolognese. IRB approved.

This is the first prospective observational study of its kind to in the field of craniocervical instability and connective tissue disorder, based on the criteria developed in our surgical practice for years. Downstream analysis includes partnership with **Stanford Genome Technology Center** and the **J. Craig Venter Institute** for advance genetics analyses and the **National Primate Research Center at Tulane University** for pathology and tissue analysis.

E. Styloid Induced Neuropathy of the Glossopharyngeal Nerve

Primary Investigator:
Dr. Bolognese. IRB approved.

The purpose of this study is to learn how styloid-induced neuropathy contributes to the pathology of patients with Chiari I malformation, Ehlers-Danlos syndrome, and related disorders. We have recently identified several patients affected by both Chari malformation and styloid hypertrophy, in whom we detected an unprecedented syndromic clinical presentation, which is different from and more complex than the known variants of Eagle syndrome. This new syndrome clinically appears to be linked to a stretch neuropathy of the glossopharyngeal nerve, where it exits the skull base and wraps around the styloid process. The clinical presentation stems from the involvement of the different segments and branches of the glossopharyngeal nerve and includes altered tongue sensation, altered salivation, cardiac irregularities, swallowing difficulty, hearing difficulty, and localized pain – overlapping with the characteristics of glossopharyngeal neuralgia and Eagle syndrome. Patients with severely debilitating symptoms that were unresponsive to conservative management were selected for surgical treatment, which is now the current standard of care. The observed co-morbidities in patients include Ehlers-Danlos syndrome (92%), Chiari malformation Type I (85%), tethered spinal cord (36%), and mast cell activation disease (41%) – thus providing empirical data supporting the hypothesis that connects styloid hypertrophy within the Chiari/EDS spectrum. A five-year follow up is underway with post-operative questionnaires.

F. Retrospective chart review of the Chiari Neurosurgical CenterConventional Treatments.

Primary Investigator:
Dr. Bolognese. IRB approved.

1. Safety analysis and complications of condylar screws in a single-surgeon series of 250 occipitocervical fusions.

A retrospective safety and complication-based analysis of occipitocervical fusion via condylar screws fixation (i.e., bone implantation) was performed. Methodical dissection of anatomical landmarks, intraoperative imaging, and neurophysiologic monitoring allowed the safe execution of the largest series of condylar screws reported to date. In the timespan of 2012-2018, a total of 250 patients underwent occipitocervical fusions using 500 condylar screws, from which no condylar screw pullouts or vertebral artery migration were observed in this series. Additionally, the sacrifice of condylar veins during the dissection at C0-1 did not cause any venous stroke. Condylar hypertrophy in a subset of patients (roughly one-third) did not prevent the insertion of condylar screws. This surgical series suggests that the use of condylar screws fixation is a relatively safe and

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reliable option in both adult and pediatric patients. Separate contributions will follow in the future to provide details about the long-term clinical outcome of this series.

2. Electromyographic assessment of condylar screw placement during occipitocervical fusion

This is a retrospective study of a series of occipitocervical fusion procedures with condylar screw fixation in which the authors investigated the utility of electromyography (EMG, free-running and triggered) as a reliable tool in assessing the positioning of condylar screws. Intraoperative free-running EMG and triggered EMG were able to correlate alerts with condylar screw placement accurately for the 197 patients with craniocervical instability who were treated within 2014-2017. A triggered EMG threshold of 2.7 mA was found to be a minimum acceptable threshold. A combination criterion of free-running EMG and triggered EMG alerts was found to enable accurate assessment of condylar screw positioning and placement.

3. Establish the role of invasive cervical testing (ICT) as an important diagnostic tool for craniocervical instability in patients with connective tissue disorder.

To guide a selection of reliable candidates for fusion/stabilization of craniocervical junction, we analyzed a cohort of over 200 consecutive patients who underwent ICT testing a single center from 2015-2021. Of note, there was a 7-to-1 preponderance of females-to-male in the patient pool. Roughly half of patients had craniocervical fusion based on ICT with ~95% of this subset diagnosed with Ehlers-Danlos syndrome. ICT of patients resulted in significant improvement in morphometric measurements of the craniocervical junction, as well as notable improvement in presenting symptoms as swallowing difficulty (85%), vision abnormalities (85%), headache (69%), breathing difficulty (65%), brain fog (54%), neck pain (53%), and fatigue (44%).

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www.southnassau.org/sn/chiari-eds

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Publications

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