The NEW ENGLAND JOURNAL of MEDICINE

Perspective

JUNE 22, 2006

ADHD in Adults

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As a child, Dr. Y often confounded her parents and teachers. She regularly brought home straight-A report cards, but the grades were accompanied by comments like "She is a very bright child but disorganized and makes careless mistakes." "I was always the space cadet of the family," recalled Dr. Y, now a 27-year-old physician doing her residency. "My sisters would get their homework done, and I would be racing around the table. I was a compulsive talker. I would wander around the house, reading. I was extremely forgetful: I would finish my little snack and always throw my spoon and my bowl in the trash. . . . I always just thought maybe I was a little weird."

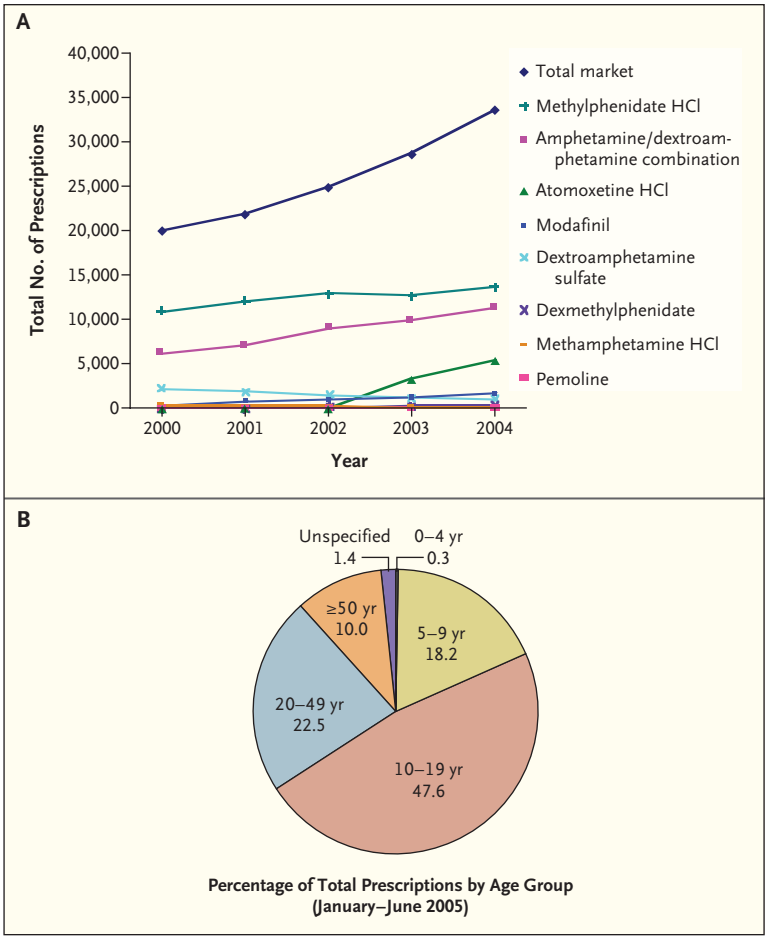
Determined to succeed, she resigned herself to spending twice as much time as her classmates did completing assignments. "For the longest time, I didn't realize how much harder I was working than everyone else to get things done," she said. As a high-school senior, she received the highest possible score, 1600, on the Scholastic Aptitude Test and was admitted to Harvard — yet when she had to organize her own college work schedule, she found herself struggling academically. She sought help from a counselor, who noticed her tendency to fidget and to talk nonstop. After a psychiatric evaluation, she was given a diagnosis of adult attention deficit–hyperactivity disorder (ADHD). "I laughed," Dr. Y told me. "I said, 'Are you kidding me? I go to Harvard — come on.'" In elementary school, she recalled, "Those kids were the bad little boys who got in trouble and ran around the room."

Although her history of academic success is atypical, many other aspects of Dr. Y's experiences are common among people with ADHD, a diagnosis that is increasingly being applied to adults. Once considered a disorder of the elementary-school years that children "outgrew" during adolescence as their brains matured, ADHD is now thought to persist into adulthood, impairing functioning, in about 50 percent of cases. Many people who were first prescribed stimulant medications for ADHD when they were young children are continuing to take them during high school, in college, and beyond. Moreover, some adults are turning to psychiatrists or primary care physicians for help with difficulties at work or in personal relationships

and are being told for the first time that they have ADHD. At a clinic for adults with the disorder at Massachusetts General Hospital in Boston, the average age of patients receiving treatment is 40.

The widespread use of methylphenidate and other stimulants to treat ADHD in children has long been controversial, and recently, their increasing use in adults has aroused concern about the possible risk of cardiovascular side effects with long-term use. Data from U.S. pharmacies, presented last February to the Drug Safety Advisory Committee of the Food and Drug Administration (FDA), indicate that the number of prescriptions given to people 19 years of age or older for eight drugs commonly used in ADHD increased by 90 percent between March 2002 and June 2005 and that adults now receive about one third of all prescriptions for these drugs (see graphs) — although they are sometimes prescribed for indications other than ADHD.

Studies suggest that in persons with untreated ADHD, symptoms of inattention, impulsiveness, and hyperactivity can impair school and work performance, damage self-esteem, interfere with relationships, and reduce the chances of success and satisfaction in many areas of life, as well as increase the risk of tobacco use, substance abuse, other psychiatric disorders, injuries, and motor vehicle accidents. But as with other mental disorders, there is no objective test for ADHD, so the decision to diagnose and treat rests on subjective factors: a patient's reported history of characteristic symptoms and functional impairment, which must have been present at least since seven years of age, and a clinician's assessment of whether the patient meets accepted diagnostic criteria (see box). Many of the symptoms are common, increasing the risk of misdiagnosis or overdiagnosis; studies of adults who present to be evaluated for ADHD suggest that only about one third clearly meet the criteria outlined in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV), and many persons with non-ADHD psychiatric diagnoses are positive on screening with commonly used ADHD rating scales.[1]



U.S. Prescriptions for Drugs Used to Treat ADHD.

Total numbers of prescriptions from 2000 to 2004 are shown in Panel A. Totals do not necessarily represent numbers of patients taking these medications for ADHD, since several of the drugs listed are also used for other indications. Panel B shows the proportions of U.S. prescriptions, for the period between January and June 2005, that were given to patients in various age groups. Data are from Vector One: National (VONA), a marketing research firm.

International psychiatric studies of children suggest that when uniform diagnostic criteria are applied and the populations studied are similar in age and sex ratios, the frequency of ADHD is similar worldwide.[2] In practice, however, diagnostic criteria vary among countries, as do cultural attitudes toward mental illness, psychiatry, and the use of psychiatric drugs, resulting in widely disparate patterns of diagnosis and treatment of ADHD. In the United States, data from the Cen-

Diagnostic Criteria for Attention Deficit–Hyperactivity Disorder.*

A. Either (1) or (2):

(1) inattention: six (or more) of the following symptoms of inattention have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

(a) often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities

(b) often has difficulty sustaining attention in tasks or play activities

(c) often does not seem to listen when spoken to directly

(d) often does not follow through on instructions and fails to finish school work, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)

(e) often has difficulty organizing tasks and activities

(f) often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)

(g) often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools)

(h) is often easily distracted by extraneous stimuli

(i) is often forgetful in daily activities

(2) hyperactivity–impulsivity: six (or more) of the following symptoms of hyperactivity–impulsivity have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

Hyperactivity

(a) often fidgets with hands or feet or squirms in seat

(b) often leaves seat in classroom or in other situations in which remaining seated is expected

(c) often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)

(d) often has difficulty playing or engaging in leisure activities quietly

(e) is often "on the go" or often acts as if "driven by a motor"

(f) often talks excessively

Impulsivity

(g) often blurts out answers before questions have been completed

(h) often has difficulty awaiting turn

(i) often interrupts or intrudes on others (e.g., butts into conversations or games)

B. Some hyperactive–impulsive or inattentive symptoms that caused impairment were present before age 7 years.

C. Some impairment from the symptoms is present in two or more settings (e.g., at school [or work] and at home).

D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorders, or a personality disorder).

* From the *Diagnostic and Statistical Manual of Mental Disorders,* fourth edition, text revision, 2000.

ters for Disease Control and Prevention indicate that in 2003, about 7.8 percent of children between 4 and 18 years of age were reported to have a history of an ADHD diagnosis, and about 56 percent of them were taking medication for the disorder. Among U.S. adults, the prevalence of ADHD is estimated to be 4.4 percent; this figure comes from a recent study of a nationally representative sample of adults 18 to 44 years of age, drawn from a much larger household survey, the National Comorbidity Survey Replication. In that study, about 11 percent of respondents who met the criteria for adult ADHD reported that they had received treatment for the disorder during the 12 months before they were interviewed.[3]

Physicians in Britain and other European countries use more restrictive diagnostic criteria, from the *International Classification of Diseases*. Medications are used to treat ADHD in children much less frequently in Europe than they are in the United States, and very few physicians diagnose or treat the disorder in adults, according to Eric Taylor, the head of the Department of Child and Adolescent Psychiatry at King's College London. For example, Taylor estimated that about 0.3 percent of children in the United Kingdom — and smaller percentages in Italy, France, and Scandinavia — are being treated with stimulants. Studies suggest that in 2001, about 1.4 percent of school-age children in Germany and 1.2 percent of children in Israel were receiving such treatment. A large, federally funded, randomized trial of children with ADHD found that treatment with stimulants, either alone or combined with intensive behavioral therapy, was more effective than behavioral therapy alone for reducing symptoms of the disorder.[4] Taylor said that he favors the early use of both medication and life-skills training for persons with ADHD but that most physicians in England would try psychotherapy or counseling before prescribing drugs. "I think, in general, the U.K. does undertreat" ADHD, Taylor said. He said the use of ADHD medications is increasing in England, "but I don't necessarily want

it to rise up to the level that prevails in the United States."

U.S. psychiatrists acknowledged that the risks of long-term stimulant use in adults must be studied more carefully, but they also emphasized that adult ADHD causes considerable suffering and that some affected adults clearly benefit from medication. "The impact of ADHD depends on what else you have going for you," such as intelligence, a congenial personality, or financial resources, said Jerrold F. Rosenbaum, psychiatrist-in-chief at Massachusetts General Hospital. Some people who have such assets can compensate for the disorder and choose not to be treated, he said. "But for a lot of people, it makes the difference between failure and making it. You go to work, and your boss gets frustrated. You don't get things completed, you don't show up on time, you lose things. . . . You let people down." Rosenbaum said life is especially hard for people who do not know they have ADHD. "They feel so bad about themselves," he said. "They spend their lives apologizing."

Despite her initial skepticism, Dr. Y soon became convinced that her own behavior and experiences fit the syndrome. "I was a terrible driver," she recalled. "I remember getting into an accident because I impulsively cut off another driver and skidded off the road." She had trouble working productively with others, sometimes hurt friends' feelings with impulsive comments, and once blew a job interview by fidgeting throughout the conversation. During a stint as a consultant after college, she had to work longer hours than her colleagues to finish her assignments. For several years, she coped with her disorganization by using strategies learned during cognitive-behavioral therapy: writing everything down in a planner and breaking projects into small tasks. Eventually, as a medical student, she began taking long-acting methylphenidate. She noticed immediate benefits — even her driving improved. "It's not a magic bullet, but it just takes the edge off. My mind was clearer. . . . I felt, instead of being really nonlinear, things just fell into an easier pattern."

However, she has also had side effects. She said that her systolic and diastolic blood pressure each rose by about 10 points, and she has episodes of tachycardia. If she is anxious, the medicine makes it worse and sometimes causes sleep problems. She recently cut back on her dose to make it easier to stay calm and to be able to sleep while on call in the hospital.

Dr. Y's case illustrates some of the tradeoffs of treating adults with ADHD medications. Three drugs — the nonstimulant atomoxetine (Strattera), mixed amphetamine salts (Adderall), and dexmethylphenidate (Focalin) — have been approved by the FDA for adult ADHD, and prescription data suggest that others are also used. "It's not clear that physicians are following guidelines and standards in the use of these medications," said Marsha Rappley, a professor of pediatrics and human development at Michigan State University College of Human Medicine. Rappley, an ADHD expert who serves on the FDA's Drug Safety Advisory Committee, said that data presented to the committee last February suggested that the cardiovascular risks associated with long-term stimulant use may be greater in adults than in children and that studies are needed to quantify the likelihood of cardiovascular events so that the risks and benefits may be weighed. And, she asks, "are there cardiovascular conditions among adults that put them at additional risk?" Guidelines issued in 2002 by the American Academy of Child and Adolescent Psychiatry on stimulant use in children, adolescents, and adults recommend monitoring the blood pressure and pulse of adults on the medications every three months. Otherwise, no separate recommendations exist for the treatment of adults, Rappley said, adding, "I think we need to move toward adoption of standards of care."

Steven Sharfstein, president of the American Psychiatric Association, said he believes adult ADHD "is a genuine syndrome" that is probably both underdiagnosed and misdiagnosed. It is successfully treated with the stimulant medications, he added, but "we don't know the long-term benefit–risk ratio" of such treatment.

Researchers have amassed considerable evidence that ADHD has a biologic basis. Family studies show that the heritability of the disorder is high, similar to that of schizophrenia or bipolar illness. Each sibling of a child with ADHD has about a 20 percent chance of having it too, and 15 to 20 percent of parents of affected children also have the disorder, said Stephen V. Faraone, a professor of psychiatry, neuroscience, and physiology at State University of New York Upstate Medical University. Anatomical studies comparing the brains of people with ADHD with those of unaffected people show reductions in

volume throughout the cerebrum and cerebellum, amounting to about a 4 percent reduction in overall brain volume. Faraone said such findings may reflect "subtle changes in neural networks." Functional brain-imaging studies in affected children show abnormal activation of a number of cerebral areas during the performance of cognitive tasks, suggesting subtle differences in brain functioning. Genetic studies have so far implicated at least seven genes in influencing susceptibility to ADHD; most code for proteins that affect the levels or functioning of a neurotransmitter — dopamine, norepinephrine, or serotonin — at nerve synapses in the brain. Stimulant drugs that are effective against ADHD are thought to work by altering the levels of dopamine and norepinephrine at the synapse. Prenatal environmental factors such as pregnancy or delivery complications, prematurity, and fetal exposure to alcohol or tobacco also appear to be risk factors.[5]

Psychiatrists say that the diagnosis of ADHD is applied to people whose symptoms range in severity and probably stem from various combinations of biologic and environmental factors. "In my view, the science is not really at the level where we can say there is a single known physiological cause," said Taylor. "There are many causes, each of small effect . . . and the model of a single disease is not well applied. What does apply is the model of chronic disability." Moreover, not everyone with ADHD needs treatment, points out Rosenbaum. "If it's not severe, you may decide that . . . you would rather live with it."

Despite the evidence of a biologic basis for ADHD, debate continues (chiefly among nonpsychiatrists) about whether some behavior that fits the syndrome may represent a variant of normal functioning that is maladaptive in today's sedentary, performance-oriented society and that has therefore been targeted for treatment. "I think adult ADHD has to be looked at in relation to the need for drug companies to create a new market," said Ilina Singh, a sociologist at the London School of Economics who has studied the marketing of methylphenidate and related stimulants. Until very recently, "ADHD was always a disorder found in childhood," she said, noting that this view may have begun to change after psychiatrists Edward M. Hallowell and John J. Ratey suggested in a popular book, *Driven to Distraction*, that Albert Einstein may have had ADHD. Diagnosing the disorder for the first time in adults "is an extraordinary shift," she said.

Singh and others express concern about the facts that pharmaceutical companies have paid for many of the ADHD treatment studies and that several leading experts on the condition have received research funding from, or have other financial relationships with, manufacturers of ADHD drugs. A recent article reported that 13 of the 21 members of the DSM-IV panel that sets diagnostic standards for ADHD and other psychiatric disorders usually diagnosed in childhood have such financial ties.[6]

Stimulants are known to increase vigilance and improve performance on learning tasks in normal persons as well as those with ADHD. Advertisements for Adderall show men apparently working as architects, scientists, or chefs and contain slogans such as "Aim higher," "Reach new heights," and "Efficacy that measures up to life's demands." "The modern advertising of these drugs is not to treat deficiency," Singh said. "It captures adults' desire to optimize their life, to enhance their life. . . . Does everybody have the right to access these drugs? What happens if more and more people in the workplace have this competitive edge?"

But physicians who regularly treat the disorder say that such skepticism reflects a lack of awareness about the ability of ADHD to disrupt the lives of affected adults as well as children. "This is not just performance enhancement that we're talking about," said Daniel Shapiro, a behavioral pediatrician who practices in Rockville, Maryland. "This is relief of genuine suffering."

Dr. Okie is a contributing editor of the *Journal*.

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