

## Treatment Intervention Advisory Committee Review and Determination

**Date:** October 31, 2014

**To:** DHS/DLTC

**From:** Wisconsin Department of Health Services Autism and other Developmental Disabilities  
Treatment Intervention Advisory Committee: Lana Collet-Klingenberg, Ph.D. (chairperson) *LC*

**RE:** Determination of Chelation Therapy as a proven and effective treatment for individuals with autism spectrum disorder and/or other developmental disabilities

This is an initial review

This is a re-review. The initial review was Date of initial review

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### Section One: Overview and Determination

Please find below a statement of our determination as to whether or not the committee views Chelation Therapy as a proven and effective treatment for children with autism spectrum disorder and/or other developmental disabilities. In subsequent sections you will find documentation of our review process including a description of the proposed treatment, a synopsis of review findings, the treatment review evidence checklist, and a listing of the literature considered. In reviewing treatments presented to us by DHS/DLTC, we implement a review process that carefully and fully considers all available information regarding a proposed treatment. Our determination is limited to a statement regarding how established a practice is in regard to quality research. We do not make funding decisions.

#### Description of proposed treatment

Chelation refers to a medical procedure that uses chemicals to remove heavy metals from the body and in this case the bodies of children with autism. The agents most commonly used are Calcium Disodium ethylenediamine-tetraacetic acid (Ca-EDTA), Dimercaptosuccinic acid (DMSA) (succimer) and 2-3-dimercaptopropane-1-sulfonate (DMPS). These man-made molecules all have a high affinity to bond metals and remove them from the body via urine when the drug itself is excreted. The administration of metal-binding molecules to treat autism is based on speculation that mercury poisoning (via administration through immunization, mercury-containing dental fillings or environmental exposure) causes autism. Therefore, the rationale is that removing the toxic metal will cure the autism or lead to an amelioration in the symptoms of autism. To “diagnose” heavy metal poisoning as a cause of these conditions, and therefore appropriate for chelation therapy, practitioners will often administer a test or challenge dose of a chelator. In a day or two, a urine test is done to measure metals. Since some metals are found in all humans, these tests are always “positive,” though they are not measured against established or medically accepted standards. These results are then used to market chelation therapy to the individuals. The American College of Medical Toxicology warns that basing chelation therapy on these types of tests is without benefit to patients and may prove harmful. It is important to note that chelation has some legitimate uses. In particular, it is indicated for removing lead from children with severe lead poisoning, and many papers in the medical literature confirm its efficacy for this purpose.

#### Synopsis of review

In the case of Chelation Therapy, please refer to the attached reference listing that details the reviewed research. The committee’s conclusions regarding Chelation Therapy include:

1. A search of the scientific literature identified that no randomized controlled trials of the use of chelation for the treatment of autism are available. Cao and colleagues studied mercury elimination in children who needed chelation with succimer for lead poisoning; they found “limited efficacy.” In a pilot study, Soden and colleagues gave DMSA (succimer) to children with and without autism. Then, they compared the amounts of arsenic, cadmium, lead, and mercury excreted in their urine before and after chelation. They reported that the results did NOT demonstrate an excess body burden of any of these metals and that “there is no evidence that any of the 15 autistic participants would benefit from chelation therapy.” The American Academy of Pediatrics issued a policy statement saying that “...unless there is clear evidence of current heavy metal toxicity, chelation by any method is not indicated outside of monitored clinical trials.” This policy was reaffirmed in December 2010.
2. In 2006, the U.S. National Institute of Mental Health (NIMH) had announced that it had begun three clinical studies of autism. One was of chelation therapy for children with autism, in part because chelation was already being administered to large numbers of children with no proof of efficacy or safety. In late 2006, a study in rodents cast doubt on the safety of succimer as it would have been used in this study. Treatment with succimer improved cognitive outcomes in rats with lead poisoning, but actually caused lasting impairment in animals without lead poisoning. NIMH re-evaluated the proposed study in light of these findings and determined that children would be put at disproportionate risk. In 2008, NIMH announced that the study was cancelled. The use of chelation therapy as a treatment for autism has been linked to at least one death in 2005 of a 5-year-old boy who during his third chelation treatment died of cardiac arrest.
3. Tonya Davis of Baylor University who co-authored an analysis published in the journal *Research in Autism Spectrum Disorders* examined 5 studies that looked at chelation treatment for children with autism. For the review, 82 people ages 3 to 14 who received chelation treatment were included across the 5 studies identified. Despite mixed or positive findings in all of the studies reviewed, the research team found methodological flaws throughout the existing science. In many cases, for example, study participants were trying several treatments in addition to chelation making it unclear what attributed to any success they experienced. The review notes that side effects of chelation include fever, vomiting and hypertension. There is also a risk of cardiac arrest with the treatment.
4. Several papers outline the opinion of the authors (listed as “pre-pilot”) who advocate a role for chelation as a treatment for autism based on personal experience (Patel and Curtis, 2007). However, there are no known scientifically-validated benefits of the administration of chelating agents, yet there are some reported risks. Known side effects of these chemicals include two reported deaths. Ten percent of DMSA-treated patients show evidence of gastrointestinal issues including elevation in liver enzymes. In short, there is not enough scientific evidence available at this time to advocate a role for chelation of heavy metals in the treatment of autism, and there is potential for adverse side effects.

In sum, it is the decision of the committee that Chelation Therapy is Level 5 - Untested (Experimental Treatment) &/or Potentially Harmful

## Section Two: Rationale for Focus on Research Specific to Comprehensive Treatment Packages (CTP) or Models

In the professional literature, there are two classifications of interventions for individuals with Autism Spectrum Disorder (National Research Council, 2001; Odom et al., 2003; Rogers & Vismara, 2008):

- (a) **Focused intervention techniques** are individual practices or strategies (such as positive reinforcement) designed to produce a specific behavioral or developmental outcome, and
- (b) **Comprehensive treatment models** are “packages” or programs that consist of a set of practices or multiple techniques designed to achieve a broader learning or developmental impact.

To determine whether a treatment package is proven and effective, the Treatment Intervention Advisory Committee (TIAC) will adopt the following perspective as recommended by Odom et al. (2010):

The individual, focused intervention techniques that make up a comprehensive treatment model may be evidence-based. The research supporting the effectiveness of separate, individual components, however, does *not* constitute an evaluation of the comprehensive treatment model or “package.” The TIAC will consider and review only research that has evaluated the efficacy of implementing the comprehensive treatment *as a package*. Such packages are most often identifiable in the literature by a consistently used name or label.

National Research Council. (2001). *Educating children with autism*. Washington, DC: National Academy Press.

Odom, S. L., Brown, W. H., Frey, T., Karusu, N., Smith-Carter, L., & Strain, P. (2003) Evidence-based practices for young children with autism: Evidence from single-subject research design. *Focus on Autism and Other Developmental Disabilities, 18*, 176-181.

Odom, S. L., Boyd, B. A., Hall, L. J., & Hume, K. (2010). Evaluation of comprehensive treatment models for individuals with Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders, 40*, 425-436.

Rogers, S., & Vismara, L. (2008). Evidence-based comprehensive treatments for early autism. *Journal of Clinical Child and Adolescent Psychology, 37*, 8-38.

### Section Three: DLTC-TIAC Treatment Review Evidence Checklist

Name of Treatment: Chelation Therapy

#### Level 1- Well Established or Strong Evidence (DHS 107 - Proven & Effective Treatment)

- Other authoritative bodies that have conducted extensive literature reviews of related treatments (e.g., National Standards Project, National Professional Development Center) have approved of or rated the treatment package as having a strong evidence base; authorities are in agreement about the level of evidence.
- There exist ample high quality studies that demonstrate experimental control and favorable outcomes of treatment package.
  - Minimum of two group studies or five single subject studies or a combination of the two.
  - Studies were conducted across at least two independent research groups.
  - Studies were published in peer reviewed journals.
- There is a published procedures manual for the treatment, or treatment implementation is clearly defined (i.e., replicable) within the studies.
- Participants (i.e., N) are clearly identified as individuals with autism spectrum disorders or developmental disabilities.

*Notes:* At this level, include ages of participants and disabilities identified in body of research

#### Level 2 – Established or Moderate Evidence (DHS 107 - Proven & Effective Treatment)

- Other authoritative bodies that have conducted extensive literature reviews of related treatments (e.g., National Standards Project, NPDC) have approved of or rated the treatment package as having at least a minimal evidence base; authorities may not be in agreement about the level of evidence.
- There exist at least two high quality studies that demonstrate experimental control and favorable outcomes of treatment package.
  - Minimum of one group study or two single subject studies or a combination of the two.
  - Studies were conducted by someone other than the creator/provider of the treatment.
  - Studies were published in peer reviewed journals.
- Participants (i.e., N) are clearly identified as individuals with autism spectrum disorders or developmental disabilities.

*Notes:* At this level, include ages of participants and disabilities identified in body of research

Level 3 – Emerging Evidence (DHS 107 – Promising as a Proven & Effective Treatment)

- Other authoritative bodies that have conducted extensive literature reviews of related treatments (e.g., National Standards Project, NPDC) have recognized the treatment package as having an emerging evidence base; authorities may not be in agreement about the level of evidence.
- There exists at least one high quality study that demonstrates experimental control and favorable outcomes of treatment package.
  - May be one group study or single subject study.
  - Study was conducted by someone other than the creator/provider of the treatment.
  - Study was published in peer reviewed journal.
- Participants (i.e., N) are clearly identified as individuals with autism spectrum disorders or developmental disabilities.

*Notes:* At this level, include ages of participants and disabilities identified in body of research

Level 4 – Insufficient Evidence (Experimental Treatment)

- Other authoritative bodies that have conducted extensive literature reviews of related treatments (e.g., National Standards Project, NPDC) have not recognized the treatment package as having an emerging evidence base; authorities are in agreement about the level of evidence.
- There is not at least one high quality study that demonstrates experimental control and favorable outcomes of treatment package.
  - Study was conducted by the creator/provider of the treatment.
  - Study was not published in a peer reviewed journal.
- Participants (i.e., N) are not clearly identified as individuals with autism spectrum disorders or developmental disabilities.

*Notes:*

Level 5 – Untested (Experimental Treatment) &/or Potentially Harmful

- Other authoritative bodies that have conducted extensive literature reviews of related treatments (e.g., National Standards Project, NPDC) have not recognized the treatment package as having an emerging evidence base; authorities are in agreement about the level of evidence.
- There are no published studies supporting the proposed treatment package.
- There exists evidence that the treatment package is potentially harmful.**
  - Authoritative bodies have expressed concern regarding safety/outcomes.
  - Professional bodies (i.e., organizations or certifying bodies) have created statements regarding safety/outcomes.

*Notes:* The American Academy of Pediatrics issued a policy statement saying that “...unless there is clear evidence of current heavy metal toxicity, chelation by any method is not indicated outside of monitored clinical trials.” This policy was reaffirmed in December 2010. The potential safety risks associated with chelation resulted in a suspension of a clinical study of chelation treatment for autism (Mitka, 2008). Additional safety issues led to NIMH cancelling a controlled trial of chelation therapy

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Date: October 31, 2014

Committee Members Completing Initial Review of Research Base: Jennifer Asmus, Brooke Winchell

Committee Decision on Level of Evidence to Suggest the Proposed Treatment is Proven and Effective:  
Level 5 - Untested (Experimental Treatment) &/or Potentially Harmful

**References Supporting Identification of Evidence Levels:**

- Chambless, D.L., Hollon, S.D. (1998). Defining empirically supported therapies. *Journal of Consulting and Clinical Psychology*, 66(1) 7-18.
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## Section Four: Literature Review

All Retrieved for Review During October 2014

Baxter, A.J., & Krenzelok, E.P. (2008). Pediatric fatality secondary to EDTA chelation. *Clinical Toxicology*, 46(10), 1083-1084. doi: 10.1080/155636507012614488

Beware of non-evidence based treatments. (2010). Retrieved from <http://autismsciencefoundation.org/what-is-autism/autism-diagnosis/beware-non-evidence-based-treatments>

Bihari, T. (2006). Assessing CAM options for treating autism. *Alternative and Complementary Therapies*, 233-7.

Boyles, S. (2008). Chelation study for autism called off. Retrieved from <http://www.webmd.com/brain/autism/news/20080918/chelation-study-autism-called-off>

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Curtis, L.T., & Patel, K. (2008). Nutritional and environmental approaches to preventing and treating autism and attention deficit hyperactivity disorder (ADHD): A review. *Journal of Alternative and Complementary Medicine*, 14(1), 79-85.

Davis, T.N., O'Reilly, M., Soyeon, K.S., Lang, R., Rispoli, M, et al. (2013). Chelation treatment for autism spectrum disorders: A systematic review. *Research in Autism Spectrum Disorders*, 7, 49-55.

Farrugia, J.M. (2013). The use or misuse of biomedical treatment approaches to autism. *Malta Medical Journal*, 25(1), 8-14

Golnik, A, E., & Ireland, M. (2009). Complementary alternative medicine for children with autism: a physician survey. *Journal of Autism Developmental Disorders*, 39(7), 996-1005.

Harrington, J.M., Boyd, W.A., Smith, M.V., Rice, J.R., Freedman, J.H., & Crumbliss, A.L. (2012). Amelioration of metal-induced toxicity in *Caenorhabditis elegans*: Utility of chelating agents in the bioremediation of metals. *Toxicological Sciences* 129(1): 49–56.

Holmes, A. (2008). Autism treatments: Mercury chelation for the treatment of autistic children. Retrieved from <http://www.healing-arts.org/children/holmes.htm>

Kidd, P. M. (2002). Autism, an extreme challenge to integrative medicine. Part 2: Medical management. *Alternative Medicine Review: A Journal of Clinical Therapeutic*, 7(6), 472-499.

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- Levy, S. E., & Hyman, S. L. (2005). Novel treatments for autistic spectrum disorders. *Mental Retardation and Developmental Disabilities Research Reviews*, 11, 131-142.
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- Whelan, D. (2010). Heavy Metals Inc. *Forbes*, 185 (1), 46-47.