

## **Townsend Letter for Doctors and Patients**

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### **The Benefits of Going Beyond Conventional Therapies for ADHD**

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Attention deficit/hyperactivity disorder (ADHD) has the distinction of being the most thoroughly studied of all the behavioral/emotional disorders of childhood.<sup>1</sup> But despite the continuing focus on this disorder, experts in the topic acknowledge that many aspects of ADHD—from its etiology to the best form of treatment—continue to be poorly understood or controversial.<sup>2, 3</sup>

Two such controversies stem from the ADHD protocols of conventional medicine, which uses subjective methods of diagnosis and mind-altering pharmaceuticals such as Ritalin and Adderall. Although these drugs are central nervous system stimulants, in the case of ADHD they have the paradoxical effect of calming the patient. Unfortunately, they also put the growing number of children and adolescents who are diagnosed with ADHD at risk of the adverse effects associated with these drugs, particularly methylphenidate (Ritalin, Concerta, Metadate, Focalin, Methylin). The negative effects range from insomnia and decreased appetite to movement disorders such as tics and the stunting of children's growth.

An analysis of orthodox medicine's approach to diagnosing and treating ADHD will reveal the benefits of using more natural methods of treating the collection of symptoms now grouped under the ADHD label.

#### **Problems of Diagnosis**

ADHD has become the most commonly diagnosed behavioral disorder of childhood, characterized by the core symptoms of inattention, impulsivity and hyperactivity. Data on its prevalence vary. The American Psychiatric Association reports that 3% to 5% of school-age children have ADHD<sup>4</sup>; the American Academy of Pediatrics reports 4% to 12%.<sup>5</sup> The most stringent estimate in a recent study by the Mayo Clinic puts the figure at 7.4% of children by age 19.<sup>6</sup> In a controversial development, the diagnosis of ADHD and use of stimulant medications have been increasing among adults.<sup>7</sup> According to one expert, the literature suggests that "ADHD is best conceptualized as a lifelong disability rather than as a childhood disorder."<sup>8</sup>

However, the diagnosis of ADHD and its treatment with pharmaceuticals have been largely concentrated in the United States (and, to a lesser extent, Canada),<sup>9, 10</sup> making ADHD an American phenomenon and raising questions about whether it is a true disorder. (It is of interest that the use of methylphenidate for ADHD has increased sharply in many other countries—mostly European ones—as well, according to the International Narcotics Control Board. Consumption in countries such as Belgium,

Germany, Iceland and the Netherlands increased by 150% to 350% in a recent five-year period. Consumption in Australia and Canada, formerly main consumer countries of methylphenidate, has leveled off or declined, although they are the only countries besides the U.S. to report significant use of amphetamines for the treatment of ADHD.<sup>11)</sup>

In diagnosing ADHD, physicians and psychiatrists use a variety of assessment tools and rating scales, such as the Conners'/CADS scales and the diagnostic criteria presented in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*. DSM-IV (1994) defines three major subtypes of the diagnosis of attention deficit/hyperactivity disorder (ADHD): predominantly inattentive, predominantly hyperactive-impulsive, and a combined type. (This condition also is referred to as attention deficit disorder, ADD. The APA replaced its former diagnosis of ADD—with or without hyperactivity—with the unidimensional ADHD diagnosis in 1987, then specified the three subtypes in 1994.)<sup>12, 13</sup>

Children with ADHD may have one, two or all three of the core symptoms of inattention, hyperactivity and impulsivity. Thus, a child may be diagnosed with ADHD even if he or she is not hyperactive. Girls, for example, often fall into the inattentive subtype.<sup>14</sup> However, a 2000 review of the diagnosis of ADHD points out that the DSM-IV criteria for this disorder are phenomenologic rather than etiologic and are much more relevant for children than for adolescents and adults.<sup>15</sup>

An easy-to-see problem with this approach to diagnosis is that the assessments are not definitive. The National Institutes of Health (NIH) believes the diagnosis of ADHD can be made reliably using diagnostic interview methods, but it also said in its 1998 Consensus Statement on ADHD that "there is no independent valid test for ADHD."<sup>16</sup> Although new testing methods are being developed, the diagnosis of ADHD remains far less objective than that of other abnormalities, where specific tools such as blood tests, x-rays and sonograms are used to determine the presence of the disorder.

Furthermore, the answers provided by parents and teachers on behavior rating scales—to questions such as how much a child fidgets or whether he/she is easily distracted—are subjective. What one person views as distractibility another may view as natural inquisitiveness. Some of the questions also are based on questionable values or assumptions. For example, the Conners' Parent Rating Scale<sup>17</sup> asks whether the child "actively defies or refuses to comply with adults' requests." In some life situations, though, disobedience is a virtue.

Another problem with the ADHD diagnosis is that it may apply a medical label to behaviors that fall at one end of a spectrum of normal patterns. The NIH says in its Consensus Statement: "Clinicians who diagnose this disorder have been criticized for merely taking a percentage of the normal population who have the most evidence of inattention and continuous activity and labeling them as having a disease. In fact, it is unclear whether the signs of ADHD represent a bimodal distribution in the population or one

end of a continuum of characteristics." The NIH observes that one of the problems of diagnosis is to "determine the appropriate boundary between the normal population and those with ADHD."<sup>18</sup>

The American Psychiatric Association states itself that the diagnosis of ADHD is not an easy one to make. The symptoms are similar to those of many other childhood disorders.<sup>19</sup> Psychiatrist Abram Hoffer, M.D., Ph.D., has stated: "You can take this same difficult child to ten psychiatrists and come back with ten different diagnoses. But no matter what the diagnosis is, they all put him on Ritalin."<sup>20</sup> To add to the complexity, approximately 65% of patients with ADHD may have one or more comorbid disorders, such as anxiety, communication, mood, conduct, oppositional defiant and learning disorders and Tourette's syndrome.<sup>21</sup>

One researcher suggests that more exact diagnostic guidelines may emerge from ADHD-related tests of executive functioning, neuroimaging and genetics that have been developed in recent years.<sup>22</sup> But any such diagnostic methods are likely to be controversial as well. According to a 2004 article, while the current evidence on the genetics of ADHD will provide important clues to its etiology, it is not sufficient to justify the use of genetic screening tests. The authors add that "genetic information on susceptibility to ADHD has the potential to be abused and to stigmatize individuals."<sup>23</sup>

Also open to controversy are the results of neuroimaging studies that have identified supposed abnormalities in structural and functional aspects of the brains of ADHD patients.<sup>24</sup> Researchers have interpreted these findings to mean that the disorder may have a biological basis. For example, a 2003 study in the *Lancet* found reduced regional brain sizes and grey-matter abnormalities in cortical components of attentional systems that may help account for ADHD symptoms.<sup>25</sup>

Research associating ADHD with brain abnormalities does not withstand a critical analysis, however. A review of neuroimaging studies published in *Clinical Neuropharmacology* in 2001 states that while the results of such studies are often used to support a biological basis for ADHD, "inconsistencies among the studies raise questions about the reliability of the findings." At the time of publication, the researchers found that "no specific abnormality in brain structure or function has been convincingly demonstrated by neuroimaging studies." They concluded that the neuroimaging literature "provides little support for a neurobiologic etiology of ADHD."<sup>26</sup>

Some doctors are already using brain-scanning technologies in the assessment of ADHD, according to a *Wall Street Journal* article. One such method even exposes the patient's brain to a small amount of radioactive material, which is used to illuminate brain activity. However, most researchers believe the use of brain-scanning techniques to diagnose ADHD is premature and impractical, given the expense of the tests and the lack of standard guidelines for interpreting the scans.<sup>27</sup>

Another more objective test of ADHD is available. The Developmental Biopsychiatry Research Program at Harvard's McLean Hospital has developed a diagnostic tool called M-MAT that monitors fine body movements during a computerized task to measure hyperactivity, impulsivity and attention. Because a child can be retested after taking a dose of medication, the test helps determine whether the drug will be effective for him or her. The researchers believe this test will address the concerns of many physicians that the diagnosis of ADHD is "too subjective, often pathologizes normal childhood behavior, and masks the detection of other important problems, such as a learning disorder."<sup>28</sup>

### **Conventional Treatment of ADHD**

Psychostimulants have become the primary treatment for those diagnosed with ADHD, fueling what the NIH has called one of the major controversies regarding this disorder. The agency noted in 1998 that the growing prescription of these drugs for the short- and long-term treatment of ADHD has led to intensified concerns about their potential overuse and abuse.<sup>29</sup>

The stimulants used to treat ADHD include methylphenidate, mixed salts of amphetamine (Adderall), dextroamphetamine sulfate (Dexedrine, Dextrostat) and, to a much lesser extent, pemoline (Cylert). The methylphenidates and amphetamines are available in short- and long-acting versions. In late 2002, Eli Lilly and Co. introduced the first nonstimulant medication approved by the FDA for the treatment of ADHD. This drug, atomoxetine (Strattera), is a selective norepinephrine reuptake inhibitor. It had the strongest launch ever for an ADHD drug and was the first such medication approved for the treatment of adults as well as children and adolescents.<sup>30, 31</sup>

Stimulant-type drugs still lead this market, however, and numerous studies document their growing prescription during the 1990s.<sup>32, 33, 34, 35, 36</sup> One study found that the use of psychotropic medications among young people had reached nearly adult utilization rates in 1996, with stimulants ranked first in the three groups examined.<sup>37</sup> Another study reported sizable increases in the use of stimulants and other medications among even 2- to 4-year-olds.<sup>38</sup>

Perhaps most disconcerting is a four-year analysis of the use of stimulants in an area of North Carolina which found that the majority of 9- to 16-year-old children who took these medications had never had any impairing ADHD symptoms reported by their parents. They did have nonimpairing symptoms and behaviors that were classified as ADHD, but "these typically fell far below the threshold for a DSM-III-R diagnosis of ADHD," say the researchers.<sup>39</sup>

One study finding evidence of overdiagnosis was conducted in southeastern Virginia, where the incidence of grade-school children receiving ADHD medications was two to three times as high as the expected rate of the disorder. By fifth grade, 18% to 20% of Caucasian boys were taking ADHD drugs.<sup>40</sup> Meanwhile, a study of the prevalence of stimulant prescriptions in

1999 found wide variations among states, ranging from a high of 6.5% in Louisiana to a low of 1.6% in the District of Columbia. The authors suggest that areas of both overuse and underuse may exist.<sup>41</sup>

The use of stimulant-type drugs to treat ADHD has grown despite a lack of understanding of their therapeutic action. Methylphenidate and amphetamines are stimulants of the central nervous system (10 milligrams of Ritalin are equivalent to 5 milligrams of amphetamine), yet in patients with ADHD the drugs have a paradoxical effect and reduce the symptoms of inattention, hyperactivity and impulsive behavior.

Researchers acknowledge that stimulants' method of action in treating ADHD is not well understood.<sup>42, 43, 44</sup> According to the *Journal of the American Medical Association*, Nora Volkow, M.D., a leading researcher in the imaging of drug effects in the brain, said of methylphenidate in 2001: "As a psychiatrist, sometimes I feel embarrassed [about the lack of knowledge] because this is, by far, the drug we prescribe most frequently to children."<sup>45</sup>

A 2001 study by Dr. Volkow and colleagues provided direct evidence, for the first time, that therapeutic doses of methylphenidate significantly increase extracellular dopamine in the human brain by blocking dopamine transporters. The researchers postulate that the drug's amplification of weak dopamine signals in ADHD patients enhances task-specific signaling, improving attention and reducing distractibility.<sup>46</sup>

Other research in this area includes a 2003 study that measured regional cerebral blood flow in ADHD patients while they were on and off methylphenidate. The results suggested that Ritalin reduces ADHD symptoms by modulating regions of the brain associated with motor function.<sup>47</sup> A study from Harvard Medical School found evidence that methylphenidate alters activity and attentiveness in children with ADHD in a rate-dependent manner. There was a clear inverse association between the severity of symptoms and the degree of therapeutic response.<sup>48</sup>

Some recent evidence about the dosages of stimulants prescribed to young people is of interest: While the common practice is to increase a child's dosage as he or she grows, this may not be necessary for all patients.<sup>49</sup> In one clinical trial, 40% of children who took half the dose of methylphenidate that had kept their symptoms stable, along with a placebo, had equally good ADHD control and fewer side effects.<sup>50</sup> Another study found that the greatest benefit in academic performance and classroom behavior came with the lowest dose studied,<sup>51</sup> while a third reported that "adolescents with ADHD may not necessarily require more medication than younger children to achieve a similar therapeutic effect."<sup>52</sup>

### **Questions Regarding ADHD Drugs**

In addition to uncertainties about the diagnosis of ADHD and the method of action of ADHD drugs, questions remain about the quality of studies of stimulant medications, the safety of these drugs and the implications of long-term use in young patients with developing brains.

In 2001, Howard Schachter and colleagues published a meta-analysis of 62 randomized trials of the efficacy and safety of short-acting methylphenidate. The trials involved 2,897 participants under age 18 diagnosed with attention deficit disorder. Their treatment lasted three weeks on average and 28 weeks at most. The meta-analysis found a significant effect of methylphenidate for each primary outcome. However, it also found that the collection of trials “exhibited low quality” based on scores from two separate indices. The analysis concluded that the drug’s “apparent beneficial effects are tempered by a strong indication of publication bias and the lack of robustness of the findings, especially those involving core ADD features.”<sup>53</sup>

An earlier meta-analysis of 77 randomized controlled trials of both pharmacological and nonpharmacological interventions for ADHD also found that studies of this disorder “have low reporting quality, methodological flaws, and heterogeneity across outcome measures and tests.” This analysis makes a noteworthy point about efficacy: It found that methylphenidate may reduce behavioral disturbance in children with ADHD, but that “academic performance does not appear to be improved with stimulants.”<sup>54</sup> Likewise, the NIH consensus statement on ADHD refers to the “consistent findings that despite the improvement in core symptoms, there is little improvement in academic or social skills.”<sup>55</sup>

Research on the long-term effects and safety of ADHD medications has been especially lacking. Schachter’s meta-analysis notes that while short-acting methylphenidate has a statistically significant clinical effect in the short-term treatment of ADHD, the “extension of this placebo-controlled effect beyond 4 weeks of treatment has not been demonstrated.”<sup>56</sup> In fact, the prescribing information for Adderall XR and Concerta state that the effectiveness of the drug beyond three weeks and four weeks, respectively, has not been systematically evaluated in controlled trials. Even so, the average number of years children are being treated for ADHD is increasing.<sup>57</sup> And according to a study of psychotropic drugs (such as stimulants, sedatives and antidepressants) used with preschoolers, earlier ages of initiation and longer durations of treatment mean that “the possibility of adverse effects on the developing brain cannot be ruled out.”<sup>58</sup>

One often cited study of longer-term ADHD treatments, the Multimodal Treatment Study of Children with ADHD, lasted 14 months. In this clinical trial, 64% of children, aged 7 to 9.9 years, were reported to have side effects from ADHD medications (mild side effects for 49.8%; moderate for 11.4%; severe for 2.9%). Interestingly, the authors say that six of the 11 severe side effects—such as depression, worrying and irritability—“could have been due to nonmedication factors.”<sup>59</sup> But as psychiatrist and author Peter Breggin, M.D., points out, placebo-controlled double-blind clinical trials have shown that the three side effects mentioned above are common adverse reactions to stimulants.<sup>60</sup>

A clearer picture of the long-term consequences of stimulant use is beginning to emerge from animal studies conducted in the past few years. These studies have found, for example, that Ritalin has the potential to cause long-lasting changes in brain cell structure and function<sup>61</sup>; that a repeated,

clinically relevant dose of methylphenidate markedly inhibits immediate-early gene expression in the brain<sup>62</sup>; that chronic exposure to methylphenidate during pre- and periadolescent development made the animals significantly less responsive to natural rewards than control animals and significantly more sensitive to stressful situations, with an increase in anxiety-like behaviors<sup>63</sup>; and that early exposure to methylphenidate causes behavioral changes which last into adulthood, including some changes that may be beneficial (less sensitivity to cocaine reward) and others that may be detrimental (increases in depressive-like signs).<sup>64</sup>

The lack of information on long-term effects isn't the only worrisome factor in the treatment of ADHD. Young people also are increasingly being prescribed multiple medications at the same time. For example, a child prescribed methylphenidate for ADHD may also take a selective serotonin reuptake inhibitor (SSRI) antidepressant.<sup>65</sup> A review by researchers at Johns Hopkins Medical Institutions found that the data supporting the use of concomitant psychotropic medication are based almost entirely on case reports and small-scale, nonblind assessments.<sup>66</sup> Other studies also document the simultaneous use of multiple psychoactive drugs by children.<sup>67, 68</sup> The Johns Hopkins review concludes: "Substantive systematic evidence is needed to clarify this increasingly common, inadequately researched child psychopharmacologic practice."<sup>69</sup>

Another shortcoming in the research on pediatric drug use may undermine safety data as well: There is no common method used to elicit and report data on adverse events in clinical studies, according to a 2003 review of 196 pediatric psychopharmacology articles published over the past 22 years. The inconsistency in the ascertainment of safety data "is a major limitation that likely impairs the ability to promptly and accurately identify drug-induced [adverse events]," state the reviewers. "Research on how best to standardize safety methods should be considered a priority in pediatric psychopharmacology."<sup>70</sup>

### **Adverse Effects**

Stimulant-type drugs generally are described as a safe treatment for ADHD, causing relatively mild side effects that may be related to dose and may decrease with time.<sup>71, 72</sup> Yet as a review published in 2002 notes, there is a substantial amount of variation both in response to these drugs and in adverse drug reactions.<sup>73</sup> Although 75% to 90% of ADHD patients respond well to amphetamine and methylphenidate, says another review, there is a subset of patients who either do not respond to the drugs or who experience side effects that preclude their use. These side effects include tics, a severe loss of appetite and marked insomnia.<sup>74</sup>

In their analysis of 62 randomized trials, Schachter and colleagues conclude that methylphenidate "has an adverse event profile that requires consideration." For almost all of the adverse events reported, patients taking methylphenidate had a higher percentage of the effects than did those taking placebo. According to data derived from parent/self-reported adverse effects, the number of study participants required for five prominent adverse events to be identified were as follows: four patients for a decreased appetite, seven

for insomnia, nine for all stomachache events; 10 all drowsiness events, and 11 for all dizziness events.<sup>75</sup>

According to a 2002 review, side effects of methylphenidate such as nervousness, headache, insomnia, anorexia and tachycardia increase linearly with dose, while overdoses can cause agitation, hallucinations, psychosis, lethargy, seizures, tachycardia, dysrhythmias, hypertension and hyperthermia.<sup>76</sup> A study of long-acting methylphenidate published in 2003 found that only two side effects, insomnia and decreased appetite, were more common at higher doses. In this group of 5- to 16-year-olds, younger and smaller children were more likely to experience sleep problems and a diminished appetite at higher dosages.<sup>77</sup>

A study of even younger children, aged 4.0 to 5.11 years, raises serious questions about the growing use of stimulants in preschoolers. In this study of 11 young children with developmental disabilities and ADHD, five who took methylphenidate experienced significant adverse effects, such as severe social withdrawal, increased crying, and irritability, especially at the higher dose of 0.6 mg/kg. The researchers state that "this population appears to be especially susceptible to adverse drug side effects."<sup>78</sup>

Another medication, Cylert, can cause acute and sometimes fatal hepatic failure. Its black box warning in the U.S. was revised in 1999, stating that Cylert should not ordinarily be considered a first-line drug treatment for ADHD.<sup>79</sup> The drug also has been withdrawn from the UK and Canadian markets (it is available with restrictions through a special access program in Canada).<sup>80, 81</sup>

What follows is a discussion of some of the side effects associated with stimulant-type drugs used to treat ADHD, particularly methylphenidate:

**Mental effects.** Stimulants can cause a variety of negative effects on mental functioning. In his book *Talking Back to Ritalin*, Peter Breggin, M.D., discusses some of the adverse experience reports for Ritalin submitted to the FDA's Spontaneous Reporting System from 1985 through March 3, 1997. Among these data, which represent only a small fraction of the total adverse events experienced by a drug's users, were reports of depression (48 reports for depression, 11 for psychotic depression); personality disorders (89); agitation (55); hostility (50); abnormal thinking (44); hallucinations (43); psychosis (38); and emotional lability (33), along with reports of amnesia, anxiety, confusion, nervousness, neurosis, stupor, paranoid reactions and, in a few cases, manic reactions.<sup>82</sup>

Dr. Breggin points out that stimulants impair the function of the basal ganglia in the brain, and this dysfunction can impede higher mental functions and cause obsessions, compulsions and abnormal movements. In two studies of stimulants, the rate of OCD symptoms was 51% and 25%, respectively.<sup>83</sup> <sup>84</sup> Another study found that 42% of children experienced obsessive over-focusing.<sup>85</sup> Parents and teachers may mistakenly see these OCD symptoms as an improvement, says Dr. Breggin, but drug-induced OCD is in fact a severe type of brain dysfunction.<sup>86</sup> Case reports also document stimulant-induced obsessive compulsiveness.<sup>87, 88</sup>

The potential for psychotic behavior in Ritalin users is included in the drug's packaging information. A 1999 chart review of children with ADHD treated in an outpatient clinic found a 6% rate of psychotic behavior among stimulant users. Six of the 98 children who took a stimulant (they were followed an average of 21 months) developed psychotic or mood-congruent psychotic symptoms during treatment.<sup>89</sup>

As for mania, a study of 34 adolescents hospitalized for this disorder found that patients who had used stimulants in the past had an earlier age at onset for bipolar disorder (BD) than those without prior stimulant exposure. In fact, those who had used at least two stimulants developed BD at a younger age than those who had been treated with one such drug.<sup>90</sup> The authors of a 2004 article also hypothesize that the earlier age of onset for BD in the United States than in the Netherlands (where the prevalence among adults and adolescents, but not pre-pubertal children, is similar to that of the U.S.) may be related to the greater use of antidepressants and stimulants for depression or ADHD by American children.<sup>91</sup>

**Movement disorders.** Children taking methylphenidate may develop involuntary muscle contractions and limb movements. A 2003 review reports that the increased use of stimulants, antipsychotic agents and antidepressants in children has inevitably led to more young patients experiencing side effects such as movement disorders. Those associated with these drugs include acute dystonic reaction and tardive dyskinesia. The reviewer states: "Unlike the isolated abnormal involuntary movements associated with drugs prescribed for epilepsy or asthma, movement syndromes...associated with psychotropic drugs are complex, difficult to recognize, and potentially seriously disabling."<sup>92</sup>

In a retrospective chart review involving 555 subjects, a total of 7.8% of those treated with stimulants developed tics (8.3% of methylphenidate users; 6.3% of dextroamphetamine users; 7.7% of pemoline [Cylert] users). The children who developed tics were significantly younger than those who did not.<sup>93</sup> Another cross-sectional analysis and chart review of 122 children with ADHD treated with stimulants found that approximately 9% developed tics or dyskinesia. One child developed Tourette's syndrome.<sup>94</sup> Other studies and case reports bear out the association between stimulants and abnormal movements.<sup>95, 96, 97</sup>

The risk of tics in stimulant users is another debated area of ADHD treatment, however. Several studies, for example, have found that the proportion of subjects with ADHD and chronic tic disorder whose tics worsened was no higher for methylphenidate than for placebo<sup>98</sup> or that methylphenidate did not produce significantly more tics than did the placebo in children with or without preexisting mild to moderate tics.<sup>99</sup>

**Growth effects.** Another disturbing side effect of stimulants is the stunting of growth that occurs in some children who take moderate to high doses over a period of years. This stunting occurs not only because stimulants can diminish a child's appetite but also because they may alter the body's natural balance of growth hormones.<sup>100</sup>

A study conducted at Yale University School of Medicine, published in 2003, examined the growth of 84 patients with ADHD who took stimulants and compared their height standard deviation (SD) scores with those of untreated biological siblings. The researchers found significant differences in mean height SD scores between treated children and siblings after two years of treatment. These findings “suggest that the prevalence of growth-suppressive effects of methylphenidate is greater than previously suspected.”<sup>101</sup>

Another 2003 study in Australia tracked 51 children treated with dexamphetamine or methylphenidate for six to 42 months. In the first six months, 86% of the patients had a height velocity below the age-corrected mean and 76% lost weight. The children’s height and weight standard deviation score (SDS) showed a progressive decline that was statistically significant after six and 18 months. During the first 30 months, height velocity was significantly attenuated (with a mean height deficit of approximately 1 cm/year in the first two years).<sup>102</sup>

Other studies have reported that stimulants do not have negative effects on growth for most children, that ADHD itself may be associated with temporary deficits in height gain which may normalize by late adolescence, or that most aspects of methylphenidate treatment are not associated with adult height or weight.<sup>103, 104, 105</sup>

**Cardiovascular effects.** Several recent studies have documented changes in cardiovascular functioning that can occur when children take stimulants. In a study of 17 boys taking methylphenidate or Adderall, diastolic blood pressure load increased significantly while the subjects were on Adderall. Systolic blood pressure and heart rate also differed between on and off medication.<sup>106</sup> A study of 14 healthy subjects found that intravenous doses of methylphenidate significantly increased heart rate, systolic and diastolic blood pressures and epinephrine concentration in plasma. The blood pressure changes were significantly correlated with increases of dopamine in striatum and of plasma epinephrine levels caused by the drug, supporting the hypothesis that methylphenidate-induced blood pressure increases are due in part to the drug’s central dopaminergic effects.<sup>107</sup>

The cardiovascular effects of methylphenidate can be deadly. According to FDA adverse reaction reports—which are notoriously incomplete—there were 160 Ritalin-related deaths between 1990 and 1997, most of them related to cardiovascular functioning. Dr. L. Dragovic, Oakland County, Michigan, medical examiner, explains that drugs such as methylphenidate stimulate the body’s adrenergic system when used repetitively, affecting everything that has as its chemical pathway mediators and transmitters such as adrenaline, noradrenaline and dopamine. The enhancement of the adrenergic system over many months or years will produce changes in small blood vessels. Some cells will be lost, and scarring will occur as the body tries to repair the area. The blood vessels will narrow. “The changes that we’re seeing in kids who have been on Ritalin for about eight years are basically the same as the changes in someone that has been abusing cocaine regularly over a period of years,” says Dr. Dragovic.<sup>108</sup>

**Potential for drug abuse.** According to the U.S. Drug Enforcement Administration (DEA), of all the psychoactive drugs prescribed to young children in the U.S., only two substances that are widely used to treat children are subject to the Controlled Substances Act (CSA): methylphenidate and amphetamine. The DEA identifies these drugs as “powerful stimulants” and places them in Schedule II of the CSA, which contains substances that have the highest abuse potential and dependence profile of all drugs with medical utility.<sup>109</sup>

In testimony before Congress in 2000, a DEA official reported that extensive research “unequivocally indicates that both methylphenidate and amphetamine have high abuse liabilities.” The data show that animals and humans cannot tell the difference between cocaine, amphetamine and methylphenidate when they are taken in the same way at comparable doses. “In short, they produce effects that are nearly identical,” he said. Improper use of methylphenidate (tablets can be abused orally, crushed and snorted, or dissolved in water and injected) poses significant risks, with high doses producing agitation, tremors, euphoria, palpitations and other problems. Abuse of this drug also has been associated with psychotic episodes, paranoid delusions and hallucinations.<sup>110</sup>

According to one review of this topic, neuropharmacologic data suggest that methylphenidate has pharmacokinetic properties which reduce its abuse potential compared with that of other stimulants, such as cocaine.<sup>111</sup> And while there is disagreement regarding the extent to which preteens and adolescents are abusing this drug,<sup>112</sup> some research indicates that the diversion of methylphenidate for illicit use increased during the 1990s and, according to a recent survey, poses a potentially serious public health issue.<sup>113, 114, 115, 116</sup> The DEA official concludes: “Probably the single most disturbing trend is that adolescents do not view abuse of this drug as serious.”<sup>117</sup>

### **Natural Therapies for ADHD**

Given the risks that children face in taking stimulant-type drugs, it stands to reason that parents may want to use more natural methods of treating ADHD symptoms. In a 2003 survey, 54% of 114 parents of children referred for evaluation of ADHD reported using complementary and alternative medicine, such as vitamins and dietary manipulation, to treat their child’s attention problems.<sup>118</sup> Natural therapies used to treat ADHD are introduced here, and they will be discussed more fully in a future article.

Many nonpharmaceutical approaches to ADHD focus on eliminating food and environmental allergens that trigger symptoms and using nutrient supplements to address deficiencies and provide the body with nutritional support. As a recent article reports: “Numerous studies suggest that biochemical heterogeneous etiologies for AD/HD cluster around at least eight risk factors: food and additive allergies, heavy metal toxicity and other environmental toxins, low-protein/high-carbohydrate diets, mineral imbalances, essential fatty acid and phospholipid deficiencies, amino acid deficiencies, thyroid disorders, and B-vitamin deficiencies.”<sup>119</sup>

A 2003 review of nutrition in the treatment of ADHD found that nutritional factors such as food additives, refined sugars, food sensitivities/allergies and deficiencies of fatty acids have been associated with this disorder. The authors say there is growing evidence that “many children with behavioral problems are sensitive to one or more food components that can negatively impact their behavior.” They conclude that, in general, diet modification “plays a major role in the management of ADHD and should be considered as part of the treatment protocol.”<sup>120</sup>

One study proving this statement found that 19 of 26 children who met the criteria for ADHD responded favorably to a multiple-item elimination diet. On open challenge, all 19 reacted to many foods, dyes and/or preservatives. Sixteen of them completed a double-blind placebo-controlled food challenge, which found a significant improvement on placebo days compared with challenge days. The researchers state that “dietary factors may play a significant role in the etiology of the majority of children with ADHD.”<sup>121</sup>

The value of nutritional therapies in addressing ADHD was demonstrated in a recent study comparing the effects of Ritalin with those of food supplements. In this study, 10 children with ADHD took the drug and 10 took dietary supplements. Subjects in both groups showed significant gains on the outcome measures used, such as the Intermediate Visual and Auditory/Continuous Performance Test. The supplements used in the study included a mix of vitamins, minerals, phytonutrients, amino acids, essential fatty acids, phospholipids and probiotics that attempted to address the biochemical risk factors of ADHD. The researchers concluded: “These findings support the effectiveness of food supplement treatment in improving attention and self-control in children with AD/HD and suggest food supplement treatment of AD/HD may be of equal efficacy to Ritalin treatment.”<sup>122</sup>

Natural therapies for ADHD, such as those discussed here, target the symptoms of this disorder without posing the risks of conventional treatment. Considering the many controversies surrounding ADHD—an unidentified cause, a subjective diagnosis and exposure to potentially harmful medications—there is clearly room for treatment options that avoid those considerable risks.

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