

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

The Diet Factor in Attention-Deficit/Hyperactivity Disorder

J. Gordon Millichap and Michelle M. Yee

Pediatrics; originally published online January 9, 2012;

DOI: 10.1542/peds.2011-2199

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/early/2012/01/04/peds.2011-2199>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2012 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



The Diet Factor in Attention-Deficit/Hyperactivity Disorder

AUTHORS: J. Gordon Millichap, MD, and Michelle M. Yee, CPNP

Division of Neurology, Children's Memorial Hospital, and Department of Pediatrics, Northwestern University Medical School, Chicago, Illinois

KEY WORDS

additive-free, attention, behavior, diet, elimination, hyperactivity, iron, ketogenic, oligoantigenic, omega-3, pediatrics, sucrose, zinc

ABBREVIATIONS

ADHD—attention-deficit/hyperactivity disorder

EFA—essential fatty acids

EPD—enzyme-potentiated desensitization

IGg—immunoglobulin G

LC—long chain

PUFA—polyunsaturated fatty acids

Dr Millichap reviewed the literature; researched and selected appropriate articles; and organized, drafted, and revised the manuscript in its final version. Nurse Practitioner Yee is clinical associate to the neurology clinic for attention-deficit/hyperactivity disorder. Yee assisted in the selection of articles and references, collected the data for the table of ω supplements, read the manuscript, and made suggestions for revision in its final form.

www.pediatrics.org/cgi/doi/10.1542/peds.2011-2199

doi:10.1542/peds.2011-2199

Accepted for publication Oct 5, 2011

Address correspondence to J. Gordon Millichap, MD, Division of Neurology, Children's Memorial Hospital, 2300 Children's Plaza, Box 51, Chicago, IL 60614. E-mail: gmillichap@childrensmemorial.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2012 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

abstract

This article is intended to provide a comprehensive overview of the role of dietary methods for treatment of children with attention-deficit/hyperactivity disorder (ADHD) when pharmacotherapy has proven unsatisfactory or unacceptable. Results of recent research and controlled studies, based on a PubMed search, are emphasized and compared with earlier reports. The recent increase of interest in this form of therapy for ADHD, and especially in the use of omega supplements, significance of iron deficiency, and the avoidance of the “Western pattern” diet, make the discussion timely.

Diets to reduce symptoms associated with ADHD include sugar-restricted, additive/preservative-free, oligoantigenic/elimination, and fatty acid supplements. Omega-3 supplement is the latest dietary treatment with positive reports of efficacy, and interest in the additive-free diet of the 1970s is occasionally revived. A provocative report draws attention to the ADHD-associated “Western-style” diet, high in fat and refined sugars, and the ADHD-free “healthy” diet, containing fiber, folate, and omega-3 fatty acids.

The literature on diets and ADHD, listed by PubMed, is reviewed with emphasis on recent controlled studies. Recommendations for the use of diets are based on current opinion of published reports and our practice experience. Indications for dietary therapy include medication failure, parental or patient preference, iron deficiency, and, when appropriate, change from an ADHD-linked Western diet to an ADHD-free healthy diet. Foods associated with ADHD to be avoided and those not linked with ADHD and preferred are listed.

In practice, additive-free and oligoantigenic/elimination diets are time-consuming and disruptive to the household; they are indicated only in selected patients. Iron and zinc are supplemented in patients with known deficiencies; they may also enhance the effectiveness of stimulant therapy. In patients failing to respond or with parents opposed to medication, omega-3 supplements may warrant a trial. A greater attention to the education of parents and children in a healthy dietary pattern, omitting items shown to predispose to ADHD, is perhaps the most promising and practical complementary or alternative treatment of ADHD. *Pediatrics* 2012;129:1–8

The role of diet and dietary supplements in the cause and treatment of attention-deficit/hyperactivity disorder (ADHD) in children is controversial, but the topic continues to interest parents and physicians who prefer an alternative to stimulant medication or seek a complementary therapy. Although prescription of medications for ADHD has shown a steady increase since their introduction in the 1960s, the popularity of various diets has risen and/or fallen in the same time period, sometimes showing a Phoenician revival. In the selection of a therapy for ADHD, physicians generally prefer a medication of value proven by controlled trial. Diets are more difficult to evaluate, and trials requiring elimination of certain foods and dyes may need the supervision of physician and dietician. The list of proposed dietary treatments includes sugar-restricted, additive- and salicylate-free (Feingold diet), oligoantigenic (elimination), ketogenic, megavitamin, and polyunsaturated fatty acid supplements (PUFA) diets. The PUFA or omega-3 supplement is the latest dietary ADHD treatment to receive positive reports, whereas the additive-free Feingold diet that enjoyed its initial popularity in the 1980s shows an occasional, smoldering revival, especially in the United Kingdom, Europe, and Australia. A recent provocative publication from Australia, the Raine study, links ADHD in adolescents with a "Western-style" dietary pattern, high in fat, refined sugars, and sodium and low in fiber, folate, and omega-3 fatty acids.¹ This review focuses on the literature concerning diets and ADHD selected from a PubMed search. Results of recent research and controlled studies are emphasized. Diet recommendations in practice are based on the data presented and on our experience in a neurology clinic for children and adolescents with ADHD. In addition to pharmacotherapy, alternative and/or complementary methods may warrant trial, including

a "healthy" diet pattern,¹ elimination of dyes or food antigens, or omega-3 PUFA supplementation.

OMEGA-3 AND -6 FATTY ACID SUPPLEMENTS

Low levels of long-chain (LC) PUFA are reported in the plasma and red cells of children with ADHD compared with controls.^{2,3} The potential mechanisms leading to abnormal essential fatty acid (EFA) levels in ADHD patients may include reduced EFA intake, reduced conversion of EFA to LC-PUFAs and increased metabolism of LC-PUFAs.⁴ These and other similar reports prompted trials of PUFA supplements in treatment of children with ADHD and learning problems.

A frequently cited trial, the Oxford-Durham study,⁵ compared the effects of dietary supplementation with omega-3 and omega-6 (in a ratio of 80% to 20%) to placebo in 117 children with developmental coordination disorder, one-third having symptoms of ADHD. Comparing the Conners' Teacher Rating Scale-L/ADHD scores, a reduction and improvement of >0.5 SD occurred during the 3-month treatment phase, whereas no change was seen in the placebo group ($P < .0001$). During a 3- to 6-month follow-up phase, a gain in reading was 3 times that expected, and

spelling advanced twice that expected. Incoordination, a common ADHD comorbidity, was not benefited. No adverse effects were reported.⁵ Although the primary aim of this study directed toward alleviation of incoordination was not met, the results demonstrate a reduction of symptoms of ADHD, an effect duplicated in other PUFA supplement trials.^{6,7} However, some studies fail to show a beneficial PUFA response,^{8,9} leading to the hypothesis of a genetically impaired fatty acid metabolism in some ADHD patients.^{10,11}

Review of 16 studies of PUFA blood levels and PUFA dietary supplementation in children with ADHD found only isolated reports from 1995 to 2006 and a flurry of interest from 2007 through 2011. Heterogeneity of design and other factors may have influenced responses and results: the type and dose of fatty acid employed (omega-3 or omega-6 or combination), method of administration, duration of treatment, and measurement of response.

On the basis of reports of efficacy and safety, we use doses of 300 to 600 mg/day of omega-3 and 30 to 60 mg/day of omega-6 FAS, continued for 2 or 3 months, or longer if indicated. Table 1 lists a sample of fatty acid supplements available and the quantities of omega-3, -6, and -9 in each. The wide variation in omega-3

TABLE 1 Omega Fatty Acid Supplements for Treatment of Children with ADHD

Supplement	Omega-3	Omega-6	Omega-9
Nordic Gummy Bears (3)	82 mg (EPA 41 mg, DHA 27 mg, other 14 mg)		
Nordic Fishes Chews (3)	136 mg (EPA 68 mg, DHA 45 mg, other 23 mg)		
Nordic ProEFA (2 softgels)	565 mg (EPA 270 mg, DHA 180 mg, other 115 mg)	224 mg LA	244 mg OA
MegaRed Krill Oil (1 softgel)	90 mg (EPA 45 mg, DHA 27 mg)		
Nutrigold (1 softgel)	380 mg (EPA 120 mg, DHA 80 mg, ALA 180 mg)	184 mg LA 76 mg GLA	100 mg OA
Nature Made 1200 mg soft gel	360 mg (EPA 180 mg, DHA 120 mg, Other 60 mg)		
Oxford/Durham study ⁵	732 mg daily (EPA 558 mg, DHA 174 mg)	60 mg GLA daily	

ALA, α -linolenic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; GLA, γ -linolenic acid; LA, linoleic acid; OA, oleic acid.

content is noteworthy. As initial or add-on therapy, we have occasional reports of improved school grades and lessening of symptoms of ADHD, without occurrence of adverse effects. Most parents are enthusiastic about trying the diet supplements, despite our explanation of only possible benefit and lack of proof of efficacy. In almost all cases, for treatment to be managed effectively, medication is also required. Additional controlled studies of PUFA are warranted, including larger numbers of patients with different age ranges (young and older children), as well as various doses of omega-3 and omega-6 fatty acid, monitored with blood levels. Subjects with and without EFA deficiency should be distinguished. We agree with other investigators¹² that although a link exists between low LC-PUFA and ADHD, the beneficial effects of omega-3 and omega-6 supplements are not clearly demonstrated.

ADDITIVE AND SALICYLATE-FREE (FEINGOLD) DIET

The history of the Feingold diet is well known to physicians who practiced in the 1970s.¹³ Amelioration of symptoms was claimed in >50% of hyperactive children treated. The enthusiasm generated by the media led to parental advocacy groups, necessitating federally supported scientific trials. Controlled studies failed to confirm the effectiveness of the diet to the extent claimed.^{14,15} Nevertheless, a small subgroup of preschool children responded adversely to additives and preservatives administered as a challenge.¹⁶ An occasional child might react adversely to dyes and preservatives in foods and might benefit from their elimination.

Interest in additives in relation to ADHD has waned in the United States. In the decade 1979–1988, a PubMed search lists 20 pertinent articles; in the 2 decades from 1990 through 2010, only 2 are recorded. Articles appearing in

2010–2011 point to a renewed interest in food additives and ADHD.^{17–19} In the latest article,¹⁹ referring to 35 years of research on dietary sensitivities and ADHD symptoms, a literature review shows that of children with suspected sensitivities, 65% to 89% react when challenged with 100 mg of artificial food colors. In addition to being sensitive to these additives, some children are sensitive to common nonsalicylic foods, and cosensitivity is more the rule than the exception. A trial combination antigen- and additive-free diet may be appropriate therapy for children with sensitivities to food antigens or allergens and to dyes.^{20,21} Atopic children with ADHD have a significantly higher response rate to a multiple-item elimination (foods, artificial colorings, and preservatives) diet than does a nonatopic group.²²

According to the Feingold diet,¹³ foods to be avoided include apples, grapes, luncheon meats, sausage, hot dogs, and cold drinks containing artificial flavors and coloring agents. Red and orange synthetic dyes are especially suspect, as well as preservatives, butylated hydroxytoluene and butylated hydroxyanisole. Foods permitted include grapefruit, pears, pineapple, and bananas, beef and lamb, plain bread, selected cereals, milk, eggs, and vitamins free of coloring. A parent wishing to follow this diet needs patience, perseverance, and frequent evaluation by an understanding physician and dietician. The same degree of patience and follow-up is required with the oligoantigenic (elimination) diet for ADHD.

OLIGOANTIGENIC (HYPOALLERGENIC/ELIMINATION) DIET

An oligoantigenic diet eliminates most known sensitizing food antigens or allergens. Foods often found to be allergenic include cow's milk, cheese, wheat cereals, egg, chocolate, nuts, and

citrus fruits. Examples of hypoallergenic foods include lamb, potato, tapioca, carrots, peas, and pears. Skin tests for allergic reactivity to foods are unreliable, and elimination diets are required to test for specific food intolerances. An early controlled trial of an oligoantigenic diet in 76 hyperkinetic children found that symptoms improved in 62 (82%), and normal behavior was achieved in 22 (29%).²³ The diet consisted of 2 meats (lamb and chicken), 2 carbohydrates (rice and potatoes), 2 fruits (banana and apple), vegetables and calcium and vitamins for 4 weeks. A subsequent double-blind study, using a "few foods" elimination diet, reported improvement in 76% patients and worsening of behavior ratings and cognitive tests after provoking food challenge.²⁴

The term "elimination diet" is now more popular than "oligoantigenic," with PubMed listing 14 articles under the former and 4 using the latter title, the majority from the United Kingdom and Europe. Interest in the oligoantigenic/elimination diet has increased, but studies have provided mixed opinions of efficacy. A partial benefit of the diet was demonstrated in a small cohort of 21 children tested with both subjective and objective measures.²⁵ The effect was significant for subjective, but not objective, measures. The oligoantigenic diet may influence only certain dimensions of the ADHD syndrome.

A more favorable effect followed a few foods elimination diet (containing rice, turkey, pear, and lettuce) in 40 children, 36 boys and 4 girls, aged 3 to 7 years, diagnosed with ADHD.²⁶ Twenty-five patients (62%) showed an improvement in behavior of $\geq 50\%$, 9 (23%) withdrew from the study, and 10 (25%) had improved parent and teacher ratings. In this controlled study, the elimination diet resulted in a statistically significant decrease in symptoms of ADHD.

The effectiveness of the diet is demonstrated by a larger randomized controlled

trial in an unselected group of 100 children²⁷ in the Impact of Nutrition on Children with ADHD study in the Netherlands. This study consisted of an open-label phase (phase 1; 5 weeks of a restricted elimination diet or healthy control diet) followed by a double-blind crossover, challenge phase (phase 2). Responders to challenge with high- or low immunoglobulin (Ig) G foods showed an increase of 20.8 points on the ADHD rating scale ($P < .0001$) and an 11.6 increase of a Conners' Score ($P < .0001$). After the challenge, relapse of ADHD symptoms occurred in 19 of 30 (63%) children, independent of the IgG blood levels.

The utility of IgG blood tests is unsupported, but the effectiveness of a supervised, restricted elimination diet is an indication of the influence of food on ADHD. For some investigators, however, the role of the elimination diet in the treatment of ADHD remains uncertain.^{28,29} The report generated criticism that the study did not permit the unqualified recommendation of dietary treatment in all children with ADHD,³⁰ and a placebo effect could not be excluded.³¹

The diagnosis of food sensitivity is complex, time-consuming, and sometimes too burdensome for patient, family, and physician. In selected patients with diligent parents, a short 2- to 3-week period of restricted elimination diet is justified. In patients benefited by the diet, restricted foods are introduced each week, 1 at a time, until the offending item or items are identified. Improvements in behavior may be delayed for 10 days to 2 weeks, and food preferred and consumed most is often the offending item.

FOOD ANTIGEN DESENSITIZATION

Terms used for food intolerance include "food sensitivity," "food allergy," or "food hypersensitivity," and "psychologically determined food aversions."³² Food allergy was investigated by a trial of enzyme-potentiated desensitization (EPD) in 40 children with food-induced

hyperkinetic behavior disorder.³³ Of 20 who received active EPD treatment, 16 became tolerant of provoking foods compared with 4 of 20 taking placebo ($P < .001$). EPD permitted children to eat foods previously known to provoke symptoms. Food allergy is a possible mechanism of the hyperkinetic syndrome, and research involving the influence of food triggers could inform clinicians on viable alternative and/or supportive immunotherapy.³⁴

SUGAR, ASPARTAME, AND ADHD

Parents of children with ADHD frequently report a worsening of hyperactivity after an excessive ingestion of candy or diet soda. Isolated reports support the parents' observations, but the majority of controlled studies fail to demonstrate a significant adverse effect of sucrose or aspartame. A PubMed search for "sugar, aspartame, and ADHD" listed 8 articles, dated 1984 through 1995. In a controlled trial involving preschool and school-age children described by parents as sensitive to sugar, diets high in sucrose or containing aspartame and free of additive had no effect on children's behavior or cognitive function.³⁵ This article provoked much correspondence, mainly critical of the negative conclusion.

The authors' subsequent meta-analysis of 16 reported studies, identified through Medline and PsychINFO databases, concluded that sugar does not usually affect the behavior or cognitive performance of children, but a small effect on subsets of children cannot be ruled out.³⁶ In preschool boys aged 2 to 6 years rated by parents as "sugar responders" and "nonresponders," neither acute sugar loading nor aspartame increased activity level or aggression, but the daily sucrose intake and total sugar consumption correlated with duration of aggression.³⁷ Inattention was increased after sugar intake, but not aspartame or saccharine. The sugar and placebo challenges were given

with a breakfast high in carbohydrate, a possible reason for the adverse effect of the sucrose challenge.³⁸ The hyperactive response is blocked if a protein meal is ingested before or with the sugar.³⁹

Reactive Hypoglycemic Response to Sugar Load

An alternative explanation for sugar-induced cognitive impairment and inattention may be a reactive hypoglycemia. Compared with adults, children are more vulnerable to the effects of hypoglycemia on cognitive function. A measure of cognitive function using auditory evoked potentials was significantly reduced when blood glucose was lowered <75 mg/dL in children but was preserved in adults until the level fell to 54 mg/dL.⁴⁰ Aspartame used as a control had no adverse effects on behavior or cognition in children with attention-deficit disorder.⁴¹ The avoidance of rapidly absorbed sucrose-containing foods in young children may prevent diet-related exacerbations of ADHD.

In a study of adolescents with insulin-dependent diabetes mellitus, mild hypoglycemia (60 mg/dL) caused a significant transient decline in performance of a battery of cognitive tests, whereas hyperglycemia had no effect.⁴² The frontal cortex, known to be involved in the control of attention, was more highly activated than other brain regions during acute hypoglycemia.⁴³ Children with food-induced ADHD show an increase in β activity in frontotemporal areas during EEG topographic mapping of brain electrical activity after ingestion of provocative foods.⁴⁴

Sugar and the EEG

The effects of sugar and especially hypoglycemia on the EEG have been studied since the late 1930s.^{45,46} Low blood sugar levels are associated with an impairment of the normal electrical activity of the cerebral cortex. A deficiency of glucose to the brain causes the

appearance of slow rhythms in the EEG, with fall in the dominant α frequency and appearance of θ and finally δ frequency. It is not surprising that a sugar load would cause an increase in faster β rhythms in the EEG.⁴⁴ An electrophysiologic approach, using EEG biofeedback (neurofeedback), in support of a possible relation between sugar and symptoms of ADHD requires additional study. However, studies of EEG biofeedback in the treatment of ADHD provide mixed results and possible benefit, with improvement in only selected attentional brain functions.⁴⁷

In practice, the link between sugar and hyperactive behavior is so universal in the opinion of parents of children with ADHD that no controlled study or physician counsel is likely to change this perception. Parents will continue to restrict the allowance of candy for their hyperactive child at Halloween in the belief that this will curb the level of exuberant activity, an example of the Hawthorne effect. The specific type of therapy or discipline may be less important than the attention provided by the treatment.²¹

The Ketogenic Diet and ADHD

The ketogenic diet, a diet high in fat content and low in carbohydrate, was introduced for the treatment of epilepsy in 1921.⁴⁸ The mechanism is still unclear, but metabolic balance studies in children with absence seizures show that the antiepileptic effect of the diet is correlated closely with a negative balance of sodium and potassium.⁴⁹ The re-introduction of carbohydrate to the diet is associated with recurrence of spike-and-wave epileptiform discharges in the EEG. In 65 children with intractable seizures, treatment with the ketogenic diet was effective in control of seizures at 1-year follow-up, and developmental quotients, behavior, attention, and social functioning were significantly improved.⁵⁰

Children with epilepsy frequently exhibit symptoms of ADHD, and children with

ADHD have a high frequency of epileptiform discharges in the EEG.⁵¹ Animals receiving a ketogenic diet show a reversible decrease in activity level.⁵² The EEG, of value in prediction of a sustained anticonvulsant effect,⁵³ may also prove indicative of a behavioral response to the ketogenic diet.

IRON DEFICIENCY AND ADHD

Iron deficiency is associated with a number of neurologic disorders, including breath-holding, restless leg syndrome, and febrile seizures. A report of low serum ferritin in children with cognitive and learning disorders⁵⁴ prompted the inclusion of a serum ferritin level in the battery of laboratory tests obtained on patients attending our neurology clinic for ADHD. In our hospital laboratory, the range of control serum ferritin levels is 300 ng/mL with a low of 22 ng/mL in males and 10 ng/mL in females. In 68 consecutive patients (aged 5–16 years; 54 male, 14 female), the mean serum ferritin level in patients with ADHD was 39.9 ng/mL and was not different from control subjects. Twelve (18%) patients had values <20 ng/mL that were considered abnormal and suggestive of iron deficiency without anemia, and a similar number had levels >60 ng/mL and were not iron deficient. A comparison of clinical characteristics of the low-ferritin and high-ferritin groups disclosed no significant difference in severity or frequency of ADHD and comorbid symptoms or response to drug therapy. In this patient cohort, a causative role for low serum ferritin and iron deficiency in ADHD was not confirmed.⁵⁵

In an earlier study of the effects of iron supplements in ADHD children in Israel, a significant increase in serum ferritin levels (25.9–44.6 ng/mL) was associated with a significant decrease in the Conners' Parent Rating Scale but not in the Teachers' Rating Scales.⁵⁶ In later studies of children with ADHD in France, the proportion with low (<30 ng/mL)

and very low (<15 ng/mL) serum ferritin levels was greater than that of our patients in the United States: 84% versus 32%.⁵⁷ Low serum ferritin levels were correlated with more severe ADHD symptoms measured with Conners' Parent Rating Scale and greater cognitive deficits. A trial of iron supplementation found improvements in behavior rating scales, but this finding did not reach significance.⁵⁸

A threshold effect may be important in the evaluation of a proposed causative role of iron deficiency in ADHD, and additional controlled studies are probably warranted. The unusually low ferritin levels (mean: 18.4 ng/mL; 23% participants <7 ng/mL) encountered in a recent study of ADHD children in Iowa City may explain the observed correlation with ADHD symptom scores.⁵⁹ Low serum ferritin was correlated with baseline inattention, hyperactivity, and impulsivity and also with the dose of amphetamine required to optimize a clinical response. Serum ferritin and iron supplementation as potential predictor or intervention to optimize stimulant therapy is a novel indication for additional study of iron deficiency and ADHD.

ZINC DEFICIENCY AND ADHD

Published reports of the role of zinc in ADHD show low zinc levels in serum, red cells, hair, urine, and nails of affected children.⁶⁰ Most reports are from the Middle Eastern countries, Turkey and Iran, areas with suspected endemic zinc deficiency. Two placebo-controlled trials, one of zinc monotherapy and the other of zinc supplementation of methylphenidate, report significant benefit.^{61,62} In one study involving children in the United States, low serum zinc levels correlated with parent/teacher-rated inattention but not with hyperactivity/impulsivity.⁶³ Zinc supplements enhanced the benefit from d-amphetamine; the optimal dose of stimulant was 37% lower with zinc than with placebo.⁶⁴

Zinc is a cofactor for metabolism of neurotransmitters and fatty acids and also regulates dopamine metabolism involved in ADHD. The relationship of zinc to EFA supplements and stimulants evaluated in treatment of ADHD found that the d-amphetamine response was linear with zinc nutrition. Fatty acids may benefit ADHD by improving or compensating for borderline zinc nutrition.⁶⁵ Although zinc supplements are of value in treatment of Middle Eastern children with ADHD associated with endemic zinc deficiency, the incorporation of zinc in the therapy of ADHD in the United States is less well defined.

OTHER ALTERNATIVE DIETARY THERAPIES FOR ADHD

The concept of orthomolecular (“right molecule”) medicine and megavitamin therapy refers to the use of a combination of nutrients and minerals alleged to provide the optimum molecular environment for the mind. The treatment, subsequently advocated for children with hyperactivity, as well as for mental retardation and Down’s syndrome,⁶⁶ is of unproven value.

In a double-blind crossover study of megavitamin therapy in 41 children with ADHD, no significant improvement was demonstrated in behavior scores, and 25% were more disruptive ($P < .01$).⁶⁷ Serum transaminase levels exceeded the upper limits of normal in 42% children while receiving vitamins. Megadoses of some vitamins are not without danger of hepatotoxicity, and their efficacy is unconfirmed. Mineral analyses, especially iron and zinc, may be warranted in children with

ADHD and learning disorders, but the need for adequate controls and blood levels is emphasized. Treatment based on inaccurate measurement techniques may lead to adverse reactions.²¹

“HEALTHY” DIET PATTERN IN PREVENTION AND TREATMENT OF ADHD

In the Australian Raine study, the relationship between dietary patterns and ADHD was examined in a population-based cohort of live births followed to age 14.¹ Two major dietary patterns were identified as “Healthy” and “Western,” according to foods considered the main contributors. (Table 2) The Western dietary pattern associated with an ADHD diagnosis contains higher intakes of total fat, saturated fat, refined sugars, and sodium and is deficient in omega-3 fatty acids, fiber, and folate. The Healthy diet pattern, not associated with ADHD diagnosis, is rich in fish, vegetables, fruit, legumes, and whole-grain foods. A higher risk of having an ADHD diagnosis, inattentive or combined types, is observed for boys compared with girls. The major specific foods in a Western diet are also contributory to an increased tendency to obesity among nonmedicated ADHD children and adolescents.⁶⁸

The relationship between a Western dietary pattern and ADHD may be mediated by other factors, such as poor family functioning and emotional distress, leading to a craving for fat-rich snack foods. Whatever the specific cause, a modification of the child’s dietary pattern may offer an alternative

TABLE 2 Foods to Avoid and Foods Preferred in Children with ADHD

“ADHD-associated” Foods to Avoid	“Healthy” Foods: Preferred
Takeaway fast foods	Fish, steamed, grilled or canned
Red meat	Vegetables
Processed meats	Tomato
Crisps, potato chips	Fresh fruit
High-fat dairy products	Whole grains
Soft drinks	Low-fat dairy products

Based on Howard AL et al.¹

method of treatment of ADHD and less reliance on medications.

SUMMARY AND CONCLUSIONS

Various alternative therapies for ADHD are offered as substitutes or supplements to medication and behavioral treatments. The evaluation of claims for therapies in a disorder such as ADHD, without a single, well-defined cause, is a scientific challenge requiring controls and appropriate neuropsychological testing. The indications for diet therapy include the following: (1) medication failure or adverse reaction, (2) parent or patient preference, (3) symptoms or signs of mineral deficiency, and (4) the need to substitute an ADHD-free healthy diet for an ADHD-linked diet.¹ Diet is one environmental etiology of ADHD that is amenable to modification.⁶⁹

Oligoantigenic, elimination, and additive-free diets are complicated, disruptive to the household, and often impractical, except for selected patients. Supplemental diet therapy is simple, relatively inexpensive, and more acceptable to patient and parent. Public education regarding a healthy diet pattern and lifestyle to prevent or control ADHD may have greater long-term success.

REFERENCES

- Howard AL, Robinson M, Smith GJ, Ambrosini GL, Piek JP, Oddy WH. ADHD is associated with a “Western” dietary pattern in adolescents. *J Atten Disord*. 2011;15(5):403–411
- Mitchell EA, Aman MG, Turbott SH, Manku M. Clinical characteristics and serum essential fatty acid levels in hyperactive children. *Clin Pediatr (Phila)*. 1987;26(8):406–411
- Colter AL, Cutler C, Meckling KA. Fatty acid status and behavioral symptoms of attention deficit hyperactivity disorder in adolescents: a case-control study. *Nutr J*. 2008;7:8
- Burgess JR, Stevens L, Zhang W, Peck L. Long-chain polyunsaturated fatty acids in children with attention-deficit hyperactivity disorder. *Am J Clin Nutr*. 2000;71(suppl 1):327S–330S
- Richardson AJ, Montgomery P. The Oxford-Durham study: a randomized, controlled

- trial of dietary supplementation with fatty acids in children with developmental coordination disorder. *Pediatrics*. 2005;115(5):1360–1366
6. Sinn N, Bryan J. Effect of supplementation with polyunsaturated fatty acids and micronutrients on learning and behavior problems associated with child ADHD. *J Dev Behav Pediatr*. 2007;28(2):82–91
 7. Johnson M, Ostlund S, Fransson G, Kadesjö B, Gillberg C. Omega-3/omega-6 fatty acids for attention deficit hyperactivity disorder: a randomized placebo-controlled trial in children and adolescents. *J Atten Disord*. 2009;12(5):394–401
 8. Voigt RG, Llorente AM, Jensen CL, Fraley JK, Berretta MC, Heird WC. A randomized, double-blind, placebo-controlled trial of docosahexaenoic acid supplementation in children with attention-deficit/hyperactivity disorder. *J Pediatr*. 2001;139(2):189–196
 9. Hirayama S, Hamazaki T, Terasawa K. Effect of docosahexaenoic acid-containing food administration on symptoms of attention-deficit/hyperactivity disorder—a placebo-controlled double-blind study. *Eur J Clin Nutr*. 2004;58(3):467–473
 10. Ng K-H, Meyer BJ, Reece L, Sinn N. Dietary PUFA intakes in children with attention-deficit/hyperactivity disorder symptoms. *Br J Nutr*. 2009;102(11):1635–1641
 11. Brookes KJ, Chen W, Xu X, Taylor E, Asherson P. Association of fatty acid desaturase genes with attention-deficit/hyperactivity disorder. *Biol Psychiatry*. 2006;60(10):1053–1061
 12. Chalou S. The role of fatty acids in the treatment of ADHD. *Neuropharmacology*. 2009;57(7–8):636–639
 13. Feingold BF. *Why Your Child Is Hyperactive*. New York, NY: Random House; 1975
 14. Conners CK, Goyette CH, Southwick DA, Lees JM, Andrulonis PA. Food additives and hyperkinesis: a controlled double-blind experiment. *Pediatrics*. 1976;58(2):154–166
 15. Harley JP, Ray RS, Tomasi L, Eichman PL, Matthews CG, Chun Ret al. Hyperkinesis and food additives: testing the Feingold hypothesis. *Pediatrics*. 1978;61(6):818–828
 16. Harley JP, Matthews CG, Eichman P. Synthetic food colors and hyperactivity in children: a double-blind challenge experiment. *Pediatrics*. 1978;62(6):975–983
 17. Connolly A, Hearty A, Nugent A, et al. Pattern of intake of food additives associated with hyperactivity in Irish children and teenagers. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess* 2010;27(4):447–456.
 18. Stevenson J, Sonuga-Barke E, McCann D, Grimshaw K, Parker KM, Rose-Zerilli MJet al. The role of histamine degradation gene polymorphisms in moderating the effects of food additives on children's ADHD symptoms. *Am J Psychiatry*. 2010;167(9):1108–1115
 19. Stevens LJ, Kuczek T, Burgess JR, Hurt E, Arnold LE. Dietary sensitivities and ADHD symptoms: thirty-five years of research. *Clin Pediatr (Phila)*. 2011;50(4):279–293
 20. Millichap JG. *Nutrition, Diet, and Your Child's Behavior*: Springfield, IL: Charles C Thomas; 1986
 21. Millichap JG. *Attention Deficit Hyperactivity Disorder Handbook. A Physician's Guide to ADHD*. 2nd ed. New York, NY: Springer; 2010
 22. Boris M, Mandel FS. Foods and additives are common causes of the attention deficit hyperactive disorder in children. *Ann Allergy*. 1994;72(5):462–468
 23. Egger J, Carter CM, Graham PJ, Gumley D, Soothill JF. Controlled trial of oligoantigenic treatment in the hyperkinetic syndrome. *Lancet*. 1985;1(8428):540–545
 24. Carter CM, Urbanowicz M, Hemsley R, et al. Effects of a few food diet in attention deficit disorder. *Arch Dis Child*. 1993;69(5):564–568
 25. Schulte-Körne G, Deimel W, Gutenbrunner C, et al. [Effect of an oligo-antigen diet on the behavior of hyperkinetic children]. *Z Kinder Jugendpsychiatr Psychother*. 1996;24(3):176–183
 26. Pelsser LM, Buitelaar JK. [Favourable effect of a standard elimination diet on the behavior of young children with attention deficit hyperactivity disorder (ADHD): a pilot study]. *Ned Tijdschr Geneesk*. 2002;146(52):2543–2547
 27. Pelsser LM, Frankena K, Toorman J, et al. Effects of a restricted elimination diet on the behaviour of children with attention-deficit hyperactivity disorder (INCA study): a randomised controlled trial. *Lancet*. 2011;377(9764):494–503
 28. Mullins RJ, Tang MLK, Dear K. Restricted elimination diet for ADHD. *Lancet*. 2011;377(9777):1567–, author reply 1568
 29. Ghuman JK. Restricted elimination diet for ADHD: the INCA study. *Lancet*. 2011;377(9764):446–448
 30. Adesman A. Restricted elimination diet for ADHD. *Lancet*. 2011;377(9777):1567–, author reply 1568
 31. Poulton AS, Babajanyan A, Nanan R. Restricted elimination diet for ADHD. *Lancet*. 2011;377(9777):1567–1568, author reply 1568
 32. Ferguson A. Definitions and diagnosis of food intolerance and food allergy: consensus and controversy. *J Pediatr*. 1992;121(5 Pt 2):S7–S11
 33. Egger J, Stolla A, McEwen LM. Controlled trial of hyposensitisation in children with food-induced hyperkinetic syndrome. *Lancet*. 1992;339(8802):1150–1153
 34. Pelsser LM, Buitelaar JK, Savelkoul HF. ADHD as a (non) allergic hypersensitivity disorder: a hypothesis. *Pediatr Allergy Immunol*. 2009;20(2):107–112
 35. Wolraich ML, Lindgren SD, Stumbo PJ, Stegink LD, Appelbaum MI, Kiritzy MC. Effects of diets high in sucrose or aspartame on the behavior and cognitive performance of children. *N Engl J Med*. 1994;330(5):301–307
 36. Wolraich ML, Wilson DB, White JW. The effect of sugar on behavior or cognition in children. A meta-analysis. *JAMA*. 1995;274(20):1617–1621
 37. Kruesi MJ, Rapoport JL, Cummings EM, et al. Effects of sugar and aspartame on aggression and activity in children. *Am J Psychiatry*. 1987;144(11):1487–1490
 38. Wender EH, Solanto MV. Effects of sugar on aggressive and inattentive behavior in children with attention deficit disorder with hyperactivity and normal children. *Pediatrics*. 1991;88(5):960–966
 39. Yehuda S. Nutrients, brain biochemistry, and behavior: a possible role for the neuronal membrane. *Int J Neurosci*. 1987;35(1–2):21–36
 40. Jones TW, Borg WP, Boulware SD, McCarthy G, Sherwin RS, Tamborlane WV. Enhanced adrenomedullary response and increased susceptibility to neuroglycopenia: mechanisms underlying the adverse effects of sugar ingestion in healthy children. *J Pediatr*. 1995;126(2):171–177
 41. Shaywitz BA, Sullivan CM, Anderson GM, Gillespie SM, Sullivan B, Shaywitz SE. Aspartame, behavior, and cognitive function in children with attention deficit disorder. *Pediatrics*. 1994;93(1):70–75
 42. Gschwend S, Ryan C, Atchison J, Arslanian S, Becker D. Effects of acute hyperglycemia on mental efficiency and counterregulatory hormones in adolescents with insulin-dependent diabetes mellitus. *J Pediatr*. 1995;126(2):178–184
 43. Smid HG, Trümper BG, Pottag G, et al. Differentiation of hypoglycaemia induced cognitive impairments. An electrophysiological approach. *Brain*. 1997;120(Pt 6):1041–1056
 44. Uhlig T, Merckenschläger A, Brandmaier R, Egger J. Topographic mapping of brain electrical activity in children with food-induced attention deficit hyperkinetic disorder. *Eur J Pediatr*. 1997;156(7):557–561
 45. Himwich HE, Frostig JP, Fazekas JF, Hoagland H, Hadidian Z. Clinical, electroencephalographic and biochemical changes during insulin hypoglycemia. *Exp Biol Med*. 1939;40(3):401–402
 46. Gibbs FA, Williams D, Gibbs EL. Modification of the cortical frequency spectrum by changes in carbon dioxide, blood sugar and oxygen. *J Neurophysiol*. 1940;3:49–58

47. Doehner M, Brandeis D, Straub M, Steinhilber HC, Drechsler R. Slow cortical potential neurofeedback in attention deficit hyperactivity disorder: is there neurophysiological evidence for specific effects? *J Neural Transm*. 2008;115(10):1445–1456
48. Wilder RM. Effect of ketonuria on course of epilepsy. *Mayo Clin Bull*. 1921;2:307
49. Millichap JG, Jones JD, Rudis BP. Mechanism of anticonvulsant action of ketogenic diet. Studies in animals with experimental seizures and in children with petit mal epilepsy. *Am J Dis Child*. 1964;107:593–604
50. Pulsifer MB, Gordon JM, Brandt J, Vining EP, Freeman JM. Effects of ketogenic diet on development and behavior: preliminary report of a prospective study. *Dev Med Child Neurol*. 2001;43(5):301–306
51. Millichap JJ, Stack CV, Millichap JG. Frequency of epileptiform discharges in the sleep-deprived electroencephalogram in children evaluated for attention-deficit disorders. *J Child Neurol*. 2011;26(1):6–11
52. Murphy P, Burnham WM. The ketogenic diet causes a reversible decrease in activity level in Long-Evans rats. *Exp Neurol*. 2006;201(1):84–89
53. Kessler SK, Gallagher PR, Shellhaas RA, Clancy RR, Bergqvist AG. Early EEG improvement after ketogenic diet initiation. *Epilepsy Res*. 2011;94(1–2):94–101
54. Halterman JS, Kaczorowski JM, Aligne CA, Auinger P, Szilagyi PG. Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States. *Pediatrics*. 2001;107(6):1381–1386
55. Millichap JG, Yee MM, Davidson SI. Serum ferritin in children with attention-deficit hyperactivity disorder. *Pediatr Neurol*. 2006;34(3):200–203
56. Sever Y, Ashkenazi A, Tyano S, Weizman A. Iron treatment in children with attention deficit hyperactivity disorder. A preliminary report. *Neuropsychobiology*. 1997;35(4):178–180
57. Konofal E, Lecendreux M, Arnulf I, Mouren M-C. Iron deficiency in children with attention-deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med*. 2004;158(12):1113–1115
58. Konofal E, Lecendreux M, Deron J, et al. Effects of iron supplementation on attention deficit hyperactivity disorder in children. *Pediatr Neurol*. 2008;38(1):20–26
59. Calarge C, Farmer C, DiSilvestro R, Arnold LE. Serum ferritin and amphetamine response in youth with attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol*. 2010;20(6):495–502
60. Arnold LE, DiSilvestro RA. Zinc in attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol*. 2005;15(4):619–627
61. Akhondzadeh S, Mohammadi MR, Khademi M. Zinc sulfate as an adjunct to methylphenidate for the treatment of attention deficit hyperactivity disorder in children: a double blind and randomized trial [ISRCTN64132371]. *BMC Psychiatry*. 2004;4:9
62. Bilici M, Yildirim F, Kandil S, et al. Double-blind, placebo-controlled study of zinc sulfate in the treatment of attention deficit hyperactivity disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2004;28(1):181–190
63. Arnold LE, Bozzolo H, Hollway J, et al. Serum zinc correlates with parent- and teacher-rated inattention in children with attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol*. 2005;15(4):628–636
64. Arnold LE, DiSilvestro RA, Bozzolo D, et al. Zinc for attention-deficit/hyperactivity disorder: placebo-controlled double-blind pilot trial alone and combined with amphetamine. *J Child Adolesc Psychopharmacol*. 2011;21(1):1–19
65. Arnold LE, Pinkham SM, Votolato N. Does zinc moderate essential fatty acid and amphetamine treatment of attention-deficit/hyperactivity disorder? *J Child Adolesc Psychopharmacol*. 2000;10(2):111–117
66. Cott A. Megavitamins: the orthomolecular approach to behavioral disorders and learning disabilities. *Acad Ther*. 1972;7:245
67. Haslam RH, Dalby JT, Rademaker AW. Effects of megavitamin therapy on children with attention deficit disorders. *Pediatrics*. 1984;74(1):103–111
68. Waring ME, Lapane KL. Overweight in children and adolescents in relation to attention-deficit/hyperactivity disorder: results from a national sample. *Pediatrics*. 2008;122(1):e1–e6
69. Millichap JG. Etiologic classification of attention-deficit/hyperactivity disorder. *Pediatrics*. 2008;121(2):e358–e365

The Diet Factor in Attention-Deficit/Hyperactivity Disorder

J. Gordon Millichap and Michelle M. Yee

Pediatrics; originally published online January 9, 2012;

DOI: 10.1542/peds.2011-2199

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/early/2012/01/04/peds.2011-2199
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Developmental/Behavior http://pediatrics.aappublications.org/cgi/collection/developmental:behavior
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://pediatrics.aappublications.org/site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: http://pediatrics.aappublications.org/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2012 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

