

Consent form for
“DMSA Treatment of Children with Autism and Heavy Metal Toxicity”

Research Team:

This study is being conducted by:

Matthew Baral, N.D., Assistant Professor Pediatrics, SCNM

James. B. Adams, Ph.D., adjunct Professor, SCNM

Walter Cinnion, N.M.D., Professor, Director of Environmental Center of Excellence, SCNM

Sanford Newmark, M.D., Director, Center for Pediatric Integrative Medicine

Purpose/Possible Benefits: The purpose of this study is to investigate the effect of DMSA and glutathione therapy on children with autism spectrum disorders. There is evidence that some children with autism have low levels of glutathione (which is a substance in the body that helps excrete toxins like mercury) and high body burden of mercury, a known toxin. It is hoped that raising the level of glutathione and reducing the amount of mercury will reduce some of the symptoms of autism in some children.

Protocol:

Phase One will involve:

- 1) Filling out the enclosed consent form
- 2) Filling out questionnaires on medical history and severity of autism (approximately 20 minutes)
- 3) Physical Examination by Dr. Matthew Baral at the Southwest Naturopathic Medical Center (Scottsdale) or by Dr. Sanford Newmark at the Center for Pediatric Integrative Medicine (Tucson).
- 4) Blood draw at Sonora Quest to determine kidney/liver function, serum transaminases, Complete Blood Count (CBC), level of glutathione, and antibodies to metals, fibrillar, chromatin, and immune complexes.
- 5) Taking the DMSA 3x/day for 3 days, and collecting urine samples before, during, and after. The urine samples will be tested for their content of toxic and essential metals. The dosage will be 10 mg/kg bodyweight, 3 doses/day.
- 6) Applying a transdermal cream to the skin for the 3 days while taking DMSA. Half of these creams will contain glutathione, and half will not contain it.

Phase Two: If a child excretes a high level of toxic metals in their urine, then they will have the option of continuing to Phase Two, which will involve:

- 1) Six more rounds of DMSA or placebo. Each round will include three days of DMSA or placebo, with 11 days of no supplementation between each round. The dosage of DMSA is 10 mg/kg bodyweight, 3x/day.

- 2) Since DMSA is excreted primarily in the urine, participants should drink a normal amount of liquids and stay well-hydrated.
- 3) A skin cream will also be applied each day during the study. Those people receiving the DMSA will also have glutathione in their cream, whereas those people receiving the placebo will not have glutathione in their cream.
- 4) There will be a blood draw to retest kidney/liver function, serum transaminases, and Complete Blood Count (CBC) at the beginning of the study, after the third round and after the sixth round in Phase Two. If those levels are abnormal, treatment will be delayed or halted.
- 5) Filling out questionnaires about the severity of autism at the beginning and end of the study, which will take about 30 minutes each time. The Autism Severity Scale (one question) will also be filled out every two weeks. The child's speech pathologist (or equivalent) will be asked to fill out the Autism Severity Scale (one question) and the ATEC form at the beginning and end of the study, which will take approximately 10 minutes.
- 6) A 1-hour psychological evaluation using the Autism Diagnostic Observation Schedule (ADOS) at the beginning and end of the study. All sessions will be videotaped so that they can be evaluated by an unbiased researcher. Also, if the parents give permission, some of the videotapes will be used for conference presentations, but that is optional for the parents.

Potential Risks:

Safety Note re. Blood Draw: There is a small risk of bruising during a blood draw. We will minimize this risk by using pediatric phlebotomists (experts who regularly do blood draws on children).

Safety Note re. Glutathione Lotion: There is a small chance (about 2%) of a topical rash developing. If this occurs, the lotion can be applied to another part of the body, or it can be discontinued if necessary.

Safety note re. DMSA: DMSA (Succimer) is a medication approved by the FDA for children as young as 1 year of age for treating lead poisoning. It is generally considered to be one of the safest medications for removal of lead and other toxic metals. **It has not been approved by the FDA for treatment of mercury toxicity or autism, so this will be an "off-label" investigational use of DMSA for those purposes.**

The Physicians Desk Reference reports the following side-effects when using DMSA for 19 days continuously: gastrointestinal upset in about 12% of patients, body aches (5%), increases in serum transaminases (4%), sore throat/cough (4%), rashes (3%), drowsiness (1%), eye/ear irritation (1%). Prolonged use can cause elevations in liver enzymes and bone marrow suppression in less than 1% of cases (which are also symptoms of lead toxicity, and all the people taking DMSA in that study had lead toxicity), which is treatable by stopping use of it. The 2004 edition also reports "No case of overdose (of DMSA) has been reported in humans;" i.e., treatment with DMSA has never been reported to result in death.

We hope to decrease the risk of adverse events by dosing for only 3 days each cycle, with 11 days between cycles. That is the treatment recommended in the DAN! Consensus report, based on extensive clinical experience. In our previous study of 221 children with autism and 18 typical children taking DMSA for 3 days, there were no reports of adverse effects. Also, by monitoring the liver/kidney function, serum transaminases and CBC (Complete Blood Count), any problems should be caught early. DMSA approximately doubles the excretion of zinc, which is why all participants will be taking at least the RDA (Recommended Daily Allowance) of zinc. Finally, there have been some anecdotal reports that DMSA may cause bacterial/yeast infections in roughly 10-20% of patients, so we will ask patients about changes in gastrointestinal function.

Alternative approaches:

Other chelators could be considered, but DMSA appears to be the one with the lowest risk of adverse effects, and one of the highest efficacies. EDTA has a similar safety record, but has little effect on mercury excretion. DMPS also has a low risk of adverse effects, and is slightly better at enhancing mercury excretion, but it is not FDA-approved. D-penicillamine is associated with a higher risk of adverse effects, and there is not much experience with it for children with autism.

Medical Care:

If adverse effects occur, participants are eligible for a free phone consultation or free office visit with Dr. Baral or Dr. Newmark. If necessary, additional phone consultations and office visits will be provided at no charge during the study. If necessary during the study, Dr. Baral or Dr. Newmark will also provide testing and treatment for gastrointestinal yeast/bacterial overgrowth. No other medical care will be provided.

Costs:

Participants will not have to pay any costs to participate in this study. They will be expected to cover their own travel costs to/from appointments.

Financial Incentives:

There will not be any financial incentives for participation in this study.

ABC Primetime Coverage: ABC Primetime has requested interviewing of families involved in this study. That is purely optional for the families.

Voluntary Participation:

Participation in this study is purely voluntary. If you choose not to participate or to withdraw from the study at any time, there will be no penalty.

Confidentiality:

The results of the research study may be published, but your name will not be used, and we will maintain confidentiality of your test results.

Questions:

Participants have the right to ask questions about the study before consenting, and to continue asking questions during the study.

Participant Access to Study Data

Participants will be given a copy of their personal test results at the end of the study, and a summary of the results of the study when available. When a final paper of the study results is completed, a copy will be sent to participants.

Access to Study Data

Only Prof. Adams, Prof. Baral, Prof. Crinnion, and their research assistants will have access to the participant’s study data. The data will be retained for at least seven years. It will be used to prepare scientific articles on the research, and for conference presentations. It raw data will not be shared with any outside group, except in the form of a publication or presentation, from which all subject identifiers are removed.

I agree to have my child _____ participate in the research study described above.

_____ date

Parent/Guardian

Note: A copy will be given to participant and their parent/guardian

James B. Adams

Matthew Baral or Sanford Newmark

Child Assent Form for
“DMSA Treatment of Children with Autism and Heavy Metal Toxicity”

I, _____, agree to take the DMSA, provide urine samples, and allow four blood draws.

Participant (if possible)

date

Note: A copy will be given to participant and their parent/guardian

James B. Adams

Matthew Baral or Sanford Newmark

Participant Information Sheet

“DMSA Treatment of Children with Autism and Heavy Metal Toxicity”

Parent/Guardian's name _____

Child's name _____

Child's birthdate _____ Gender: _____

Child's Ethnicity: Asian/Pacific Islander American Indian/Alaskan Native

Black (not Hispanic) Hispanic Multi-Racial White (not Hispanic) Other

Child's primary diagnosis (autism, Asperger's, PDD/NOS) _____

Person who made diagnosis and their profession: _____

Other co-existing conditions: _____

Mailing Address: _____

City: _____ State _____ Zip _____

Phone: _____ Email: _____

Other mental/physical health conditions:

Current Medications:

Current Vitamin/Mineral Supplement:

1. name
2. amount of zinc
3. length of time taking it

During the last two months, has there been any change in your child's medications, supplements, diets, behavioral therapy, or any other therapy? If so, please explain.

Does your child have any gastrointestinal problems, such as chronic diarrhea or chronic constipation? _____ If yes, is it mild, moderate, or severe? _____