

## CHAT WITH DR. SWOBODA 28<sup>TH</sup> JULY 2004

### QUESTIONS AND ANSWERS

<b>Question</b>	Which kind of food (natural food or formulas) do you usually suggest for a 3 years SMA 1 child with a PEG button? From 1 year of age till now (35 months old) my SMA1 daughter has been fed with NUTRINI by Nutricia (1 ml – 1kcal). Which way do you suggest to introduce natural food for passing to a mixed or natural feeding? What kind of food and which way (boluses, continuous)?
<b>Dr. Swoboda</b>	Regarding diet questions, I encourage you to download the recent presentation I gave at the FSMA meeting. I think natural foods are best if the child can swallow. However, many type 1 and some type 2 child need supplemental formulas. Which formulas are the best, whether it is an elemental or whole formula is not yet clear.
<b>Question</b>	I have already your Power Point file. Which way do you suggest to introduce natural food for passing to a mixed or natural feeding? What kind of food and which way (boluses, continuous)?
<b>Dr. Swoboda</b>	It really depends on the child. Do you have a child with SMA 1 or 2, and does he or she have a g-tube and Nissan, or just a g-tube, and remind me what you are feeding now, and how.
<b>Question</b>	SMA1 with a low profile gastrostomy button fed in continuous with Nutrini (1 ml – 1kcal)
<b>Dr. Swoboda</b>	In a child with SMA 1, who has a gastrostomy button without a Nissan, I'd be very cautious and introduce one new whole blended food at a time and watch very carefully, since you might see worsening of reflux. I wouldn't introduce more than one new food: say baby vegetables or fruits to start, no more quickly than every 2 weeks. If you have been giving it continuously, I'd blend it together with the formula and continue that strategy. Don't forget to include some meat or other food that contains carnitine.
<b>Question</b>	Hi Dr. Swoboda- Do you know of how much of a calorie restriction one needs to maintain weight. I know that I do not need as many calories as a person without sma. I am 27 walk pretty well and I weight 135. I would like to lose 10 lbs, but I really do not know how many calories I should take in. Thanks
<b>Dr. Swoboda</b>	The exact calorie needs for a particular SMA individual depends on their lean body mass and degree of physical activity. Certainly, if you are in a chair all day, you will need less calories than a type 3 subject who is up walking. In general, I start with recommending about 70% of the caloric intake recommended based on your weight and height..then we go from there.
<b>Question</b>	Hi Dr. Swoboda - My question is about g-tubes. My son is 11 months old with Type I. He still eats and swallows well and hasn't had any respiratory problems to date. I've heard many people say to get the g-tube before you need it. What are your thoughts? Thanks
<b>Dr. Swoboda</b>	I have changed my strategy over the years on this point. I am a proponent of getting a g-tube early in an SMA 1 child, as I've seen several children deteriorate in the setting of losing their swallow over a short period of time, sometimes a day or two. Sometimes it is an infection that causes this worsening, and the big problem is maintaining nutrition adequately during this period.
<b>Question</b>	In reference to the g-tube adn ksykoras question do you feel the same way about an 11 month old type II
<b>Dr. Swoboda</b>	In type 2 children the choice is not so clearcut, since many of these children with type 2 will be able to maintain the integrity of swallow and protecting their airway.

	However, I try to choose what is best for each particular child. If you don't get a g-tube, then you must have a very low threshold for taking your child in to the ER when she/he stops eating due to illness. I begin IV fluids and amino acid (TPN) supplementation on these kids no more than 12 hours after they stop eating, sometimes sooner.
<b>Question</b>	How can I tell if my type II/III child is aspirating with her newly placed g-tube w/out Nissen?
<b>Dr. Swoboda</b>	Regarding assessing swallow, you should watch your child carefully for any signs of coughing or choking with eating, or coughing in the 30 minutes following eating. This can indicate either reflux or aspiration or both. Sometimes aspiration is "silent" meaning that small amounts of material are being aspirated when swallowing. This can cause chronic changes in the lungs over time if not detected. I recommend a formal swallow study in any child or adult in whom this may be a concern.
<b>Question</b>	How do you recommend is the best way to test for aspiration? I was told to have my daughter do a Bronchoscopy and a BrovoPHcapsul study? How do you feel about that?
<b>Dr. Swoboda</b>	Two tests are commonly used to detect aspiration. Aspiration from above can be detected using a barium swallow or video fluoroscopy. Aspiration from reflex from below is best detected with a 24 hour pH probe study. A bronchoscopy shouldn't be necessary, but can help to visualize chronic lung changes caused by aspiration.
<b>Question</b>	Doctor,what do you think about homeophatics preparation.I think it works.We use them for a year.My son is 2.5,and at the moment he is doing well.
<b>Dr. Swoboda</b>	I apologize, I don't really know what homeophatics is.
<b>Question</b>	What do you think of anticatarrhal vaccine for SMA1?
<b>Dr. Swoboda</b>	By anticatarrhal vaccine are you referring to the RSV vaccine. I recommend all my type 1 patients to be on it every winter, and in my weaker type 2 kids, at least through age 2 yrs.
<b>Question</b>	What is RSV? Immunoglobuline?
<b>Dr. Swoboda</b>	Regarding the RSV shot, it is an immunoglobulin shot that must be received once per month during the typical months of Oct or so to April
<b>Question</b>	I have heard about abnormalities in fatty acid synthesis for SMA 1. What does it mean? How can we adequate the diet?
<b>Dr. Swoboda</b>	Regarding abnormalities in fatty acid oxidation....there have been observations the urine metabolite studies performed in children with SMA show abnormal patterns, often with a dicarboxylic aciduria....these are fatty acids that are excreted in the urine and can imply a problem with fatty acid metabolism. We don't know the exact perfect diet recipe for a child with SMA, but making sure it isn't too high in fat would seem important in light of these abnormalities. However, children need some fat to make myelin and other critical things...so excessively restricting fat isn't good either. I'd aim for no more than 30% calories from fat, and limit transfatty acids and saturated fatty acids in processed foods like cookies, crackers, etc.
<b>Question</b>	Sometimes, after having slept all the night with the Bi-PAP, my SMA 1 daughter is slightly sweaty and she and her clothes smell of ammonia. Is there any reason for this particular smell?
<b>Dr. Swoboda</b>	SMA individuals do seem to sweat excessively on the head, back and palms and soles, especially when they sleep. I don't really know why her clothes smell of ammonia, but it could be the excessive sweating, and excretion of dicarboxylic acids...they do have a certain odor, and these kids probably excrete them in sweat to a small degree as well as urine.
<b>Question</b>	Whether there are recommendations for carrying out of therapy with dolphins and whether there were such experiments for patients SMA?

<b>Dr. Swoboda</b>	Regarding therapy with dolphins I don't have experience with that, but I'm a big fan of any water therapy, and animal therapy also has tremendous potential...especially with kids.
<b>Question</b>	Have you noticed/studied the fine hand tremors in SMA patients? Can that be controlled to some extent?
<b>Dr. Swoboda</b>	For the most part, I haven't had people complain about their tremors. Nearly every SMA child/adult has them to varying degrees, but no one has ever asked me to try and treat them. It would be very difficult, because the tremor in SMA is basically a physiologic normal tremor that everyone has...it is amplified when nervous or upset, and is more prominent especially in type 2 and 3 subjects because the individual motor units are bigger than normal due to reinnervation. I know that is technical and I apologize.
<b>Question</b>	Greetings from Wisconsin, USA. I have Type II and am age 60. I met you, Dr. Swoboda, briefly at the SMA conference. My question is: I recently had a blood test indicating an elevated ANA (anti-nuclear antibody) 3 x that of normal..the compliment levels were normal. My physician and I are puzzled as I have no other obvious symptoms of auto-disease, though I have many, many allergies. Is this elevated ANA commonly seen in SMA or is this totally unrelated to the disease? Thanks much. Correction to my question: I meant to say "auto immune disease".
<b>Dr. Swoboda</b>	That is not a particularly high ANA, and it can sometimes be nonspecifically elevated. This is not common in SMA to my knowledge, but then again it hasn't been investigated. There is some data regarding increased inflammatory response in spinal cord of SMA mice - don't know what that means as yet for patients.
<b>Question</b>	Thank you for joining us today Dr. Swoboda. Our 21 month old daughter has type 2, and I was wondering what specialists our daughter needs to see, and how often. She currently sees a neurologist, a pulmonologist, and a physiatrist. They all would like to see her every three months. I really do not like the idea of taking her out during flu season.
<b>Dr. Swoboda</b>	Regarding the 21 month old with type 2, there is no firm recipe. She should probably be seen at least every 6 months by your coordinating primary care physician. Depending on how healthy she is, she may need to be monitored more or less closely for nutrition, feeding issues, onset of scoliosis, recommendations regarding therapy and assistive devices. I recommend all type 2 children receive a stroller or standing Danny as weight bearing is important for hip development, prevention of scoliosis.
<b>Question</b>	I have noticed that in individuals with SMA 3 and similar levels of muscle weakness, some have significant respiratory involvement requiring BiPap use, while others seem to be free of respiratory symptoms. Does SMA 3 affect different individuals at different spinal levels?
<b>Dr. Swoboda</b>	Absolutely, type 3 is not type 3...everybody is unique. Some individuals may be more vulnerable than others; some may have had chronic injury to the lungs from prior infections, and some may have weaker muscles in the chest wall "the intercostal muscles" than others with type 3. Some type 3 patients lose ambulation at less than 10 yrs, some after several decades, and some are still walking well after 50!
<b>Question</b>	Father of 21 month old type 2 daughter Hello Dr. Swoboda, what are the indications for prescribing BiPap? She uses In/Exsufflator nightly or more often and we perform cpt regularly, as needed. No apparent breathing abnormalities and pulmonologist has no concerns.
<b>Dr. Swoboda</b>	Indications for prescribing BiPAP typically are based on a formal sleep study to look for evidence that your daughter is either desaturating her oxygen level at night or retaining too much carbon dioxide. However, sometimes the decision is made on

	clinical observations. Almost any child with any dependence on abdominal breathing can benefit from BiPAP.
<b>Question</b>	I was also told to place my SMA daughter on Fosamax to increase bone density...it is not FDA approved for children. Lindsey recently had a very bad femur break. Do you currently have SMA children taking Fosamax?
<b>Dr. Swoboda</b>	No formal studies have been performed using fosfamax or similar agents in children with SMA, but some of us are beginning to use this in the clinical setting, particularly for children who have fractures, or in whom we anticipate doing spinal surgery on in the next year or two. Regarding the fosfamax again...we don't know, and I guage this case by case. I am regularly performing DEXA scans on my SMA paitents to try to get a better handle on this issue.
<b>Question</b>	My daughter age 19, type II. Clinical trials with valproic acid will soon start here where we live in Barcelona, Spain and her name is down as interested in participating with controls every 3 months. What prospects does this have and what about the side effects ?
<b>Dr. Swoboda</b>	Regarding the valproic acid, we are currently pursuing safety trials. So far, we have about 40 individuals with SMA, most of them relatively young children with types 2 and 3, and it has been tolerated very well. There are so possible concerns, though, about toxicity. We have found that carnitine levels can be depleted very quickly on the valproic acid, and need to be monitored very closely. Carnitine deficiency could lead to severe liver failure or just worsening of muscle weakness, which is exactly what we don't want.
<b>Question</b>	does that mean no new studies opening soon to start kids on the valproic acid?
<b>Dr. Swoboda</b>	No, we are intending to begin additional studies with valproic acid in the near future with the Project Cure Consortium.
<b>Question</b>	Hi Dr. Swoboda. In works on therapy by new drugs it is mentioned only SMN2. Whether influences valproic acid and phenylbutyrate on copies SMN 3, 4? What sort the progression is reached at application valproic acid and phenylbutyrate and as far as long she is kept at patients? Thanks
<b>Dr. Swoboda</b>	We each have two types of SMN genes, SMN 1 and SMN 2. The number of SMN 2 copies does seem to play a role in modifying the severity of the disease, although the correlation is not 100%. For instance, most type 1 babies have only 2 SMN 2 copies, while most SMA 2 and 3 subjects have 3 or more copies.
<b>Question</b>	Dr Kathy i have type 2 and i would like to know if anything will be able to help in my life time
<b>Dr. Swoboda</b>	Yes, I do think you as a type 2 individual will have medications that will help you in your lifetime..I am very optimistic about this in light of the exciting work going on both in current trials and in the research laboratories around the world.
<b>Question</b>	Hi Doctor, I know that a lot of work that you do are with children. Do you anticipate that any of the clinical trials will be available for adults? Do you think the current studies will be applicable to adults with type 3 sma?
<b>Dr. Swoboda</b>	Yes, I absolutely do anticipate that some of the trials will be dedicated to adults with SMA. We will be working on that with Project Cure. Dr. Kissel at Ohio State University, who is part of the Project Cure Group, has been involved in studies on adults with SMA in the past, and he will certainly do so at some point.
<b>Question</b>	Is ther anything going to be available in Ontario Canada
<b>Dr. Swoboda</b>	We do have a Project Cure Site in Montreal that is targeting type 2 kids at the present time. I don't know yet about Ontario.
<b>Question</b>	Is the hypothesis for the medications to increase lifetime, strength, functional ability, or anything I failed to mention?

<b>Dr. Swoboda</b>	Depending on the medication, that will vary. We hope for medications that increase SMN2 gene expression that we will see benefits in all these areas...we just don't know as yet if the current medications are strong enough to make a significant impact, or any impact at all...or if we need to look at other medications.
<b>Question</b>	Dr Swoboda, what do you think of application of valproic acid on patients carrying SMN1 point mutations. I mean: do you think this mutant SMN1 protein will be induced as well, just as SMN2?
<b>Dr. Swoboda</b>	I would think that patients with one point mutation and one gene deletion would have a similar response to these medications.
<b>Question</b>	Whether the virus reason of damage of a gene was investigated? For example, at carrying out of a preventive inoculation against a poliomyelitis in 0,5 years. Whether such inoculation suppression protein and could lead to initialisation SMA?
<b>Dr. Swoboda</b>	We know that children with SMA are very vulnerable to deterioration when they get a viral infection of any sort. To my knowledge, no one has described clear deterioration in a child with SMA due to gene deletion in response to the polio vaccination. The live polio vaccine has occasionally resulted in a child with an active polio infection, which can certainly cause anterior horn cell disease and mimic SMA.
<b>Question</b>	Do you think that it is possible for a sma type 3 patient still walking climbing steps with handrail is possible to build strength through exercise? How to strengthen patients with Type III. What nutrients, vitamins etc., exercises, electro-stimulation might be helpful?
<b>Dr. Swoboda</b>	We don't know the answers to all these questions as yet. I would check the carnitine levels, and make sure those are okay. It is reasonable to take a multivitamin with folate, and regular exercise does seem to help maintain energy levels, joint mobility and general well-being.
<b>Question</b>	I have only one question. Every time I see a specialist, or any medical professional for my son, they say that We are very close to a cure and we will find a cure in five years. Is it true? Or are they just giving false hope?
<b>Dr. Swoboda</b>	Regarding a cure in 5 yrs, of course no one can say that. Cure is a hard step to accomplish; however, I am very confident we will have medications that will lead to some benefit during that time period.
<b>Question</b>	Considering current research and clinical trials, should an adult with clinical SMA 3, but a negative genetic test, expect any benefit from these outcomes? Many trials require a positive genetic test result to be included.
<b>Dr. Swoboda</b>	Type 3 individuals who have one deletion of one copy of SMN 1 and a point mutation in the other copy should have the same benefit. However, SMA can be caused by other genes, so it depends.
<b>Question</b>	Whether is time to enter new international classification SMA except for as by age criterion, and in maximum function achieved (MFA), i.e. to enter types SMA III a. SMA III b (work by B.S. Russman, MD and others)? It will give additional hope and confidence for parents.
<b>Dr. Swoboda</b>	Regarding the classification types of SMA, I agree that that would be helpful. The problem is that children can cross sometimes from one type to another. It may give additional hope to some parents, and less to others. View your child/family member as an individual first, and don't try to squeeze them into too tight a label or compare them too closely to other children with the "same type". All SMA individuals are different, although there are certainly commonalities we can use to guide ourselves in monitoring.
<b>Question</b>	Hello Dr. Swoboda. I have read several places that the motor neurons die, other places that they become dormant or that the axons are dysfunctional because they haven't matured. What is your opinion on this, and how does it relate to treatment in terms of

	reactivating the neurons?
<b>Dr. Swoboda</b>	I think again it depends on the type and severity of SMA. In children with SMA 1 who die very early, we know that there is significant cell death that has occurred in the spinal cord. However, there does seem to be a discrepancy between how much cell death and how severe the weakness is, leading some to hypothesize that a percentage of these cells may be "rescuable"...that is, able to respond once a medication increases SMN gene expression. In type 2 and 3 subjects, this discrepancy is likely to be greater, with an even bigger population of "rescuable" nerve cells that may have had axons (nerve fibers) that have died back, but could potentially send axons back out again.
<b>Question</b>	To a terminology question. Centromeric and telomeric copies (cSMN and tSMN) of SMN1 and SMN2, or cSMN and tSMN are both SMN1 or exists the another copies named SMN2, 3, 4? If diagnosed homozygous deletion 7, 8 exons, what copy of a gene participates in make protein and whether there will be an effect of therapy at such diagnosis?
<b>Dr. Swoboda</b>	tSMN is SMN1 and cSMN is SMN2; there is no SMN 3 or 4, but a child can have 3 or 4 or even 5 SMN2 copies. Both SMN 1 and SMN 2 make some full length SMN protein, but in the case of SMN 2 gene, only about 10% of the SMN protein is full length, vs nearly 100% for SMN1.
<b>Question</b>	Healthy carriers have only one SMN1 copy resulting in presumably 50% wt SMN level. Is this gene upregulated in any way since you mention a case of 5 SMN2 copies resulting in app. 50% wt SMN level in SMA3 patients? If so, do we have any idea of how the cell upregulates the SMN1 gene to possible use the same mechanism to upregulate the transcription of SMN2?
<b>Dr. Swoboda</b>	I have seen some individuals with 5 SMN 2 copies who are either type 3 or unaffected...so again, there is a modification, but not predictable by any specific formula. We don't really know all the details yet that go into regulating SMN 1 and 2 expression, but many researchers are working hard on these issues. Obviously, having one SMN 1 copy is enough to prevent progression to SMA in carriers.
<b>Question</b>	Whether is necessary to carry out research for an establishment deletion a gene NAIP, presence of number copies SMN2 for the further therapy, or deletion 7, 8 exons of SMN is universal criterion?
<b>Dr. Swoboda</b>	We really don't know how much impact deletion of NAIP contributes to SMA severity, if at all. We are currently exploring that issue further in our Project Cure Studies in collaboration with Dr. Alex McKenzie
<b>Question</b>	I know that stress levels can interfere with the type of alternative splicing seen in the SMN2 gene. Do you think people with SMA should be more aware of stress levels or is this of minor importance?
<b>Dr. Swoboda</b>	I am not aware of the evidence that stress levels changes splicing in the SMN2 gene. Not sure.
<b>Question</b>	Whether is research on revealing healthy people was carried out with deletion 7, 8 exons of SMN?
<b>Dr. Swoboda</b>	We are trying to identify any family members who may carry a homozygous deletion of SMN 1, but don't have symptoms. They may be expressing other genes which are working to minimize the effects of SMN deficiency, and they are extremely important individuals to identify to try to find out what those genes are.