

## **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,