



News About...

Chiari Type 1/Syringomyelia Research

Fall 2005



Welcome from Dr. Marcy Speer



On behalf of the entire CM Research Team here at Duke, I'd like to welcome you to this latest edition of "News About...Chiari Type 1/Syringomyelia." This newsletter is for the families who so generously contribute their time to support our research into Chiari Type 1/Syringomyelia and the genes that may influence CM1/S. None of the work we are doing would be possible without your help. Thank you!

Marcy Speer, PhD
Study Director and
Principal Investigator



Candidate Gene Update

Candidate genes are genes scientists know something about, such as their exact location on a particular chromosome and their function. Candidate genes for Chiari Type 1 Malformation/Syringomyelia include genes known to be involved in the development of the skull and nervous system, or known to cause other conditions related to CM1/S such as Paget's disease. Currently we are focusing on two of these Paget's disease genes: sequestome 1 (SQSTM1) and tumor necrosis factor receptor super family member 11A (TNFRSF11A).

Genome Screen Update

We have completed the first stage of our genomic screen looking for regions in the genome which are common between people with CM1/S. This screen included more than 170 people from 30 families with more than one person with CM1/S. As we complete the second stage with more people utilizing a newer technology, the screen and MRI study will help us determine where to find candidate genes for further study.

Visits from Study Personnel



In many cases, we are able to visit families in person to complete their enrollment in the CM1/S study. During visits with families, we answer any questions participants have about our study, draw blood samples, and complete any other paperwork. We will be traveling to one or two states each month and can most often accommodate the scheduling needs of the family, including evening or weekend visits. Please contact us to schedule a visit or to check your family's enrollment status.

New Study Contact Information

Phone: (toll free) (877) 385-2626

Phone: (direct) (919) 668-1972

E-mail: chiari@chg.duhs.duke.edu

Web: <http://www.chg.duke.edu/diseases/chiari.html>



MRI Study

Head and spine MRIs from CM1/S patients and their family members provide us a unique opportunity to study the condition. By comparing the size and position of certain structures we are hoping to clarify what aspects are common among CM1/S patients and what features are similar between relatives. We can also measure the volume of the posterior fossa to try to determine if this space is smaller in CM1/S patients. Combined with the genomic screen information we are hoping to determine which genes may be contributing to the size of the brain or foramen magnum, for example.

If the brain is thought of like a house, one group of genes may decide how big to build the foundation and another determines how many floors it will have. A one-story house can comfortably hold your family if the foundation is big enough, but if it's not you could feel cramped. If we can find the genes that contribute to building the house we may be able to figure out which types of houses are likely to develop CM1/S.

If any of your family members have had a head or neck MRI, even if it was unrelated to CM1/S, please contact us toll free at (877) 385-2626, or direct at (919) 668-1972, or by e-mail at chiari@chg.duhs.duke.edu. These are critical to our research!

Recent Publications

Chiari Type I Malformation With or Without Syringomyelia: Prevalence and Genetics

Speer MC, Enterline DS, Mehlretter L, Hammock P, Joseph J, Dickerson M, Ellenbogen RG, Milhorat TH, Hauser MA, George TM. Journal of Genetic Counseling 12(4):297, 2003.

We collaborated with clinicians and scientists from Duke University Medical Center, Children's Hospital in Seattle, WA, and The Chiari Institute in Manhasset, New York to report our experience and to review the scientific literature to summarize the current definitions of Chiari Type I with or without Syringomyelia (CM1/S). This scientific report reviewed the prevalence, symptoms, diagnostic methods and current treatment of CM1/S for clinicians in genetics. We hypothesized that in a subset of families, CM1/S may be genetic (inherited) in nature based on several factors including evidence from three areas:

1. Familial Aggregation. Familial aggregation refers to "clustering" of

a trait or medical condition within a family, meaning two or more members have CM1/S.

2. Twin Studies. Twin studies can be a valuable component in determining the genetic contribution of a trait or medical condition. When a condition is genetic, we expect to see the condition more frequently among identical twins than fraternal twins. We reported our experience thus far with 6 sets of twins and 3 additional cases in the literature in which at least one member had CM1/S. This data is consistent with a genetic hypothesis for CM1/S. Additional twin studies are needed to add power to these findings.

3. Cosegregation. Cosegregation is said to occur if two traits or medical conditions occur in the same individual, such as Chiari Type I and Klippel Feil Syndrome. Cosegregation may happen by chance or because the two conditions could be due to the same or similar cause. Of particular interest to geneticists is whether CM1/S cosegregates with other known genetic syndromes.

In many people, CM1/S occurs independently of any other health condition and is said to be isolated. However, in other individuals, another genetic syndrome may also be present. In this published paper, we summarized 21 genetic conditions in which CM1/S has also been reported (most likely accounting for a very small percent of all CM1/S cases). This information may be helpful in targeting regions of the genome for further research.

We hope this paper has served to bring CM1/S to the attention of health care providers and researchers, stressing that importance of determining the potential genetic causes of CM1/S. And, we believe that this paper has helped patients and families educate their health-care providers that CM1/S can be genetic, and therefore, symptomatic relatives should be offered MRIs. This knowledge may shed light on the development of CM1/S, predictive testing, treatment strategies and the risk for recurrence (CM1/S occurring again) within a family.

Please Update Us

Please keep us in mind when important changes happen in your family. We like to ensure that all of our family trees and mailing lists are accurate. We would like to know if you move or if there are any major changes in the health status of family members, such as someone diagnosed with a new medical disorder, if another family member is diagnosed with Chiari Type 1 Malformation and/or Syringomyelia or if there are new members of your family. Please give us your updates by calling us toll-free at (877) 385-2626, or directly at (919) 668-1972, or you may e-mail us at chiari@chg.duhs.duke.edu. Thanks!

Who pays for the research?

Conducting the genetic research studies that create CM1/S breakthroughs is painstaking and expensive work that relies on funding support from both public and private sources. Substantial funding is typically only granted to researchers with strong research plans and programs already in place. With the participation and support of nearly 275 families, you have helped us to develop one of the strongest CM1/S genetic studies in the nation.

Since the genetics of Chiari Type 1 Malformation with or without Syringomyelia study began in 1994, the Duke CHG team has been awarded research funds or grants from Bobby Jones Open Fund, the National Institutes of Health HD33400, NS26630, the American Syringomyelia Alliance Project (ASAP), and from families that are enrolled in the study or whose lives have been touched by Chiari Type 1 Malformation and/or Syringomyelia.

On occasion, we are asked if we can accept donations to support the CM1/S research, sometimes in honor or memory of a loved one with CM1/S. If you or someone you know would like to make a gift, the Center for Human Genetics has created the Duke CHG CM1/S. Research Fund. To make a financial gift to CM1/S research, you may visit the secure web site of the gift records office at <http://www.giftrecords.duke.edu/>, or you can send your tax-deductible donation to:

Center for Human Genetics
Chiari Type 1/Syringomyelia Research Fund
Box 3445
Duke University Medical Center
Durham, NC 27710

Duke Center for Human Genetics

The 120,000 square foot Center for Human Genetics building took \$41 million and 2 years to complete. The building opened in February 2002. It provides CHG researchers with unparalleled laboratory, computing, and office facilities that make our work to identify genes involved in Chiari Type 1 Malformation and/or Syringomyelia and other disorders possible.





Additional Information

Please note that our research is concentrated on studying genetic causes of CM1/S. With research as our primary focus, we are not in a position to communicate medical advice. If you are seeking answers to clinical, surgical or symptom-related questions, or are interested in obtaining information about particular institutions or physicians, please call your physician. In addition, there are many organizations that provide factual information about Chiari Type 1 Malformation and syringomyelia for individuals and families. Here are some you may find useful:

American Syringomyelia Alliance Project

The ASAP national network, founded in 1988, offers support, networking, and information for individuals with syringomyelia

PO Box 1586

Longview, TX 75606-1586

Phone: (800) 272-7282 toll-free; (903) 236-7079

Fax: (903) 757-7456

Web: www.asap.org

Canadian Syringomyelia Network

69 Penny Crescent

Markham, Ontario L3P 5X7

Contact Person: Barbara Forrestall, Chair and Founder

Phone: (905) 471-8278

Fax: (905) 882-8367

E-mail: csn@passport.ca

Web: www.csn.ca

National Organization for Rare Disorders

PO Box 8923

New Fairfield, CT 06812-8923

Phone: (800) 999-6673 toll-free; (203) 746-6518

Web: www.rarediseases.org

National Institute of Neurological Disorders and Stroke

Federal Building, Room 814

7550 Wisconsin Avenue

Bethesda, MD 20892

Phone: (301) 496-5821

Fax: (301) 402-0302

Web: www.ninds.nih.gov

A Warm Thanks to All Families!

We are indebted to all the individuals and family members who have so generously agreed to participate in this ongoing genetic research study for Chiari Type 1 Malformation with or without Syringomyelia. Each individual and, in turn, each family that participates, helps the pieces of this research puzzle fall into place. The research described in this newsletter is only possible because of the many, many individuals and family members who agree to participate. We look forward to continuing to work with all of you over the next few years. Together, we will move closer to our common goal of understanding why and how Chiari Type 1 Malformation and/or Syringomyelia develop.

We also want to thank all of the families who have helped spread the word about our research. We have received many phone calls and e-mail messages from families who learned about the study through other families already enrolled in the study. Please keep telling other families about the study, as we continue to enroll additional interested families.