Interview: Dr. Marcy Speer

Genetic Researcher, looks for a Chiari gene

DNA, genetic testing, stem cells, gene therapy. These words are everywhere in the media today. Genetics is a hot topic with a lot of promise and maybe a little hype. Yet, for those affected by Chiari and syringomyelia, genetics touches on some of the most personal issues there are: Will my children get this condition? Did I already pass it on to them? Is there any way to find out?

If anyone can help us understand the genetic aspects of these conditions, it is Dr. Marcy Speer. Dr. Speer is an Associate Professor in the Section of Medical Genetics at Duke University, a genetic epidemiologist, a board certified Ph.D. medical geneticist, and a board certified genetic counselor. In other words, she knows what she's talking about.

We put Dr. Speer In the Spotlight to see if we could shed some light on the subject:

How and when did you first become interested in genetics?
S: I became interested in genetics in high school when I learned about Mendel's laws and about population genetics. Both the biological and mathematical aspects of genetics were appealing to me.

How did you get interested in studying Chiari/SM?
S: I was approached by ASAP (American Syringomyelia Alliance Project) several years ago. I'm not sure how they found me, maybe my work on Spina Bifida. ASAP was interested in pursuing the genetic contribution to the condition.

Could you describe your current work on Chiari/SM?
S: We're interested in two things. First, identifying if there is a genetic contribution to Chiari, both with and without syringomyelia. Once that is established, we want to identify the genes that predispose people to these conditions in families.

Can you draw any early conclusions from your work yet?
S: Yes, we've done a couple of things. One, we've established that there is a genetic component in at least some cases. In the first part of our research, we collected detailed information on families - medical records, MRI's, etc.- and identified more than 100 families where two or more people are affected. This is consistent with a genetic basis for the condition in some cases. Second, we eliminated a few candidate genes and performed a genomic screen to identify regions of interest.

If you discover a Chiari gene or genes, is developing a test straightforward?
S: Yes, a test for whether someone carries the alteration is straightforward. Interpreting what the genetic alteration means in a given individual is difficult - when will they become symptomatic, how badly, etc.?

Is it important to develop a test?
S: I don't have tunnel vision about the importance of genetics in CM/SM. A lot of families have more pressing issues just in coping with daily life. But, for life planning, having children, knowledge can be important to some people, not all. Also, sometimes identifying the genetic basis of a disorder can provide information about mechanisms and this can give insight into better interventions.

Do you believe that Chiari is a complex disorder (multiple genes, gene-environment interaction)?
S: Complicated question, my guess is that the underlying genetics are "simple" in nature, that within a family with a genetic predisposition, risk is due to the involvement of a single gene. What will be complex about this condition is that there is tremendous variability as to how it manifests itself within families who would carry the same altered gene. When do people become symptomatic? What defines what Chiari is? Who gets a syrinx and is it just chance or under genetic influence? That's probably where either other genetic or environmental influences play into it – the presentation of the condition.

If you discover a Chiari gene or genes, how do you determine what percent of cases it accounts for?
S: By studying large groups of individuals who are carefully phenotyped and then looking at whether they have a particular genetic alteration or not. That part can be straightforward.

Is it expensive or cheap to determine the percent of genetic contribution?
S: Depends on the genetic change, some are easy and straightforward, some are more subtle. So the approach is straightforward, but the expense is variable.

Given the relationship between Chiari Type 2 and Spina Bifida, do you think that Folic Acid might play a role in Chiari malformations?
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Qualifications:
- Genetic Epidemiologist
- Board Certified Ph.D.
- Geneticist
- Board Certified Genetic Counselor

Education:
- Ph.D., Statistical Human Genetics, Duke University, 1993

Research Interests:
- Chiari 1/SM
- Spina Bifida
- Muscular Dystrophy
- Asthma
- Bipolar Disorder

Selected Publications:
- Speer MC, George TM, Enterline DS, Franklin A, Wolpert CM, Milhorat TH. A Genetic "Hypothesis for Chiari Type 1 Malformation with or without Syringomyelia (CM1/S)". Neurosurgery Focus 8(3); March 2000.

Editor's Note: Dr. Speer's work extends beyond the laboratory as she freely donates her time and energy to help patient organizations.

You are also a genetic counselor; what is a genetic counselor?
S: A genetic counselor is typically a master's level person who works with a physician (medical geneticist) in dealing with patients and families either diagnosed with or at-risk for a genetic condition. Genetic counselors provide educational information - what's the disease, what's the recurrence risk - as well as psychosocial assistance, dealing with the stresses associated with the condition under question. I did primarily genetic counseling in prenatal cases, for example advanced maternal age, family history of birth defects, and for muscular dystrophies.

Currently, some states screen all newborns for a number of genetic conditions. If a test were developed for a “Chiari gene”, would you recommend that it be added to the newborn screening?
S: The ideas about newborn screening are evolving so rapidly that I'm not sure. Currently, most newborn screening involves situations where either treatment/intervention is available following diagnosis; or identifying cases early enough can provide important reproductive risk counseling for at-risk couples. I'm not sure that Chiari would fit either of these categories. On the other hand, genetics and genomics is advancing so rapidly that our ideas of what information is “useful” is evolving.

Under what circumstances would you recommend that the siblings, parents, or children of a newly diagnosed patient have an MRI or a genetic test?
S: Right now, I think if there's any question of symptoms of the condition. One of the early issues that ASAP presented to me is that sometimes symptomatic relatives were being denied diagnostic testing because “it wasn’t genetic”, and hopefully some of our work has helped to prevent that knee-jerk response.

There appears to be an enormous gap between developing genetic screening tests and developing effective gene therapies. Has anyone been successful in curing a disease through gene therapy?
S: Yes, there have been some important successes ... There are lots of trials on-going, and a few interventions, we now call it gene transfer, have had really good success.

Is the genetic research community getting frustrated at the complexity of using the information that has been uncovered in the human genome?
S: Yes, everyone’s frustrated . . . the science is moving incredibly rapidly – really at lightning speed for research – but we have limited successes in making it real from the interventional perspective.

Do you believe there is, or has been, too much hype surrounding genetic testing and gene therapies?
S: Depends on one’s perspective. I think that the promise is there, and geneticists know that the real “pay-off” is about 10-15 years away. The risk is having the public think that the pay-offs are sooner than we can really deliver, and then people getting frustrated. From the patient’s perspective, really anyone who’s waiting for results, the progress is interminably slow.

Do you ever get concerned that the increasing pace of scientific discovery is not giving society a chance to work through the ethical issues surrounding new discoveries and technologies?
S: Yes, it’s a big issue. There’s a difficult balancing act between bench science and practical applications.

What should be done about this?
S: The government has done a lot, NIH (National Institute of Health) has a whole group dedicated to these issues. In first world countries, like the US, Canada, Britain, there are very sincere and dedicated efforts to identify, understand, and think through the implications of the work we do.

How do you feel about Pres. Bush’s stem cell decision?
S: Brilliant political move. He walked a very fine line. He kept the door open without completely alienating his conservative base.

Are stem cells overhyped?
S: No, they offer great promise.

As a good scientist you probably don’t like to speculate, but as an expert, please speculate on the following:

Will you develop a Chiari genetic screen?
S: I think that testing for Chiari from the genetic perspective will definitely become available.

Is there any chance for a gene therapy cure for Chiari? If so, how far in the future?
S: Not likely with today’s gene therapy techniques.

Many people are diagnosed just as they are starting families. Should passing on this disease be a consideration for patients thinking about having children? Or for children who grow up with the disease as they become adults?
S: Wow, tough questions! One of the powers of this kind of work is that it offers the option of additional information. One of the things that I’ve learned from genetic counseling is that no one can predict, not even the
individual themselves, how they will utilize information. My own perspective is that I think that the option for utilizing information should be available and access should be by individual choice and not dictated by society.

You’ve been known to choke up when thinking about the children affected by the disease you study – are they your motivation?

S: A big motivation. My motivation is I want to do things that can be translated to real efforts and make a difference; that’s why I focus on genetic abnormalities. The reproductive issues are near and dear to my heart.