

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

KEY POINTS

- Families of children with autism spectrum disorders (ASD) commonly use complementary and alternative medical (CAM) treatments.
- CAM treatments are selected to promote wellness, treat specific symptoms, avoid side effects of conventional medicine, or promote resolution of core symptoms of ASD.
- Commonly used categories of CAM are natural products, mind and body therapies and other biomedical treatments.
- Conventional studies document that some CAM treatments are ineffective, whereas others require further study.

OVERVIEW

Autism spectrum disorders (ASD) are common neurodevelopmental disorders (affecting 1 in 68 children)¹ with a significant impact on the quality of life of child and family, owing to the constellation of core and associated symptoms. ASDs

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Abbreviations	
ASD	Autism spectrum disorders
CAM	Complementary and alternative medical (treatments)
NCCAM	National Center for Complementary and Alternative Medicine
NHIS	National Health Interview Survey

have characteristic core deficits in communication-socialization and behavior, with a wide range of severity of symptoms.² Many treatments are recommended through collaborative medical, behavioral, and educational practice, but selection of treatment strategies is complicated by the impact of core deficits and frequently associated comorbid psychopathology.³ Current scientific evidence strongly supports multifactorial genetic etiology,^{4,5} with environmental factors also having an etiologic impact.⁶ Thus for many children the specific causes are often not known. Furthermore, symptoms are behaviorally defined and heterogeneous, and will change over time with acquisition of developmental skills. As a result, families of children with autism and related disorders may find that the clinicians who diagnose their child's autism may sound vague about both cause and prognosis. This vagueness may turn families to therapies not based on conventional medical or psychological practice, proponents of which may present the treatment options as more concrete, definitive in etiology, and optimistic in outcome.⁷

This article provides an overview of commonly used complementary, alternative, or integrative health treatments that families of children with ASD may pursue. Many of these health care approaches are conceptualized outside of mainstream Western or conventional medicine⁸ either to replace standard medical care or to supplement it. The combination of conventional practice and complementary techniques is often called integrative medicine. For ease of discussion, this article uses the term complementary and alternative medicine (CAM) to encompass all treatments that would fall under this integrative medicine rubric (not just biologically based medical treatments). This review discusses the reasons why families seek CAM, review the commonly used CAM therapies for ASD, and describes how conventional practitioners might work with patients who use CAM treatments.

The National Center for Complementary and Alternative Medicine (NCCAM) was established in 1991 as part of the National Institutes of Health to promote scientific study of CAM treatments, which it has promoted through education and direct support of research (www.nccam.nih.gov). NCCAM groups CAM therapies into 2 domains: Natural Products and Mind and Body Practices. Not included in these categories is the use of biological or biomedical treatments, which would also refer to psychopharmacologic or other pharmacologic agents used off-label to address a nonstandard hypothesis.

The use of CAM treatments by adults in the United States remains high. Analysis of data from the 2002 and 2007 National Health Interview Survey (NHIS) revealed rates of 36% and 38%, respectively, of any type of CAM treatment (excluding prayer) by United States adults.^{9,10} Population-based data on the use of CAM treatments in children were available for the first time from the 2007 NHIS, reporting that 11.8% of children used CAM therapy in the 12 months before the survey.⁹ This figure is likely to be an underestimate. Other reviews have reported a wide range of CAM use (2%–50%) in children, but these data are derived from selected groups and are not population based (as in the NHIS survey)¹¹

TYPES OF TREATMENTS IN USE

Table 1 lists the categories and types of CAM treatments classified according to NCCAM and how they are administered, empirical evidence for effectiveness, and advantages and disadvantages of each therapy. CAM in adults is big business. In 2007, adults in the United States spent \$33.9 billion out of pocket on purchases of CAM products, practitioner visits, and other related activities,¹² an increase from \$21.2 billion in 1997.¹³ The most commonly used CAM treatments in adults are in the category of natural products (17.7%) and mind and body practices (6.1%–12.7%).⁹ Most often, adults use CAM to treat musculoskeletal pain and other chronic conditions.

WHO USES COMPLEMENTARY AND ALTERNATIVE TREATMENTS AND WHY

Studies report that children with chronic illnesses, such as cancer, asthma, rheumatoid arthritis, attention-deficit/hyperactivity disorder, genetic disorders (eg, Down syndrome), cerebral palsy, and other neurodevelopmental disorders are treated with CAM therapies at higher rates (24%–75%).^{7,14–17} Families of children with ASD have even higher rates of usage (28%–95%).^{18–20} The occurrence of comorbid disorders and increased severity of symptoms of autism is associated with increased use of CAM.^{18–20}

The most commonly used CAM treatments for ASD reflecting similar patterns of use in adults and children with other chronic disorders are^{18,21}:

- With natural products: 13% to 54%
- Special diet: 17% to 33%
- Mind and body practices: 25% to 30%

As in adults, the most commonly used treatments in the 2007 NHIS survey of CAM use in children were mind and body practices and natural products. Children whose parents used CAM were 2 times more likely to use CAM than those whose parents did not.

CAM treatments include therapies used in combination with mainstream approaches (complementary) and, less commonly, in place of conventional treatments (alternative) (www.nccam.nih.org). Reasons for use of CAM treatments vary, but usually target treatment of hypothetical causes of specific disorders or illnesses or for general wellness purposes.^{9,22} Studies of CAM in adults have started to differentiate these purposes, but studies in children have not advanced to this level. A recent study by Davis and colleagues²² identified respondents to the NHIS 2007 survey as nonusers (75%) and CAM treatment users (25%). Users were categorized into treatment only, health promotion only, and mixed users, and the investigators identified different characteristics of health behaviors and utilization. It was estimated that:

- 17.4% of adults used CAM to treat illness
- 27.4% used CAM for health promotion
- 13% were mixed users

By self-report, health promotion users were healthier, treatment users had higher rates of conventional use of medical care, and treatment users consumed more services. As already described, it appears that few adults are using these treatments as alternative care.

There are more specific reasons for use of CAM treatments beyond treatment of disorders and general wellness. Goals of treatment may include⁹:

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).

- Relief of specific symptoms (eg, pain, musculoskeletal symptoms, gastrointestinal symptoms)
- Alleviation of side effects of conventional treatments
- Philosophic reasons (eg, holistic health philosophy)
- Wanting greater control over health management

Many CAM treatments are perceived as “natural,” without the potential side effects of conventional medical treatments.^{23,24}

Use of Complementary and Alternative Medical in Families of Children with Autism Spectrum Disorder

Families of children with ASD may have wellness promotion among their reasons for electing nonstandard therapies, but they use CAM to treat symptoms of autism in general, comorbid symptoms (such as attention, hyperactivity, irritability, moodiness, gastrointestinal symptoms, seizures, sleep, and tactile sensitivity).^{25,26} In some instances they select CAM when conventional therapies do not seem to affect core symptoms in an attempt to provide more comprehensive treatment.¹⁵ Other families report the use of CAM to address concerns about negative side effects of conventional treatments.⁷ Most importantly, most families who use CAM use more than 1 CAM treatment. Clinicians must be aware of this and must monitor for interactions of therapies, and the impact the cost and energy to provide CAM therapies may have on prescribed treatments.^{19,27}

Despite the increasing trend for children with chronic illnesses such as ASD to be served in a primary care practice that can be a “medical home” where families can develop relationships with a clinician, most families continue to obtain their information about CAM from other sources. A survey of parents by Wong and Smith²⁸ reported the frequency of sources of information about CAM treatment:

- Family and the community members: 35%
- Physicians: 23%
- Other nonmedical professionals: 4% to 27%
- Internet: 23%
- Books: 15%

It is most notable that families reported that they rarely asked physicians for information about CAM. The proliferation of Internet-based lay communities and Web sites that are promoting untested treatments have increased the exposure of families to large volumes of information about treatments with potential harm. Sites often promote the use of bioactive substances without medical monitoring, and this has added stress to the relationship between families and medical providers. Conventional clinicians may not feel comfortable advising patients about treatments with little scientific basis in the conventional literature,¹⁵ and this has a direct negative impact on the likelihood of shared decision making between medical providers and families about treatment choices. Many families do not tell their physician that they are using CAM. Reasons for lack of disclosure include a perception of physician’s lack of knowledge about CAM therapies, lack of time for discussion, not seeing the necessity of reporting the use of other therapies, and concern regarding disapproval by the physician.^{15,28}

EVIDENCE FOR COMPLEMENTARY AND ALTERNATIVE THERAPIES

Given the frequency of use of CAM treatments and that many families may not inform their provider of such use, practitioners must be aware of factors associated with the use, methods to evaluate evidence for efficacy and/or effectiveness, and how to

negotiate with families for safe care. **Table 1** lists categories of CAM treatments and examples of each, providing an overview of available research, and advantages and disadvantages of the treatments.

For the purposes of this article, the authors have reviewed the available literature regarding CAM treatments (with emphasis on advances since the previous article)⁷ and have assigned a grade for the strength of the research. In many instances a comprehensive systematic review was not possible because the evidence or studies did not exist and could not be compared. The authors have followed the recommendations of the GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group, focused on rating the quality of evidence through systematic review to enable providers to develop and present recommendations for treatment.²⁹ The working group has graded evidence as³⁰:

- High: several high-quality studies or randomized trials
- Moderate: one high-quality study or several with some limitations
- Low: study or studies with severe limitations
- Very low: no direct research evidence or expert opinion

For consistency, after reviewing the evidence for different treatments (consistent with the rubric of GRADE ratings) the authors have assigned scores for studies involving CAM treatments (**Box 1**). **Table 2** provides an overview of evidence-based support for selected treatments.

Natural Products

Natural products include a variety of products available to consumers over the counter, for which no prescription or recommendation by a licensed clinician is needed. These products may be administered as an oral or topical preparation, and are often sold as dietary supplements or nutraceuticals. Such products are consumer driven; that is, there is easy access by families. However, in many cases guidance or encouragement for their use may come from non-peer-reviewed sources (such as the community, lay press, or Internet), and this may play a role in lack of guidance or monitoring for potential side effects. Medical practitioners often lack the knowledge to guide consumers if they are informed by families of these products.

Mind and Body Practices

Mind and body practices are a diverse group of procedures or techniques administered or taught by a trained practitioner or teacher, on an individual or group basis. Most require ongoing treatment or support by trained practitioner. Acupuncture is administered individually, by a licensed acupuncturist. Hypnotherapy may be administered by a licensed provider (therapist or medical provider). Equine therapy may be provided in the context of a physical or occupational therapy treatment program or by an independent provider. Massage therapy is singular, administered by a variety of

Box 1	
Scores for studies involving CAM treatments	
Score	Qualifications
A	>1 high-quality study with consistent results or 1 large multicenter trial
B	1 high-quality study or several studies with mild limitations
C	1 study with severe limitations
D	No evidence/theories/multiple studies with very severe limitations

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
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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

Yoga ^{115,116}	Small study or manualized approach with measured benefit in behavior using standard outcome measures	Randomized trials of adequate size with characterized patients needed to extend beyond pilot data Low risk, potential benefit	C
Biologically Based Practices			
Anti-infectives (antibiotics, antifungal, antivirals), ^{117–130} minocycline ¹³¹	Antibiotics for intestinal overgrowth unproven Antiviral therapies untested Trial of minocycline may affect neurotrophic growth factors but did not affect clinical symptoms	No evidence for antibiotic or antifungal use for intestinal overgrowth, no studies on antiviral therapies Larger DB PC trial of minocycline indicated it as a psychopharmacologic agent No FDA-approved product on market with this clinical indication at present	C
Immunoglobulins ^{78,87,92,122,132–142}	IVIG did not alter behavioral symptoms in small open trials using valid outcome measures; a DB PC clinical trial of oral IgG did not affect behavior or GI symptoms	Data do not support using immunoglobulins for treatment of symptoms of ASD. Current research suggests that prenatal immune events may affect fetal brain development placing infants at risk for ASD No FDA-approved product on market with the clinical indication of altering immune function at present	C
Chelation agents: DMSA ^{92,143–150}	One case report of death with intravenous NaEDTA. Trial of DMSA chelation terminated because of concern about toxicity. Case series with methodological compromise suggested improvement after 6 mo of chelation	No evidence supporting the use of chelation Risk high. Use is not recommended outside of approved DB PC trials No FDA-approved product on market with this clinical indication at present	D
Digestive enzymes ^{151,152}	One RCT (N = 43) did not demonstrate clinical improvement, slight improvement in food variety	No FDA-approved product on market with this clinical indication at present	D
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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.

individuals ranging from trained massage therapists to parents, and there may be inconsistencies in the administration, making study challenging. Music therapy may be provided on an individual or group basis by a music therapist, who may not be trained in working with children with ASD. Chiropractic manipulation is administered individually by a licensed chiropractor. Craniofacial manipulation is administered by a variety of licensed professionals including chiropractors, occupational therapists, and physical therapists.

These treatments are also consumer driven, with direct access by families (but not necessarily covered by insurance). Guidance for or promotion of their use for the treatment of symptoms of autism may come from non-peer-reviewed sources (community, lay press, or Internet). Again, medical practitioners may not be sufficiently knowledgeable about these therapies to guide consumers in terms of their application in the treatment of autism symptoms. Owing to their lack of knowledge or experience, clinicians may not be open to reciprocal discussion (shared decision making). Some treatments (especially those involving physical manipulation) may not be adequately regulated by an oversight body or certification of providers.

Other Biomedical Treatments

Readers are referred to a recent review of biomedical complementary treatment approaches for autism by Robert Hendren³¹ for further details about biomedical treatments and the purported mechanisms that they would target. Biomedical treatments represent diverse types of medical or biologically based therapy, which likely present the most potential for negative side effects. These agents may be divided into 2 broad categories: off-label prescribed medications (eg, anti-infectives, immunoglobulins, chelation agents, digestive enzymes, oxytocin, secretin) and other medical treatments (eg, specialized diets without known medical indications, hyperbaric oxygen therapy, stem cell transplantation, transcranial magnetic therapy, vagus nerve stimulation). These treatments require a licensed clinician (physician, nurse practitioner) to prescribe the medication or administer the treatment.

Off-label medications may be over the counter (such as digestive enzymes and certain chelation agents) but are most often prescribed by a licensed medical provider, but used for an unapproved indication, age, or dosage as indicated by the Food and Drug Administration. Depending on the medication, they may be provided orally (antibiotics, antifungals, antivirals, chelation agents, immunoglobulins, among others), intranasal (oxytocin), rectal (chelation), intravenous (immunoglobulins, secretin) or transdermal (secretin). A frequently used intervention without medical guidance is elimination diet(s), most commonly the gluten-free/casein-free diet. This therapy may be totally consumer driven, and may be implemented without medical support for monitoring side effects such as nutritional deficiency. Other procedures such as hyperbaric oxygen therapy are implemented using a hyperbaric chamber, administered by a technician. The patient may be alone or with a caregiver. This treatment is often prescribed by a medical provider, but units can be purchased online or consumers can find directions to build one. Stem cell transplantation is intravenous or intrathecal, prescribed by complementary medical professionals. Families may travel to other countries to obtain stem cell transplantation that does not have the oversight that professional practice does in the United States. Transcranial magnetic therapy is provided individually, directed by a licensed medical professional as part of a registered clinical trial. It is not commercially available for ASD at present. Vagus nerve stimulation is derived from a specialized treatment for intractable seizures, using a medically implanted device for seizure control, with demonstrated efficacy for seizure control.

These treatments all have high potential for negative side effects and complications. Complementary providers and families may lack a mechanism to monitor for side effects. Most promotion for use comes from the community, lay press, or Internet, and precludes adequate peer review for evidence of efficacy. Medical practitioners are often not knowledgeable enough to guide consumers and may not be open to reciprocal discussion (shared decision making). These treatments are expensive (usually out of pocket), although in some instances insurance companies might cover some of the costs. Another cost to the patient is that the expenses to obtain these treatments may interfere with the ability to obtain other treatments (costs = time and money).

Some novel interventions, such as transcranial magnetic therapy, are investigational so may demonstrate a therapeutic effect after appropriate clinical trials. Many CAM approaches are rapid responses to new scientific observations that have not been critically examined or appropriately tested using appropriate clinical trial methodology.

WORKING WITH FAMILIES WHO CHOOSE COMPLEMENTARY AND ALTERNATIVE MEDICAL

The literature indicates that families of children with ASD often do not tell their health care provider that they are using nonstandard therapies unless directly asked. Many families do not think that their allopathic providers are knowledgeable about CAM while others do not want to tell their providers they are using products or approaches the provider might not approve of. It is important for the health care provider to routinely and nonjudgmentally ask about all interventions that a family is using to ensure that potential side effects are considered and families helped to navigate the choices related to expense and time commitment. It is common for users of CAM to assume that there are no or few side effects. Loose stool, for example, may be a side effect of supplements containing magnesium. This sign may be perceived as a medical comorbidity of the ASD if a full evaluation of supplements used does not take place. The American Academy of Pediatrics published recommendations for clinicians working with families who elect to use CAM for their children with special health care needs. The tenets of this document are: respect for family beliefs, listening to concerns, maintaining a dialogue with the family, ensuring the safety of the child, and being knowledgeable about how to evaluate the literature used to support CAM interventions.^{13,32}

Health care providers need to understand how to interpret the literature regarding novel therapies. Clinical trials evaluating new therapies are increasingly published in peer-reviewed sources. Physicians use print literature (68%) and colleagues (60%) as their most common sources for updating their medical information, and report that medical conferences and physician-directed Web sites (both 42%) are also common sources of new information. This percentage is the same as that for the use of general Web-based searches.³³ By contrast, the Internet is the first source of medical information in almost two-thirds of families. The lay literature often used to promote CAM therapies may be based on anecdotal evidence and scant data, thus the health care provider may need to counsel the family regarding the components of an acceptable clinical trial. Peer-reviewed scientific reports should include information on the recruitment and characterization of the participants. The methods of study need to be described, and it should be noted if group assignment was random and the assessment and treatment was double-blinded. Treatments should use consistent dosing. If a nonbiological intervention was used, it should be described and noted if delivered in a standard fashion. Outcome measures need to be valid (ie, measure what they say they measure).¹⁵ If no high-quality clinical trials inform the safety or efficacy of an intervention, the clinician can help the family understand the available data to enable them

Table 3	
Working with families who select CAM use	
Principles	What to Do
Discussion with families	Ask about all treatments
Family disclosure of CAM use to provider ¹⁵	Partnering to promote discussion
Choice of treatments	Shared decision making
Selection of non-evidence-based treatment	Educating about evidence and informed consumer practices ¹⁵
Sources of information ²⁶	Provider awareness of potential sources of information (family, friends, nonmedical community, Internet) ¹⁵
Provider comfort and knowledge about CAM treatments	Seek out sources of education Reviews of CAM treatment Educational opportunities

to make an informed choice on whether to use a novel therapy. **Table 3** lists some suggestions about working with families.

MONITORING INTERVENTIONS

Regardless of whether the literature supports an intervention, it may or may not be successful for an individual patient. It is important to establish the symptoms a novel therapy is used to address, and to define the expected benefits and potential side effects. Families should be counseled on the expected length of time until a therapeutic effect can be expected. With this knowledge they, and the program staff, can determine the impact of a specific intervention. It is important for interventions to be introduced one by one so that the effects can be correctly attributed.

SUMMARY

There are many treatments in current use for core and associated symptoms of ASD. This review discusses categories of CAM treatments commonly used for children with ASD, including natural products, mind and body practices, and other biomedical treatments. The focus is on factors associated with the use of CAM, the empirical evidence for the most frequently used treatments, and how to work with families who choose CAM treatments. Families choose CAM to promote wellness, to treat specific symptoms or co-occurring disorders of ASD, to avoid untoward symptoms of conventional medicine, and, in some cases, under the hope or assumption of resolution of core symptoms of ASD. Some treatments have been proved to be ineffective, some have unacceptable potential side effects, and others require more study in depth.

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