New And Complementary Therapies for Autism: Opening Doors and Covering Quacks Part 1: Biological Interventions

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Some definitions

- Conventional medicine – evidence-based, accepted by mainstream medical providers
- Complementary medicine – treatments that are used ***together with*** conventional medical treatment. Example: diet and exercise along with medication to treat diabetes
- Alternative medicine – treatments that are used ***instead of*** conventional medicine.
- Integrative medicine – a comprehensive, evidence-based approach mixing complementary and conventional methods

Acronym **CAM** is often used to describe these treatments

Why do people use CAM?

- Dissatisfaction with conventional medicine due to
  - Lack of efficacy
  - Adverse effects
  - Cost
- Prefer something "natural"
- Information received from sources other than health provider, including
  - Social media (podcasts, TikTok, etc.)
  - Friends and family
  - Direct to consumer marketing

How common is CAM use? Pain as an example

- In 2002, 19.2 percent of people used at least one approach for pain, whereas in 2022, 36.7 percent of people did.
- Use of yoga, meditation, and massage therapy increased the most from 2002 to 2022.
- Use of yoga increased from 5 percent in 2002 to 9 percent in 2012 to 15.8 percent in 2022.
- Meditation increased from 7.5 percent in 2002 to 17.3 percent in 2022, and it was the most used approach in 2022.
- Use of acupuncture, which was increasingly covered by insurance, increased from 1 percent in 2002 to 2.2 percent in 2022.

JAMA. 2024;331(7):613-615.

How common is CAM in autism?

28% reported any use;

17% report special diets;

20% report other CAM.

Higher rates of CAM use were associated with gastrointestinal symptoms, seizures, and externalizing behaviors.

Perrin JM, Coury DL, Hyman SL, Cole L, Reynolds AM, Clemons T. Complementary and alternative medicine use in a large pediatric autism sample. Pediatrics. 2012 Nov;130 Suppl 2:S77-82. doi: 10.1542/peds.2012-0900E. PMID: 23118257.

What is the basis for CAM treatments for ASD?

- Most CAM are based on theories of cause of ASD
- The CAM treatment then addresses this proposed cause
- Most evidence presented is anecdotal and / or testimonial; very little data
- Data presented is weak if present

What causes autism?

WE DON'T KNOW - but we know of many associated factors

Strong genetic component

Identical twins – if one has ASD, there is a 60 – 90% chance the other twin will have ASD

Several hundred candidate genes have been identified, but having one of these does not always result in ASD

Environmental influences are a concern

Increased exposure to air pollution

Vaccines DO NOT CAUSE AUTISM

- Dozens of studies across multiple countries have confirmed this

Thimerosal does not cause autism

- Institute of Medicine review failed to find an association between vaccines or thimerosal and autism (2003)
- Three articles in *Pediatrics* September 2004 failed to confirm relationship between thimerosal and autism

What are some CAM promoted for autism?

- Hyperbaric Oxygen Therapy (HBOT)
- Sauna treatments
- Nutritional treatments – diets, supplements
- Biofilm treatment
- Chelation of heavy metals
- These have been promoted over the past three decades

Hyperbaric Treatment for Autism

If you're struggling with autism and have not found answers, consider seeking help from Dr. Johnson.

Contact us today to learn more and schedule a consultation.

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COMPREHENSIVE AUTISM CARE WITH HYPERBARIC THERAPY

Conditions we treat

Emergency Conditions
Carbon Monoxide Poisoning
Neurological Conditions
Stroke Recovery and Treatment
Hyperbaric Treatment for Autism
Orthopedic Conditions
Scuba Diving Complications
Sports Injury
Traumatic Brain Injury & Concussion
Other FDA-Approved Conditions
Other Worldwide Uses

Accessed February 5, 2026

CHILLRx CRYOTHERAPY

Research Articles
Far-Infrared Saunas Help Reverse Autism

. . . everyone, including children, should be doing saunas – especially those with autism

HTTPS://REDBANK.CHILLCRYO.NET/RESEARCH/FAR-INFRARED-SAUNAS-HELP-REVERSE-AUTISM/

ACCESSED FEBRUARY 5, 2026

Current Popular Proposed Treatments for ASD

- Testing for heavy metals, vitamin levels, trace metals, mycotoxins
- Supplements
- Lab testing – folate receptor antibody, folate levels, genetic
- Leucovorin

Chelation of heavy metals

- Hypothesis: that individuals with autism spectrum disorder (ASD) have higher levels of toxic heavy metals in their systems than their peers
- However, this hypothesis is unproven.
- Associated hypothesis: mercury in vaccines causes vaccine
- This hypothesis has been disproved.
- Chelation is not approved for treating autism.
- Chelation has resulted in at least one death when used to treat autism.

Zeolite

Zeolite minerals contain mainly aluminum and silicon compounds

These are often used as drying agents and are used in products such as cat litter

Theory: this will attract and absorb toxins such as heavy metals and biotoxins in the GI tract, and will release calcium and magnesium in the process

The zeolite with the toxins is then excreted from the body

Special Diets

- Gluten free, casein free (GFCF) diet
- Specific carbohydrate diet (SCD)

Many people with ASD have selective diets, often due to sensory issues (food color, food texture, taste, smell).

Many studies have shown fecal bacteria populations are often different from those without ASD. This is often called gut dysbiosis.

Special diets aim to correct gut dysbiosis

Supplements

Many have been recommended for various reasons

- Magnesium – to promote sleep
- Vitamin D
- Zinc
- Vitamin A
- Turmeric – to reduce inflammation
- Curcumin – to reduce inflammation
- Probiotics

Vitamin D

2011 study – In NHANES adults the overall prevalence rate of vitamin D deficiency was 41.6%, with the highest rate seen in blacks (82.1%), followed by Hispanics (69.2%) (Forrest et al, 2011 PMID: 21310306.)

Meta-analyses consistently demonstrate that children with ASD have significantly lower vitamin D levels than typically developing controls

Clinical trial evidence suggests **modest improvements in behavioral functioning and hyperactivity** with vitamin D supplementation. Effects on core social communication symptoms remain inconsistent across studies.

Probiotics

- **Probiotics show modest but statistically significant improvements in behavioral symptoms of autism**, with multi-strain formulations appearing more effective than single-strain products.
- The evidence for gastrointestinal symptom improvement is stronger and more consistent than for core behavioral symptoms.
- Lactobacillus, Bifidobacterium, and Streptococcus strains show the most promise, with approximately 66% of studies reporting improvements in behavioral and gastrointestinal symptoms.

Lewandowska-Pietruszka Z, et al

Microbiota in Autism Spectrum Disorder: A Systematic Review.

International Journal of Molecular Sciences. 2023.

Folate, Folinic Acid, Cerebral Folate Deficiency and Neurodevelopment

- Role of folate in neurodevelopment well known; trials reported in 1980 and 1981 showed folate taken prenatally led to reduction in neural tube defect recurrence by 72%.
- Folic acid supplementation has been recommended by USPHS since 1992, and wheat flour has been fortified since 1998 with population reductions in spina bifida.

Cerebral folate deficiency (CFD)

Multiple disorders leading to reduced folate in CSF

Inherited defects in folate transporters can result in profound reductions in CSF folate

This can lead to severe neurocognitive and developmental deficits and intractable seizures

HOWEVER

- There is no established level for CSF folate below which neurocognitive deficits are consistently observed

Cerebral folate deficiency (CFD)

- There are two folate-specific transported systems in the choroid plexus that lead to CFD.
- FOLR1-CFTD is the one that FDA has announced as an indication for leucovorin
- Hereditary folate malabsorption is caused by PCFT (proton-coupled folate transporter). This form can cause CFD and also systemic folate deficiency
- There is no evidence linking variants or mutations of either gene with autism.

Cerebral folate deficiency (CFD)

Requires CSF to measure folate levels

There have been reports of autoantibodies to FOLR1 protein in autistic persons; this has suggested that these antibodies are impairing folate transport into CSF.

In those patients where CSF folate has been measured, levels were within normal range.

Some propose that high FOLR1 antibody titers could be a surrogate biomarker for CFD and could be used as an indication for leucovorin treatment

Most autism experts feel the evidence is inconclusive

What are some concerns about FRAT testing in autism?

Currently one lab where testing can be performed (Religen)

- Inability to verify results with another lab

Unclear correlation between serum FRAA levels and CSF MTHF

- Two types of autoantibody: blocking and binding
  - Some decrease with age, others don't
- Milk downregulates FRAA expression
- Wide variation between studies

The Folate Receptor Antibody Test (FRAT)

Not FDA certified; still considered experimental

Thus, insurance usually won't cover cost

Recall earlier points:

- Antibody test as surrogate for actual CSF folate level is conjecture
- Limited data has been inconsistent

Randomized Trials of Folinic Acid in Autism

First Author	Year	Participants	Reference
Frye, RE	2018	23 folinic acid; 25 placebo	Mol Psychiatry PMID 27752075
Renard, E	2020	9 folinic acid; 10 placebo	Biochimie PMID 32387472
Batebi, N	2021	28 folinic acid + risperidone; 27 placebo + risperidone	Child Psychiatr Hum Dev PMID 33029705
Panda, PK	2024	40 folinic acid; 40 placebo	Eur J Pediatr PMID 39243316 **RETRACTED 1/29/26**
Zhang, C	2025	49 folinic acid; 27 placebo	Nutrients PMID 40362912

149 treated – 40 retracted = 109 treated
28 also treated with risperidone = 81 treated without other medication reported

Compiling the Literature

- Findings
  - Children with ASD *may* be more likely to have increased FRAA than TD children*
  - Leucovorin *may* improve verbal communication for *some* children*
    - Effect more pronounced for autistic children with higher FRAA levels
    - Serum FRAA levels are *inconsistently* inversely correlated with CSF 5-MTHF
  - Leucovorin mostly well tolerated, but follow-up periods short

Characteristics of Current FRAA/Leucovorin Studies

single site studies; N is often < 50

Leucovorin often used in combo with other supps.

Wide variety of outcome measures used

- Hard to compare across groups
- **Large heterogeneity!**

Self referential

Inconsistency with intention to treat analysis

Follow up periods often 1 year or less

What are some concerns about leucovorin use in autism?

- Uncertainty about dosing
- No phase 3 clinical trials conducted
- Uncertainty about duration of treatment
- Uncertainty regarding side effects
- Opportunity Cost
- Potential Shortage Issues
- Cost/Lack of Insurance Coverage

NEJM
Jan.21, 2026

"any future expansion of FDA approval for leucovorin to include autism must be based on evidence from large-scale, well designed clinical trials that include biomarker measurements, appropriate clinical end points, and preregistration analysis plan, with the final data made available to the scientific community for independent analysis and comment. "

Studies using FOLR1 autoantibodies as a biomarker for CFD and leucovorin response in autism should also include CSF folate measurements to establish whether FOLR1 antibodies are in fact indicative of a substantial reduction in CSF folate levels.

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Cerebral Folate Deficiency, Autism, and the Role of Leucovorin

I. David Goldman, M.D.,[1] and Bruce A. Chabner, M.D.[2,3]

Position Statements

- American Academy of Pediatrics
- Society for Developmental and Behavioral Pediatrics
- Coalition of Autism Scientists
- Autism Science Foundation

Resources

- Association for Science in Autism Treatment (ASAT) (asatonline.org)
- Autism Science Foundation (autismsciencefoundation.org)
- Autism Speaks (autismspeaks.org)
- Organization for Autism Research (researchautism.org)