SEEKING THE BEST

In 2003 Soraya and her sister Sylvana started communicating on-line with an MSUD Support-Group. Every two years, this group would host a symposium to discuss the disease and to exchange information with interested parties. Meanwhile, the Fernandes family was organizing their own symposium in their city, Natal. Even though it was small, this symposium was of vital importance because they had invited one of the world's most respected MSUD physicians, Dr. Kevin Strauss, an American who would give a presentation about MSUD and also examine some Brazilian children who had the disease. Artur's condition was so weak and his immune system so compromised that the trip to the symposium could be very risky, so we decided not to take him with us. We knew that a metabolic crisis could be fatal. Even though Artur would be staying in Fortaleza with Andrea, we wanted to be prepared for a meaningful meeting with Dr. Straus. So, Soraya compiled a file with all the lab reports, photos, diet, etc. The agenda had Dr. Strauss explaining the disease on the first day and examining the children on the second. The Fernandes handled the event professionally and arranged for a translator, Dr. Celma, to help us understand his lecture.

I'll never forget Dr. Straus' first lecture during which he emphasized the importance of knowing the consequences of MSUD when patients are not being treated properly. When MSUD is not properly treated, internal damage to cells systems will result in the destruction of the cells. To make us understand this type of crisis, he drew an analogy comparing a human cell to a corral and the essential amino acids to the bulls that would live in the corral. To be in balance, each corral (cell) has the capacity for eight types of animals (amino acids). In other words, he meant that a cell requires eight amino acids (he called them the 'bulls'), each with different weights, to achieve the perfect cell balance. Hence, a perfect body with normal metabolism naturally maintains a normal balance of amino acids. Without this balance, the cell would be destroyed.

To help us visualize, Dr. Stauss drew an empty corral surrounded by the bulls, naming them for each of the amino acids essential to a human body: **Isoleucine**, **Leucine**, Lysine, Methionine, Phenylalanine, Threonine, Tryptophan and **Valine**. He then continued. "I want all of you to consider that each bull has its' own transporter, like a car, to get it into the corral."

Pointing to his drawing on the screen, he continued. "This bull, called **Leucine**, is the strongest one and it has a very powerful transporter, like a brand new Ferrari. All the others have transporters like 1967 VW Beetles. And don't forget that the corral has a defect; it cannot get rid of the excess of three specific bulls, the **Leucine,** the **Isoleucine** and the **Valine**."

To finalize his comparison, he showed us the exact moment when a cell becomes toxic. "It is logical that the Ferraris, with the Leucine bulls, will arrive at the corral first followed by the others. In normal cells, these amino acids are naturally metabolized and any excess is excreted through feces, urine and sweat, thereby keeping the cell in balance. But in the case of cell with MSUD, the other bulls that enter the corral will be expelled because this corral has a defect and cannot get rid of the three bulls cited previously. So what will occur in a short period of time is that all of the Leucine will enter the corral followed by Isoleucine and Valine as space permits. Some of other bulls may be present in this corral, but as I said, **Leucine** is the fastest and the strongest and it will soon block the entrance for the others. The corral cannot support the pressure and bursts. This is just what happens in the abnormal cells of an MSUD patient. The excess of these amino acids cannot be metabolized because of a defective enzyme and the affected cells are destroyed, causing a severe metabolic crisis for the patient. And to make it

worse, this destruction occurs first and very aggressively in brain cells, which often can cause the death of an MSUD patient. Just a single infection, like a cold, can cause the cell's destruction, known as a catabolism, causing brain damage, and often death.

Keeping an MSUD patient's amino acids balanced, especially the Leucine, is a very difficult task. Close monitoring of the amino acid levels via blood tests is the only way to do it. When blood tests indicate that acid levels are not properly balanced, immediate action can be taken to prevent or mitigate a metabolic crisis. A special solution, called TPN, and some other drugs must be administered until the levels come back into balance…"

Even though we had done our own extensive research on MSUD, everything that Dr. Strauss had told us was completely new to me. I think I was stunned by his explanations and I found myself even more desperate to get answers to the many questions we had about Artur's condition. This symposium had become like a revelation for me; my eyes were finally opened. Dr. Strauss was the only doctor who provided a clear explanation about this terrible disease and that it could easily result in Artur becoming an invalid and even dying. But could this doctor control the amounts of these amino acids (bulls) in each cell (corral)? Later, I would find that these equations could not easily be balanced.

During the course of the symposium, we found that we were smart for not having brought Artur with us. Dr. Strauss explained that stress can initiate a metabolic crisis and, since we did not know how Artur would react to the trip to Natal and another examination, his amino acids levels would have had to be monitored constantly. And no equipment for such monitoring was available at the symposium. Plus, according to Dr. Strauss, metabolism in humans is a steady, rapid process with amino acid levels changing every second.

Dr. Strauss' presentation left us feeling like our treatment plan for Artur was severely lacking. In Brazil, we knew just two laboratories that could run the amino acids test, known as chromatography. One machine was in Porto Alegre and the other one in São Paulo. To make it worse, the laboratories had no interest in running these specific tests because the demand for them was very small. Also, to run the amino acid test, this multi-purpose equipment had to be reconfigured, a time-consuming process which delayed the results from 4 to 7 days. MSUD patients could not be treated effectively on such a lab schedule. A patient could be dead in that amount of time! At Dr. Strauss' clinic, these lab tests would be available in about one hour, so any imbalance would be known and the patient could be treated right away.

Because of the small number of MSUD patients, the Brazilian labs claimed that performing these amino acid tests was not financially viable for them. After collecting the blood and sending it to the lab, we literally had to beg the staff in Porto Alegre to run the tests. Even then, the results took days to be reported.

During one of the symposium breaks, we had the opportunity to have a little chat with Dr. Strauss. When we told him how Brazil was treating its MSUD kids, he was surprised. "It is impossible to effectively treat your patients on this basis. As I said, metabolism is a very fast process and cells react quickly and with great intensity. A fast turnaround by the lab is the only way we can know how to balance the cells, thereby avoiding a severe toxic situation and hospitalization."…