Attention Deficit Hyperactivity Disorder  
Evidence Based Prevention  
(As of 10/01/09)

Risk factors for attention deficit-hyperactivity disorder (ADHD) are difficult to firmly establish due to the uncertain nature of the condition. A great deal of controversy exists related to its biological cause and diagnosis (1). Without the knowledge of its etiology or objective tests for diagnosis, it is difficult to properly design a study to determine risk factors. Consequently all evidence relating to risk factors are primarily observational in nature and must be evaluated on that basis.

RISK FACTORS AND PREVENTION STRATEGIES

1. Family (C): Up to one third of parents of children with ADHD are themselves affected by ADHD (2). As a result many researchers have concluded there is a strong genetic link. Twin studies and genetic research support this hypothesis although no genetic marker has been clearly established (3). Other researchers argue the familial link to ADHD is more a result of environment than genetics. A few of the many family related factors which appear to be associated with ADHD include television viewing of other than educational programming before age 3 (4), low educational levels of parents (5), parental antisocial behavior, parental substance abuse (6) and high maternal anxiety between 12 and 22 weeks of pregnancy (7). A very interesting finding in a study by Braun et al. was the observation that there was an increased likelihood that children attending daycare or preschool were more likely to develop ADHD (OR 2.4) (8).

3. Prenatal maternal smoking/alcohol use (C): Prenatal maternal smoking has been identified as having a strong relationship with ADHD in several studies (9;10). Additionally a cross-sectional study of 4704 children using the National Health and Nutrition Examination Survey (NHANES) found the adjusted odds ratio for developing ADHD was 2.5 when exposed to prenatal environmental tobacco smoke. Interestingly females seemed to be more susceptible to the effects of tobacco smoke than males. Surprisingly no relationship was found in this study between postnatal tobacco smoke and ADHD (8). Alcohol use was found to be associated with ADHD in 2 reviews (11;12) and not associated in a third review (13).

4. Lead and other chemical toxins (C): Lead exposure has been associated with ADHD in several studies including the NHANES study mentioned above (8;14;15). Other chemicals that have been identified as possible contributors to ADHD are mercury (16;17), dioxins (18), manganese (19) and polychlorinated biphenyls (20).

4. Nutrition (C): Insufficient levels of several nutrients have been associated with ADHD in a variety of studies although the strength of evidence of these
studies is weak. Suboptimal levels of **omega 3 fatty acids** (21;22), **vitamin E** (23), **vitamin D** (24), **iron** (25), **carnitine, zinc and vitamin B6** (26) have all been associated with ADHD. A review of 16 studies that evaluated sugar challenges and the symptoms of ADHD found 4 studies that demonstrated worsened symptoms, 11 showed little change and 1 showed improvement (27). **Food additives** have also been implicated but remain controversial. Bateman et al. reported adverse effects of food coloring and benzoate preservatives on 3 year old children based on parental reports but not on clinic assessment (28). This study addressed hyperactivity but purposely avoided the term ADHD. Two other studies lend support to the adverse effects of food additives (29;30) while a consensus panel did not (31).

5. **Other (C):** Several other factors may increase the risk for ADHD but have limited, strongly conflicting or marginal evidence. They include **aspartame** (32), **low birth weight** (33;34), **birth trauma** (35;36), **viral infection** (35) and **brain trauma** (37). **Thimerosal**, an ethylmercury preservative used in vaccines, has also been implicated as a risk factor for ADHD. However a longitudinal study published in 2004 which had over 14000 subjects could not associate thimerosal with ADHD (38).

**Reference List**

(1) Furman LM. Attention-deficit hyperactivity disorder (ADHD): does new research support old concepts? J Child Neurol 2008 Jul;23(7):775-84.


(3) Furman L. What is attention-deficit hyperactivity disorder (ADHD)? J Child Neurol 2005 Dec;20(12):994-1002.


Attention deficit-hyperactivity disorder (ADHD) has been defined as “the inability to marshall and sustain attention, modulate activity level and moderate impulsive actions” (1). A commonly used diagnostic protocol for the primary care physician is the American Academy of Pediatrics (AAP) “Clinical Practice Guideline: Diagnosis and Evaluation of the Child With Attention-Deficit/Hyperactivity Disorder” (2). This guideline includes the following 6 recommendations:

**RECOMMENDATION 1:** In a child 6 to 12 years old who presents with inattention, hyperactivity, impulsivity, academic underachievement, or behavior problems, primary care clinicians should initiate an evaluation for ADHD.

**RECOMMENDATION 2:** The diagnosis of ADHD requires that a child meet the *Diagnostic and Statistical Manual of Mental Health Disorders, Fourth Edition* (DSM-IV) criteria.

**RECOMMENDATION 3:** The assessment of ADHD requires evidence directly obtained from parents or caregivers regarding the core symptoms of ADHD in various settings, the age of onset, duration of symptoms, and degree of functional impairment.

**RECOMMENDATION 4:** The assessment of ADHD requires evidence directly obtained from the classroom teacher (or other school professional) regarding the core symptoms of ADHD, the duration of symptoms, the degree of functional impairment, and coexisting conditions. A physician should review any reports from a school-based multidisciplinary evaluation where they exist, which will include assessments from the teacher or other school-based professionals.

**RECOMMENDATION 4A:** Use of these scales is a clinical option when diagnosing children for ADHD.

**RECOMMENDATION 4B:** Use of teacher global questionnaires and rating scales is not recommended in the diagnosing of children for ADHD, although they may be useful for other purposes.

**RECOMMENDATION 5:** Evaluation of the child with ADHD should include assessment for coexisting conditions.

**RECOMMENDATION 6:** Other diagnostic tests are not routinely indicated to establish the diagnosis of ADHD.

While the above recommendations appear to be straightforward there are other complexities which confront the practitioner attending a child he/she suspects has ADHD. The DSM-IV requires all the following for a diagnosis of ADHD (3):

1) An evaluation of 18 behavioral symptoms and finding 6 of 9 present in the hyperactive/impulsive domain and/or 6 of 9 present in the inattentive domain persisting for 6 months.
2) Onset of symptoms before age 7.
3) Clear evidence of functional impairment in two settings or more.
4) No other explanation for the symptomology.

The specific criteria of the DSM-IV can be found at: http://www.cnsspectrums.com/aspx/articledetail.aspx?articleid=1118

Diagnostic difficulties become more apparent when one considers there are three subtypes of ADHD. They are predominately hyperactive-impulsive, predominately inattentive type and combined type (4). Additionally comorbidities abound with up to 50% of the inattentive subtype also experiencing anxiety and depression and 80% of the combined subtype experiencing oppositional defiant disorder/conduct disorder (5).

Another complexity of the diagnostic process in ADHD is the different diagnostic challenges facing the physician when evaluating a preschool child as opposed to the school aged child, adolescent or adult.

Implementation of the AAP guidelines and use of the DSM-IV criteria have been less than successful. In a national survey sample of 861 primary care physicians only 28% used the DSM-IV criteria (6). A separate study showed only 4% of clinicians and nurse practitioners used all of the AAP diagnostic guidelines (7).

Considering the complexities of diagnosis and the impact on the life of the ADHD patient, unless the physician is well trained, current with the literature and experienced in using the diagnostic protocols of ADHD, a referral to a mental health specialist may be the best diagnostic option.

CLINICAL TESTING

1. **Rating scales (C):** Several different rating scales have been developed to aid in the diagnosis of ADHD. The following list contains but a few: Connors Rating Scale, Brown Attention Deficit Disorder Scale (BADDS) for Children and Adolescents, Vanderbilt ADHD Rating Scale, the Swanson, Nolan and Pelham IV, the Child Behavior Checklist, Early Childhood Inventory and the Preschool Age Psychiatric Assessment. The Connors is available at www.mhs.com ($265.00), BADDS at www.addwarehouse.com ($199.00), Vanderbilt www.aap.org ($200.00 or $250.00) and Swanson, Nolan and Pelham IV at www.adhd.net (free). Each test has their individual strengths and weaknesses (8-11) and none appear to be clearly superior according to the literature.

2. **Imaging (C):** Although some studies have evaluated functional MRI as a promising tool in the diagnosis of ADHD current expert opinion considers all diagnostic imaging protocols of little value in the diagnosis of ADHD (2;12;13)

3. **Laboratory testing (C):** Laboratory testing is of little value in the diagnosis of ADHD based on expert opinion but may play a role in ruling out other pathology such as lead poisoning (2).
4. **Electroencephalography (EEG) (C):** EEG cannot be used to diagnosis ADHD but is considered a promising technology (14).

Reference List


(9) Furman LM. Attention-deficit hyperactivity disorder (ADHD): does new research support old concepts? J Child Neurol 2008 Jul;23(7):775-84.


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Concerns pertaining to the use of psychostimulants for children have lead many parents to seek alternatives for the treatment of attention deficit hyperactivity disorder (ADHD). Up to 64% of children with ADHD have been treated with some form of alternative therapy (1). Although diet therapy, chiropractic and homeopathy are the most common interventions (2;3), good quality studies on any alternative intervention are limited.

Pharmacological interventions are considered to be the primary treatment option by many medical physicians but significant concerns remain relating to safety issues, abuse, side effects and long term effectiveness.

With the exception of behavioral training, all conservative interventions are graded C due to a lack of good quality randomized controlled trials (RCT) which are necessary to fully evaluate effectiveness.

**CHIROPRACTIC AND OTHER CONSERVATIVE TREATMENT**

1. **Cognitive/behavioral therapy (B):** A technical report reviewing treatment for ADHD from the American Academy of Pediatrics found 14 studies relating to either cognitive or behavioral therapy (C/BT). None of the studies, except one by Carlson (4), gave evidence these interventions performed as well as pharmacological treatment and C/BT combined (5).

2. **Essential fatty acids (C+):** Several studies have examined the effect of essential fatty acids (EFA) on the symptoms of ADHD. A variety of dosages and combinations have been tested. One review author stated the evidence was “shaky” (6) while another stated current studies “do not support the use of EFA’s” (7). One randomized controlled trial (RCT) divided 166 children, aged 9 to 12, into two groups. The treatment group received 3600 mg of docosahexaenoic acid (DHA), and 849 mg of eicosapentaenoic acid (EPA) daily for 3 months. There was no effect on boys at the end of the study but girls exhibited decreased impulsivity (8). Another smaller RCT using 345 mg of DHA in 6 to 12 year olds was unable to detect improvement (9). The most positive study was a placebo controlled one-way crossover design of 75 children aged from 8 to 18. The treatment group received 558 mg EPA, 173 mg DHA, 60 mg gamma linoleic acid and 10.8 mg vitamin E. Although the authors consider the overall outcome of this study as negative, they did state 1 in 8 of the treatment group showed considerable improvements with a reduction in symptoms of 50% (10). Several other RCT’s have reported modest improvements in a limited number of outcome measures (11-13).

3. **Nutraceuticals(C):** A review published in 2009 identified several nutritional supplements that may have value in the treatment of ADHD. The authors of this review caution the reader that the evidence is primarily from small trials providing limited information often with mixed results. They identified the following as having possible benefit (14):
A. Magnesium, in children (3mg/lb) (15)
B. Zinc, in children (150 mg as zinc sulfate) (16)
C. SAM-e, in adult males (2400 mg) (17)
D. Carnitine, in male children (100 mg/kg) (18)
E. Iron, in children (80 mg as ferrous sulfate) (19)
E. Multivitamins, in children (20)

4. Spinal manipulation (C): Several small case series were located that indicate spinal manipulation may be of value in treating ADHD (21-23). None of these studies were RCT’s so a cause and effect relationship can not be established.

5. Biofeedback (C): Biofeedback as a treatment for ADHD has been examined in several different forms. Neurofeedback, hemoencephalography and EEG feedback have been investigated with encouraging, although not convincing results (24-26). The strongest of these trials was an RCT of 102 children comparing neurofeedback to attention skills training. Statistically significant differences were reported in favor of neurofeedback (25).

6. Homeopathy (C): Three small RCT’s were located that provided mixed results relating to effectiveness. Two demonstrated positive results (27;28) and one reported no differences (29). Two separate systematic reviews concluded the evidence for homeopathy was not convincing as a treatment for ADHD (30;31).

7. Herbal therapy (C): Although 20% of ADHD patients have used herbal therapy (32), very little evidence was located to establish effectiveness. Two very small studies reported ginkgo biloba may be of benefit (33;34) and one RCT found methylphenidate (Ritalin) to be superior to ginkgo biloba (35). A 54 subject RCT of hypericum perforatum (St. John’s Wort) found no improvement when compared to a placebo after 8 weeks (36).

8. Diet intervention (C): Since the introduction of the Feingold diet in the 1970’s a debate has raged over the role of food additives, artificial sweeteners and sugar in ADHD. The evidence is strongly conflicting. An early study published in 1981 which utilized a crossover design of 11 children found no effect of artificial food coloring on the symptoms of ADHD (37). A 1994 RCT of 25 children found neither dietary sucrose or aspartame effect the symptoms of ADHD (38). A follow up meta-analysis reached similar conclusions (39). Yet a RCT of 26 children demonstrated elimination of certain foods, dyes and preservatives resulted in improvements in 73% of cases (40). A more recent small trial reported effectiveness of an elimination diet in children (41). In 2004 Bateman et al performed a double blind crossover study of 277 three year old children utilizing an elimination diet. They conclude there is “an adverse effect of artificial food coloring and benzoate preservatives” as detected by parents (42). An editorial in the Lancet considered this study to be seriously flawed and stated “we strongly believe that unnecessary diets should not be instituted for hyperactivity” (43).

9. Other (C): Many other interventions have been touted as treatments for ADHD but have limited evidence to support efficacy. These include music therapy (44;45),
noise therapy (46), movement therapy (47), therapy balls (48), Bach flower therapy (49), hypnosis (50;51), yoga (52), massage therapy (53), exercise (54) and green outdoor activities (55).

Attention Deficit Hyperactivity Disorder  
Evidence Based Pharmaceutical & Invasive Treatment  
(as of 11/5/09)

Although pharmaceutical interventions are considered the treatment of choice for most of the medical establishment, there remains significant opposition from within the medical community relating to issues of safety and long term effectiveness. Lydia Furman, M.D. is among this group of dissenting physicians and has published several papers voicing her concerns (56;57). Among these concerns are:

1. There is no evidence any pharmacologic treatment is superior to another. Consequently choice is primarily physician driven (57).
2. Pharmaceutical firms fund or have financial ties to many researchers involved in ADHD studies. For example over 50% of the principle investigators in the recent National Institutes of Mental Health Multimodal Treatment Study of Children with Attention Deficit Hyperactivity Disorder had financial links to pharmaceutical companies (57).
3. At least 1 side effect was reported in 22% of children in one study (57).
4. Long term studies to determine effect on growth until adulthood have not been performed. One follow-up study (58) reported an average of 2.0 cm loss in height and 2.7 kg loss in weight over 36 months compared to expected patterns (57).
5. In 1995 2% of 4-year olds were receiving stimulant medication (59). Only six controlled trials with about 200 total patients have been performed in children of preschool age. The effect on brain development and personality is unknown (56).

The evidence for stimulant medications is rated as an A and they are considered first line agents (60). This rating is based on the number and quality of trials performed. The most commonly utilized stimulants are methylphenidate (Ritalin, Methylin), dexamethylphenidate and dextroamphetamine. A second line agent is atomoxetine and third line agents are antidepressant medications. The evidence for the effectiveness of antidepressants is limited (60).


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