COMPLIMENTARY AND ALTERNATIVE MEDICINE THERAPY IN THE SETTING OF ASD

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COMPLIMENTARY AND ALTERNATIVE MEDICATION USE

- Between 28-95% of kids with ASD have 1+ complementary therapy, whether or not the family may share this with you
  - Children with chronic diseases tend to have higher rates of CAM use (24-74%)
- Families often reluctant to share interest or use with providers

APPEAL OF CAM THERAPY

- Romantic advertisement promising more than what traditional therapies might
- Promoters not held to the same regulatory compliance rules as traditional therapies

CAM IS BIG BUSINESS

- $33.9 billion out of pocket in 2007
- Increased 60% from the decade before

CAM = NATURAL ≠ WITHOUT HARM

- Many CAM treatments are perceived as "natural," ie avoid the potential side effects of conventional medical treatments
- Part of this is because of the regulatory and reporting mechanisms for CAM

HOW TO DISSECT CAM TX?

Table 1
Types of CAM treatments

Type of Products[a]	Provider Based or No Provider	Efficacy/Effectiveness	Advantage	Disadvantage	Cost
Natural Products Herbs Vitamins, minerals, supplements Probiotics	No provider	Little research validation of efficacy or documentation of side effects	Consumer driven	Not FDA regulated No oversight of potential side effects or management Consumer driven	Out-of-pocket expenses
Mind and Body Practices Auditory integration Acupuncture Equine therapy Healing touch Hypnotherapy Massage therapy, qigong Music therapy Physical manipulation Yoga	Provider based	Little research validation of efficacy or documentation of side effects	Consumer driven Low potential for negative side effects and complication	Guidance nonmedical Lack of knowledge by medical practitioners Lack of regulatory oversight in some treatment	Out-of-pocket expenses
Other Biomedical Treatments Off-label prescription medications Other medical treatments Specialized or elimination diets	Provider based	Little research validation of efficacy or documentation of side effects	Perception of "cure"	High potential for negative side effects and complications Most guidance for use in community, lay press, or Internet Guidance nonmedical Lack of knowledge by medical practitioners Lack of regulatory oversight for some treatments High cost may interfere with ability to obtain other treatments	Out of pocket, may be expensive

Abbreviation: FDA, US Food and Drug Administration.
[a] Classified according to the National Center for Complementary and Alternative Medicine (www.nccam.nih.gov).

RESEARCH INTO CAM

- The National Center for Complementary and Alternative Medicine (NCCAM) established in 1991 as part of the NIH
  - Natural products
  - Mind and Body practices

Complementary and Alternative Medicine Treatments for Children with Autism Spectrum Disorders

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KEYWORDS

• Autism • Autism spectrum • Complementary and alternative treatments
• Evidence based

Table 2
Evidence-based support for treatments

Treatments	Evidence	Comments	Rating of Evidence
Natural Products			
Herbal products[34]	No specific studies of herbs and autism	No studies; no recommendations	D
Vitamins/minerals/supplements[35,36]	Randomized DB/PC trials with vitamin mineral supplement. Outcome measures included PGI-R and symptoms of hyperactivity, tantruming, and changes in biotin and vitamin K	Significant methodological problems	C
Vitamin A[37]	No evidence; theories	No evidence of effectiveness; significant potential for harm	D
Vitamin C[38–40]	2 DB PC trials showing improved sensorimotor, sleep, and GI symptoms and differences in vitamin C levels Other reference theoretic, ascribing cause(s) of ASD associated with oxidative stress	Some preliminary evidence; toxicity not significant	B
Vitamin D[35,41–47]	Treatment based on circumstantial evidence: symptoms of ASD during 2nd and 3rd year of life when vitamin D may be low; correlation of UV-B doses in USA with prevalence; relationship of vitamin D hormone (calcitriol) and serotonin and correlations of 25(OH)-vitamin concentration and scores on the Autism-Spectrum Quotient	Primarily hypothetical theories. Methodological problems: observational, epidemiologic assumptions	D
Vitamin B_6 and magnesium[38,48–54]	Cochrane review 2005 of existing studies: 3 studies; Owing to small number of studies, methodological quality of studies, and small sample sizes, no recommendation can be advanced regarding the use of B_6-Mg as a treatment for autism. Update in 2010 came to same conclusion.[52] Study in 2006 with 33 children, poorly defined diagnosis, changes seen in blood studies; control by typical children; unblinded	Poor quality of studies precludes recommendations for treatment Potential neurotoxicity of B_6 and/or magnesium; report of death from combination of multiple supplements with magnesium	D

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Table 2
(*continued*)

Treatments	Evidence	Comments	Rating of Evidence
DMG[55–57]	2 studies published: 1999 DB/PC crossover pilot of low-dose DMG, N = 8; no differences between groups. 2001 DB/PC trial, N = 37 no difference	Small studies, without benefit; no further evidence Parents report side effects of hyperactivity	C+
Amino acids[7,58,59]	No peer-reviewed studies of taurine, lysine, GABA administration Carnosine: most literature based on bench research. One study in humans, of L-carnosine (2002) DB/PC trial N = 31 children, improvement in GARS and other measures. No further trials reported	Inadequate study to make recommendations for treatment	C
Omega-3 FA[60–67]	Several systematic reviews examining nutritional and environmental factors. Studies of supplements have reported benefits, but many methodological problems. Cochrane review reported 3 studies (N = 37 children) with randomized, DB/PC; other studies excluded owing to nonrandomization or no controls. No evidence impact on social interaction, communication, stereotypy of hyperactivity	Not yet high-quality evidence that omega-3 FA supplementation is effective for improving core and associated symptoms of ASD. More study needed based on promising effects in other populations	C
Vitamin B_{12}[39,68–77]	Except for a small pilot study, with open-label extension, No additional studies since 2008 review Bertoglio study: 12 wk DB/PC, crossover clinical trial of injectable methyl B_{12}. N = 30; no differences in behavioral measures or laboratory tests; in a subgroup 30% improvement. No correlations of response to number of infections, GI symptoms, or food allergies	Need further study to delineate a responder group; may be related to measures used to examine outcome in a group of children with intellectual challenges	C+

Melatonin[78–89]	Multiple studies including (1) cohort study (Anderson, 2008); (2) open-label dose escalation (Malow, 2012); (3) biochemical analyses and susceptibility genes in ASD vs controls, showing differences in the 2 groups	Good physiologic evidence and some medium-quality observational and open-label studies Few side effects	B
Probiotics[90–95]	No specific studies of treatment of children with ASD. Literature explores link between gastrointestinal dysfunction and associated symptoms. Theory that probiotic bacteria would restore normal gut microbiota or that probiotics would provide "detoxification"	No evidence to support need for detoxification. No recommendations for treatment	D+
Mind and Body Practices			
Auditory integration[96–100]	7 clinical trials with varied outcome measures; 5 do not demonstrate benefit	Randomized, blinded trial with adequate sample size, manualized approach, and valid outcome measures would be needed to demonstrate support Risk low, unlikely benefit	B
Acupuncture[101,102]	RCTs suggest benefit when combined with language and other therapies; varying results when compared with wait-list controls	Randomized trials of adequate size with characterized patients and valid outcome data are needed Risk for infection, injury in uncooperative patients. Potential for benefit for comorbid conditions possible. No evidence to support use for ASD	B
Equine therapy[103]	Case series identified improvement in teacher-reported behavioral scales while riding program in effect	Randomized trial with appropriate control activity with valid outcome measures needed. With appropriate attention to safety (helmet, trained assistants) risk is relatively low; potential benefit for symptoms or as leisure activity	C

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Table 2
(*continued*)

Treatments	Evidence	Comments	Rating of Evidence
Hypnotherapy	Case reports only	Randomized trials of adequate size with characterized patients, manualized treatment, and valid outcome data needed Low risk, potential benefit	D+
Massage[104–106] Qigong[104,105,107–110]	Small studies without characterization of participants, standardization of treatments, or valid outcome measures. Benefits reported in parental perception and sensory and behavioral skills	Randomized trials of adequate size with characterized patients, manualized treatment, and valid outcome data needed Low risk, potential benefit	C
Music therapy[111,112]	Small trials and case series with suggestion of increased verbalizations in melodic-based interventions. Data do not demonstrate improvement in language or behavior	Randomized trials of adequate size with characterized patients, manualized approaches, and valid outcome measures needed Low risk, limited evidence for potential therapeutic benefit. (Note: outcome measures on use of music as cue for behavior may be warranted, eg, effect of Barney "Clean Up" song)	B
Chiropractic[113,114]	No trials in the literature to inform a recommendation for chiropractic for symptoms of ASD	Randomized trials of adequate size with characterized patients, manualized treatment, and valid outcome data needed Low risk (if no spinal abnormalities, eg, atlanto-occipital instability of Down syndrome), potential benefit for comorbid medical conditions possible	D
Craniosacral manipulation	No adequate clinical trials support this intervention in ASD. No evidence that external manipulation alters flow of spinal fluid	No clinical trials support this intervention or the underlying construct Risk low, no evidence of benefit	D

Table 2
(*continued*)

Treatments	Evidence	Comments	Rating of Evidence
Oxytocin[153,154]	7 RCTs, small samples; benefits in emotional recognition, eye gaze. One trial with benefit at 6 wk	Longer-lasting products needed that can be tested in appropriate clinical trials No FDA-approved product on market with this clinical indication at present	C+
Secretin[92,155–171]	>900 children have been evaluated in DB PC trials. No behavioral benefit	No FDA-approved product on market with this clinical indication at present Risk from intravenous route, stress. No benefit documented	A
Gluten-free/casein-free diet[93,172–190]	Single-blind trials suggested potential benefit in children 5–7 y of age with GI symptoms DB trial without demonstrable benefit	Provided by parents with/without professional guidance DB randomized trial with characterization of patients and standard outcome data would be needed to clarify utility of this intervention Risk for nutritional compromise with restriction of calcium, vitamin D in milk products, and other nutrients with additional restrictions. Can be delivered in a nutritionally sound fashion. Suggest consultation with registered dietitian	B
Hyperbaric oxygen therapy[76,191–196]	Two randomized trials, conflicting results. Statistics might be interpreted differently, impact of other therapies possible	Randomized trial, DB of well-characterized patients using manualized approach and valid outcome measures would be needed to determine efficacy No FDA-approved product on market with this clinical indication at present	B

Stem cell transplantation[197–200]	Open-label treatment claims improvement in 21 of 36 patients in one report and 23 of 37 in another. Seizures as side effect reported to be managed with medications	No FDA-approved product on market with this clinical indication at present	D
Transcranial magnetic stimulation[106,201–207]	Dorsomedial prefrontal cortex activation improved social relatedness and anxiety in adults with ASD over 2-wk trial with short-term follow-up, compared with sham treatment. Data supported by other small series Safe in context of clinical trials	DB randomized trial with characterization of patients and standard outcome data would be needed to clarify utility of this intervention. Long-term efficacy and safety data needed to support pediatric use No FDA-approved product on market with this clinical indication at present for general clinical use in children Potential for risk, potential for benefit	B
Vagus nerve stimulation[208–210]	Anecdotal case reports for improved behavior. Prospective data suggest that patients with ASD may have improved mood	Use of questionnaires and direct observation may be helpful in documenting behavioral change with implantation of vagal nerve stimulators in patients with ASD and epilepsy. If demonstrable benefit, may justify trials for behavior alone Risk with procedure, benefit unknown relative to ASD, benefit for seizure control	D

Abbreviations: ASD, autism spectrum disorders; DB, double-blind; DMG, dimethylglycine; DMSA, dimercaptosuccinic acid; FA, fatty acid; FDA, US Food and Drug Administration; GABA, γ-aminobutyric acid; GARS, Gilliam Autism Rating Scale; GI, gastrointestinal; IgG, immunoglobulin G; IVIG, intravenous immunoglobulin; NaEDTA, sodium ethylenediaminetetraacetic acid; PC, placebo-controlled; PGI-R, Parental Global Impressions—Revised; RCT, randomized controlled trial; UV-B, ultraviolet B.

MARIJUANA

- Increasing interest from the public
- Medical marijuana legal now in 33 states, including Utah
- Efforts to push for recreational marijuana continue
- **Prescribers in difficult position to counsel patients re efficacy for all the CAM reasons discussed above**

HOUSE BILL 3001: UTAH MEDICAL CANNIBUS ACT

- Recently passed, Dec. 2018
- ID cards to be issued to patients
- QMP* to prescribe for specific conditions
- Establishes mandatory ongoing training every 2 years
- Licensed pharmacies to dispense

*QMP (Qualified Medical Provider): MD, DO, NP, PA

UTAH MEDICAL CANNABIS

QUALIFYING CONDITIONS (26-61A-104)

Individuals with the following conditions are authorized under the Utah Medical Cannabis Act to receive a medical cannabis patient card:

- HIV or acquired immune deficiency syndrome (AIDS)
- Alzheimer's disease
- Amyotrophic lateral sclerosis
- Cancer
- Cachexia
- Persistent nausea that is not significantly responsive to traditional treatment except for nausea related to: pregnancy, cannabis-induced cyclical vomiting syndrome, or CBD hyperemesis syndrome
- Crohn's disease or ulcerative colitis
- Epilepsy or debilitating seizures
- Multiple sclerosis or debilitating muscle spasms
- Post-traumatic stress disorder (PTSD) that is being treated and monitored by a mental health therapist and that: has been diagnosed by a health care provider or mental health provider by the VA and documented in the patient's record; or has been diagnosed or confirmed by evaluation by a psychiatrist, doctorate psychologist, a doctorate licensed clinical social worker, or a psych APRN
- Autism
- Terminal illness when the patient's remaining life expectancy is less than 6 months
- Condition resulting in the individual receiving hospice care
- Rare condition or disease that affects less than 200,000 individuals in the U.S., as defined in federal law and this is not adequately managed despite treatment attempts using conventional medications (other than opioids or opiates) or physical interventions
- Pain lasting longer than two weeks that is not adequately managed, in the qualified medical provider's opinion, despite treatment attempts using conventional medications other than opioids or opiates or physical interventions
- If a patient does not have a qualifying condition specifically named, they may petition the Compassionate Use Board for approval of their medical cannabis card.

WHY IS MARIJUANA HARD TO STUDY?

- Plant with more than 100 cannabinoid compounds
- Endocannabinoid receptors throughout the body
- Though it has been around for centuries, isolated cannabinoids have not been studied hence varied report of efficacy.

SUPPLY IS NOT RELIABLE

- Different marijuana strains will have different cannabinoid profiles
- Access to reliable supply and formulations have also been limited even from licensed dispensaries
- Legal definitions of what is allowed also varies

HEALTHY

I Tried Cooking With CBD Oil for 7 Days and Here's What Happened

Am I calmer now? Am I zen? Am I being haunted by hippos?

BY JOE SEVIER

March 26, 2018

Hard to counsel specifically because it is so ubiquitious!

RESEARCH RESTRICTIONS

- Considered a class 1 drug
- Federally illegal still

CANNABINOIDS

- More common natural forms
  - CBD
  - THC

CBD oil can have up to 0.3% THC in the state of Utah

RX FORMULATIONS:

- Dronabinol – tx of chemotherapy induced nausea, appetite
- Nabilone – tx of chemotherapy induced nausea, appetite issues
- Epidolex – seizures type Dravet and Lennox Gastault

REVIEW OF CANNABIS*

Conclusive effect	Moderate effect	Limited effect	Inconclusive
Chronic pain	Sleep disturbance	Appetite and weight gain	Cancer
Chemotx induced nausea and vomiting		PTSD	Epilepsy
Multiple sclerosis spasticity		Anxiety	Neurodegenerative disorders
		Tourettes	IBS
			Addiction

*From the National Academies of Sciences, Engineering and Medicine. Research difficult as most of the evidence relates to the pharmaceutical cannabinoids – dronabinol, nabilone, and nabiximols. Recommendations also limited by scope of DBPC trials.

TECHNOLOGY ASSISTED INTERVENTIONS

MEDIA AND ASD

- ASD youth as compared to peers
  - Watch more TV
  - Play more video games
  - Prefer video games to TV watching
  - Avg 4.5 hours screen time a day, and <2 hours nonscreen time

Most are not using ESM for social purposes

BENEFITS

- Parents often report "splinter" skills
- Some studies do who that children with ASD perform better with ESM than traditional media
- Learning may be more efficient as well
- Specific programming might help with language, social deficits, academic and adaptive functioning

CAVEATS

- Obesity
- Sleep
- Internet addiction
- Risk for cyberbullying
- Legal/safety issues
- Cognitive issues
- Social issues

RESOURCES AND REFERENCES

https://health.utah.gov/wp-content/uploads/MedCanFactSheet4-8-19.pdf

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