Tell me briefly about your daughter; she was initially diagnosed with epilepsy? GLUT 1 isn't a form of epilepsy or related to it, is it?

Macie is a delightful 14 year-old. She is the bravest and strongest person I know. My husband and I often say that she is our hero for many reasons.

Macie seemed to be a perfectly normal infant. She started having seizures at around her first birthday. We weren't sure what they were at the time. Her seizures were very quick little stares and jerks, always worse when she was tired or hungry and the during the first couple of hours of each day. She also had a few typical absence seizures, and she was eventually diagnosed with epilepsy at 22 months of age. By this time, she was having hundreds of these little seizures every day. She would often seem to be in a fog when she was having several seizures in a short period of time - slow speech, uncoordinated, couldn't concentrate or finish sentences. She was late to walk (16 months), but otherwise on target for her milestones. The first drug we tried didn't seem to help her seizures, and made her tired and wobbly. Other drugs were added, and some seemed to give temporary seizure improvement - but never for long. The drugs were not kind to her, and it seemed she was always either trying to wake up or trying to go to sleep - which is not a good place to be stuck for those who have seizures. After failing 5 drugs, we asked to try the ketogenic diet. Her neurologist at the time did not recommend the diet because he felt it was too difficult, so we found a doctor who did offer it (4 and a half hours away from our home). Macie started the diet and became seizure free as soon as she got into ketosis. She took to the diet like a champ. She enjoyed almost two years of complete seizure freedom and came off all of her medications. She truly blossomed, and it was like the fog had lifted. Just as we started talking about weaning the diet, her seizures returned. We tried lots of tinkering, and even changed neurology centers hoping to better fine tune the diet and get her seizures under control again. Unfortunately, we were not successful and after another two years we gave up the diet. She then went on to try and fail several more drugs, and we even revisited some of the ones she had tried before. She progressively worsened and started having multiple seizure types. She became unable to attend school. She was diagnosed at one point with Myoclonic Astatic Epilepsy (Doose Syndrome), then another doctor diagnosed Lennox-Gastaut. We were told that they had done all they could do for her and we needed to try the Vagus Nerve Stimulator, which we did. It was ineffective against her seizures as well and in fact seemed to aggravate them.

During the time we thought Macie had Doose Syndrome, we went to a Pediatric Epilepsy Syndromes conference in California to hear presentations from experts from all over the world. It was a wonderful experience, and the conference raised questions for us as to whether Macie really did have Doose. I was also active on the Yahoo group for Doose for quite some time, and I happened to catch part of a conversation between a mother in New Zealand and a mother in Australia. One of them had a friend whose child had Glut1 Transporter Deficiency Syndrome. One of the things she mentioned

was that this child always had seizures worse when he was hungry, and food often cleared them up. We had been telling doctors this about Macie for a long time. I began trying to find out all I could about Glut1 Deficiency. There isn't a lot of information out there, and a good deal of it is much more technical than I can understand, but the more I read, the more I thought she had it. We began asking her doctor about the possibility of investigating Glut1 Deficiency, but he was sure she didn't have it so he did not want to pursue any testing. I contacted the doctor who identified Glut1 (Dr. DeVivo), and he didn't think she sounded like a classical case either. He wanted her test results to review, but of course we didn't have any because we couldn't convince her doctor to do any testing. Finally, after some reshuffling of doctors at her neurology center, her wonderful nurse practitioner worked with us and got an appointment with a metabolic neurologist. He eventually began the testing process for Glut1 Deficiency, and yet another new doctor assigned to Macie was willing to explore the possibility that she had it. After about 18 months of testing and waiting, we got a confirmation through a DNA analysis that she did indeed have it. We started on a Modified Atkins diet and saw lots of improvements, and then after a while decided to go to a more classical ketogenic diet. She remains on the diet and does well, although she is not seizure free. We were concerned whether the diet would work for her again since it had stopped working before, and we are grateful that it is helping....we just hope it continues. We hope how quickly they discover another way to treat it.

According to experts, Glut1 Deficiency does fall under the epilepsy umbrella, and it is a metabolic disorder that causes other symptoms in other neurological domains as well (behavior, cognition, movement). There is a breakdown in the body's ability to transport glucose (fuel) across the blood-brain barrier, so the brain starves for energy. This energy crisis can lead to seizures, developmental delays, movement disorders, and other issues. The ketogenic diet provides an alternate fuel source as ketones instead of glucose. One of Macie's doctors likened it to getting a gasoline engine to run on diesel fuel.

Most patients with Glut1 Deficiency have seizures. Dr. Klepper from Germany (one of the world's top experts on Glut1 Defciency), says this on the German Glut1 parent group website:

http://www.glut1.de/html-uk/index.htm

The disease

(J. Klepper, Aschaffenburg; updated 01.2007)

GLUT1 deficiency syndrome (GLUT1 DS) was first described in 1991. It is one of the few epilepsies in childhood that can be treated effectively by initiating a special “ketogenic” diet. For this reason this condition should be excluded in any child with intractable epilepsy by means of a fasting lumbar puncture.

So, in a sense, Macie still has intractable epilepsy, it is just that now we know the cause, and she has other issues attributable to the Glut1 Deficiency condition.

What are her symptoms (speech/handwriting difficulty?); what is the treatment is she getting and how successful has it been?

Macie's main symptom has always been and continues to be the seizures, though for some other Glut1 Deficiency children the movement disorders are more pronounced than the seizures. She also does have difficulties with handwriting and other small motor skills, and she walks slightly with her toes pointed in and flexed. She has mild to moderate developmental delays along with academic difficulties. Math is especially difficult for her. She also has some obsessive compulsive tendencies. She is very social and loves to talk, although she has weaknesses in certain language areas (word recall, word associations and categorization, pacing and speed, etc.). She qualifies for OT, PT, and speech services and loves going to therapy. Her therapists have helped her fine tune her skills and build her confidence. She also participates in Special Olympics.

The diet has given Macie a great deal of relief from her seizures. Her mind just seems clearer, and she is more alert, energetic, talkative, and can focus and concentrate more on her school work. She is also better coordinated and her speech flows better. She still has a bad day with seizures occasionally (100 or so), and this seems to affect all of the other areas I've mentioned, sometimes to the point where she cannot walk or function. She continues to be home-schooled, which helps her so much. She is able to wake up in the morning when she is ready, rest and nap when needed, and eat frequently. It also best suits her unique academic needs.

The site says that the keto diet is the best treatment so far, although "individuals treated with the diet still experience neurological, mental, and physical difficulties." What are these difficulties, and is gaining excessive weight one of them? Does your own daughter suffer from any adverse effects from the diet?

The ketogenic diet gives the body an alternate source of fuel, which helps most readily with the seizures. Although most patients improve in other areas as well, the diet doesn't seem to be as effective for the movement disorders and cognitive issues. The severity of symptoms varies widely among GLUT 1 DS patients, and so does improvement with the diet. The diet helps with the symptoms of Glut1 Deficiency, it doesn't fix the problem.

Weight gain could be an issue with the diet, and so could weight loss (it is like Atkins in many ways). The diet is carefully calculated by a dietitian for each individual child, taking into account activity levels, calorie needs, and growth rates. Children are given daily allotments of protein, fat, carbohydrates, and calories, which are divided

into meals. There is just enough protein for growth, and then the fat and carbohydrate amounts are calculated to meet a prescribed diet ratio. For instance, a child may have a 3:1 ratio, which means for every 3 grams of fat in a meal there is only 1 gram of protein and carbohydrates combined. Dietitians and caregivers use some form of a computer-based meal planner or exchange formula to build meals to match all of the requirements. Patients often monitor blood ketones to gauge the effectiveness of the diet.

Weight gain has not been an issue for Macie. However, she does have an elevated cholesterol level. Other side effects of the diet are increased acidity (which can lead to kidney stones) and constipation. She takes a medication to help with the acidity. The diet is deficient in many vitamins/nutrients, so it is necessary to give good nutritional supplements while on it. This is especially true for our Glut1 Deficiency children, who stay on the diet much longer than most children who are using it for seizure control alone. Patients are monitored for liver and kidney function while on the diet, as well as cholesterol and other vitamin/mineral levels. Adjustments can be made as needed. The diet is the best treatment available for now, but we all desire a better alternative – and one that brings a cure.

How are GLUT 1 patients accurately diagnosed?

The first step is a lumbar puncture (spinal tap). A blood sample is taken at the same time, and the levels of glucose in the spinal fluid and the blood are compared. For Glut1 Deficiency patients, the levels of glucose in the blood look normal, but the level in the spinal fluid is greatly reduced - so the level of glucose reaching the brain is reflected in the spinal fluid. Some have gotten a diagnosis of Glut1 Deficiency from the one test. For us, we followed with a few more tests before getting a concrete diagnosis. After the spinal tap, Macie was scheduled for a video EEg. We had her go without eating, and they watched her brain activity. We then fed her a meal of high carbohydrates (grilled cheese, french fries), and then compared the EEg activity before and after the meal. The improvement was dramatic. They then ordered a DNA analysis, which took several months. They checked for the Glut1 mutation as well as a separate gene mutation that causes Dravet Syndrome and GEFS+ (familial epilepsies). While we were waiting for the results of the DNA test, Macie had a PET scan done to see how effective her brain was at taking up glucose. Once the DNA tests were in, they were a bit inconclusive. She did have the gene mutation for GLUT 1 DS (the other gene was normal), but it wasn't exactly like any they had seen before....so, they ordered DNA analysis for her father, her little sister (because she has had a couple of complex febrile seizures), and me. After another few months, it was found that the rest of us did not have the mutation, and Macie's mutation was the cause of her Glut1 Deficiency symptoms.

There is also an erythrocyte assay test that can be given to aid in the diagnosis. Macie did not have this test.

What is your advice for parents of kids with this? What is your advice for patients who may have it but aren't sure (where should they go for diagnosis / treatment)?

For parents of Glut1 Deficiency children, I'd highly recommend getting involved with a research group, either with Dr. Pascual in Dallas, Dr. DeVivo in New York, or Dr. Klepper in Germany. The more we add to the data, the better the chances that we can help our children. Also, the support group online has been a tremendous help. It is great to be able to compare things and ask for help with every day issues in dealing with this condition. I have learned more from other parents than in any doctor's office. I'd also suggest doing regular internet searches for new information and articles about Glut1 Deficiency.

If you suspect that your child may have this, talk to your doctor. You may have to educate your doctor about the condition. I printed off articles I found online and highlighted all the things from the articles that made me think Macie may have it. I gave copies to anyone who would take one who was involved in her care (and mailed copies to those who wouldn't take one!). Be persistent, and ask them to investigate the condition further. If your neurologist is unwilling to consider it, talk to your child's pediatrician about other options and avenues.

For all parents, my advice is to always, always be an advocate for your child. Even if you have a fantastic doctor, that doctor isn't going to have the level of personal interest in your child that you do. They may understand the medical side of things more clearly, but you know your child better than anyone. If you know a treatment isn't working for your child, speak up. Sometimes that means finding an alternative on your own and making suggestions to the doctor. If there are unusual symptoms, keep mentioning them. I have tried to always keep a good relationship with our doctors and work as a team, but at times I know I have come across as "that crazy, aggravating mother".....that's OK! Looking back, there are times that I wish I had been more outspoken about her. My husband and I are often the only voice that Macie has, and we want to make sure we are doing all we can for her. It is an awesome responsibility, really.....but it is one that all parents of special needs children share.

What do you want neurologists (who don't treat this) to know about it?

I think that Dr. Klepper's comments sum it up:

The disease

(J. Klepper, Aschaffenburg; updated 01.2007)

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I want them to keep Glut1 Deficiency in the back of their minds and consider the possibility in any child with treatment resistant epilepsy or other unexplained movement disorders and developmental delays. Also, if parents mention any connection with food to alertness, muscle tone, and/or seizure activity, consider that it might be Glut1 Deficiency. I know that Macie's current neurologist has discovered a second case of Glut1 Deficiency in one of his patients just because the mother mentioned that her child improved with meals.

Any other comments as you see fit (for our patient audience).

There is much to be learned about this condition. We are so very grateful for those few experts who are devoting themselves to finding answers and to helping our children. Hopefully, one day we will look back and know that we have helped them lay the groundwork for a cure, and that we have managed to help other families along the way.