

Diagnosis and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents

Larry S. Goldman, MD; Myron Genel, MD; Rebecca J. Bezman, MD; Priscilla J. Slanetz, MD, MPH;
for the Council on Scientific Affairs, American Medical Association

Objective.—To deal with public and professional concern regarding possible overprescription of attention-deficit/hyperactivity disorder (ADHD) medications, particularly methylphenidate, by reviewing issues related to the diagnosis, optimal treatment, and actual care of ADHD patients and of evidence of patient misuse of ADHD medications.

Data Sources.—Literature review using a National Library of Medicine database search for 1975 through March 1997 on the terms *attention deficit disorder with hyperactivity, methylphenidate, stimulants, and stimulant abuse and dependence*. Relevant documents from the Drug Enforcement Administration were also reviewed.

Study Selection.—All English-language studies dealing with children of elementary school through high school age were included.

Data Extraction.—All searched articles were selected and were made available to coauthors for review. Additional articles known to coauthors were added to the initial list, and a consensus was developed among the coauthors regarding the articles most pertinent to the issues requested in the resolution calling for this report. Relevant information from these articles was included in the report.

Data Synthesis.—Diagnostic criteria for ADHD are based on extensive empirical research and, if applied appropriately, lead to the diagnosis of a syndrome with high interrater reliability, good face validity, and high predictability of course and medication responsiveness. The criteria of what constitutes ADHD in children have broadened, and there is a growing appreciation of the persistence of ADHD into adolescence and adulthood. As a result, more children (especially girls), adolescents, and adults are being diagnosed and treated with stimulant medication, and children are being treated for longer periods of time. Epidemiologic studies using standardized diagnostic criteria suggest that 3% to 6% of the school-aged population (elementary through high school) may suffer from ADHD, although the percentage of US youth being treated for ADHD is at most at the lower end of this prevalence range. Pharmacotherapy, particularly use of stimulants, has been extensively studied and generally provides significant short-term symptomatic and academic improvement. There is little evidence that stimulant abuse or diversion is currently a major problem, particularly among those with ADHD, although recent trends suggest that this could increase with the expanding production and use of stimulants.

Conclusions.—Although some children are being diagnosed as having ADHD with insufficient evaluation and in some cases stimulant medication is prescribed when treatment alternatives exist, there is little evidence of widespread overdiagnosis or misdiagnosis of ADHD or of widespread overprescription of methylphenidate by physicians.

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This report is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all the facts and

circumstances involved in an individual case and are subject to change as scientific knowledge and technology advance and patterns of practice evolve. This report reflects the scientific literature as of March 1997.

Reprints: Linda B. Bresolin, PhD, Council on Scientific Affairs, American Medical Association, 515 N State St, Chicago, IL 60610 (e-mail: linda_bresolin@ama-assn.org).

ATTENTION-DEFICIT/hyperactivity disorder (ADHD) is a common neuropsychiatric syndrome with onset in childhood, most commonly becoming apparent (and thus coming to medical attention) during the first few years of grade school. ADHD may be associated with a number of comorbid psychiatric conditions as well as with impaired academic performance and with both patient and family emotional distress. While it was previously thought that the disorder remitted before or during adolescence, it has become well established that many patients will have an illness course that persists well into adulthood. Pharmacological treatment, particularly with stimulant medication, is the most-studied aspect of management, although other forms of treatment (eg, behavior therapy, parent training) are important parts of good clinical care.

Despite an enormous body of research into this disorder, various aspects of ADHD have generated controversy over the years. Three features of ADHD in particular seem to have contributed to the controversy: (1) like most mental disorders, its diagnostic criteria involve patient history and behavioral assessment without the availability of laboratory or radiologic confirmation; (2) like many chronic illnesses of childhood, it has an early onset and extended course, thus requiring at times treatment of children and adolescents over many years; and (3) its treatment often includes stimulant medications that have abuse or diversion potential.

Members of the Council on Scientific Affairs at the time this report was written include the following: Mitchell S. Karlan, MD, Los Angeles, Calif (chair); Ronald M. Davis, MD, Detroit, Mich (chair-elect); Roy D. Altman, MD, Miami, Fla; Rebecca J. Bezman, MD, Chicago, Ill; Scott D. Deitchman, MD, MPH, Decatur, Ga; Myron Genel, MD, New Haven, Conn; John P. Howe III, MD, San Antonio, Tex; Nancy H. Nielsen, MD, PhD, Buffalo, NY; Joseph A. Riggs, MD, Haddon Field, NJ; Priscilla J. Slanetz, MD, MPH, Boston, Mass; Michael A. Williams, MD, Baltimore, Md; Donald C. Young, MD, Iowa City; Larry S. Goldman, MD (staff); Robert C. Rinaldi, PhD (secretary); Linda Bresolin, PhD (assistant secretary).

Debate has centered on the appropriate assessment and "labeling" of children: there have been allegations that the diagnosis is merely applied to control children who exhibit unwanted behaviors in the classroom or elsewhere and that medication is simply used to control such behavior. Along similar lines, concerns have been expressed about whether thorough enough evaluations are being performed by physicians prior to prescribing medication. Apart from diagnostic issues, concerns have been raised about young children taking medications for lengthy periods of time. In addition, some critics have complained that overemphasis on psychopharmacological treatment has led to neglect of other treatment modalities or served as a distraction from family problems or school shortcomings. It should be stressed that these issues have been raised polemically or theoretically, rather than on the basis of particular scientific findings.

Another concern has been raised by the dramatic increase in methylphenidate (Ritalin) hydrochloride production and use in the United States in the past decade. This has raised questions about whether there has been a true increase in the prevalence of ADHD in this time period; a change in diagnostic criteria affecting practice; improved physician recognition of the disorder; a broadened spectrum of indications for use of stimulants; and an increase in stimulant abuse, diversion, and prescription for profit.

Debate over ADHD within the research and medical communities has been mild and mostly concerned with nuances in the diagnostic and treatment paradigms.¹ By contrast, highly inflammatory public relations campaigns and pitched legal battles have been waged (particularly by groups such as the Church of Scientology) that seek to label the whole idea of ADHD as an illness a "myth" and to brand the use of stimulants in children as a form of "mind control."^{2,3} These efforts, which have been widely reported in the news media, have created a climate of fear among physicians, parents, and educators and have sown anxiety and confusion among the general public.^{4,5} It is thus most important to separate legitimate concerns raised by scientific studies from abstract, distorted, or mendacious information from other sources.

There are 6 main questions that underlie this professional and public concern and that this report will address by reviewing the pertinent research:

1. Is there an agreed-on set of diagnostic criteria for ADHD that reflects sufficient reliability and validity so as to delineate a clinically meaningful syndrome?

2. What is the epidemiology of ADHD, and how can the apparent disparities in prevalence in different populations be explained?

3. What is the course of the illness, and what are the adverse consequences of the illness that would justify treatment?

4. What constitutes optimal treatment for ADHD, and how do stimulants fit into it?

5. What are the adverse consequences of using stimulants, and in particular, what is known about the risks of abuse and diversion?

6. Are children being appropriately assessed and treated in clinical settings to ensure that diagnostic criteria are being used appropriately; ie, is there evidence of underdiagnosis, overdiagnosis, or misdiagnosis?

METHODS

The National Library of Medicine database was searched for 1975 through March 1997 for English-language articles covering school-aged children. Search terms were *attention deficit disorder with hyperactivity, methylphenidate, stimulants, and stimulant abuse and dependence*. Articles concerned with diagnostic and outcomes issues were used. Drug Enforcement Administration (DEA) data also were incorporated.

DIAGNOSIS OF ADHD

Hyperactivity in children was first described clinically in 1902, and the first report of stimulant use to treat hyperactivity in that condition was in 1937.⁶ The high frequency of "soft" neurologic findings led to designating the condition "minimal brain dysfunction," with the expectation that a consistent neurologic lesion or set of lesions would eventually be found.⁷

The first empirically based official set of diagnostic criteria for what is now referred to as ADHD was delineated in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders (DSM-III)* in 1980.⁸ Early focus on the centrality of hyperactivity shifted toward giving weight to attentional problems and impulsivity as well, which was later reflected in the 1987 revision (*Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition [DSM-III-R]*).⁹ The current classification (*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV]*) of the disorder now allows subtyping as predominantly inattentive type, predominantly hyperactive type, or combined type.¹⁰ These successive changes in diagnostic criteria reflect a combination of empiri-

cal research findings and expert committee consensus. The complete *DSM-IV* criteria can be found in Table 1.

The *DSM-IV* criteria emphasize several factors:

The symptoms specified in the criteria must be present for at least 6 months, ensuring that persistent rather than transient symptoms will be included.

The symptoms must be "maladaptive and inconsistent with developmental level." This ensures that the symptoms are of sufficient severity to cause problems and that the child's age and neurodevelopment are considered in evaluating symptoms.

The symptoms must be present across 2 or more settings, ie, school problems alone do not meet criteria for the diagnosis.

The symptoms are not better explained by another disorder, such as mood disorder, psychosis, or pervasive developmental disorder (autism).

Taken as a whole, these criteria require an illness pattern that is enduring and has led to impairment. To make this diagnosis appropriately, the clinician must be familiar with normal development and behavior, gather information from several sources to evaluate the child's symptoms in different settings, and construct an appropriate differential diagnosis for the presenting complaints. This helps, for example, to distinguish children with ADHD from unaffected children whose parents or teachers are mislabeling normal behavior as pathological. The diagnostic criteria as used by appropriate examiners demonstrate high interrater reliability of individual items and of overall diagnosis.¹¹

A number of other psychiatric, medical, and neurologic disorders (eg, traumatic brain injury, epilepsy, depression) can lead to disturbances in attention and/or activity level.¹² Thus, the diagnosis of "primary" ADHD is made when there is no evidence from the history, physical examination, or laboratory findings of another condition producing the clinical picture.

The goals of the actual examination of the child are to determine whether he or she meets diagnostic criteria and to look for conditions other than ADHD that might simulate it. Too much focus on a child's behavior in the physician's office or the child's own observations may lead to a missed diagnosis, while overreliance on parental reports of abnormal behavior alone may lead to overdiagnosis.¹³

A number of rating scales and psychological testing instruments may be used in the assessment of suspected ADHD, but none of these should be used in isolation to make or refute the diagnosis. Scales such as the Conners, SNAP-IV,

Table 1.—Diagnostic Criteria for Attention-Deficit/Hyperactivity Disorder*

- A. Either (1) or (2):
- (1) inattention: 6 (or more) of the following symptoms of inattention have persisted for at least 6 mo 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 schoolwork, 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 (eg, 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: 6 (or more) of the following symptoms of hyperactivity-impulsivity have persisted for at least 6 mo to a degree that is maladaptive and inconsistent with developmental level:
 - (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
 - (g) often blurts out answers before questions have been completed
 - (h) often has difficulty awaiting turn
 - (i) often interrupts or intrudes on others (eg, butts into conversations or games)
- B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before age 7 y
- C. Some impairment from the symptoms is present in 2 or more settings (eg, 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 (eg, mood disorder, anxiety disorder, dissociative disorder, or a personality disorder)

**Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*,¹⁰ code based on type: 314.01 Attention-Deficit/Hyperactivity Disorder, Combined Type: if both criteria A(1) and A(2) are met for the past 6 months; 314.00 Attention-Deficit/Hyperactivity Disorder, Predominantly Inattentive Type: if criterion A(1) is met but criterion A(2) is not met for the past 6 months; 314.01 Attention-Deficit/Hyperactivity Disorder, Predominantly Hyperactive-Impulsive Type: if criterion A(2) is met but Criterion A(1) is not met for the past 6 months. Coding note: For individuals (especially adolescents and adults) who currently have symptoms that no longer meet full criteria, "In Partial Remission" should be specified.

and Disruptive Behavior Disorder Scale are more helpful in assessing and monitoring response to treatment than in making a diagnosis. Neuropsychological tests that focus on sustained attention such as the Continuous Performance Task, the Wisconsin Card-Sorting Test, Test of Variables of Attention, the Matching Familiar Figures Test, and the Wechsler Intelligence Scale for Children-Revised are similarly not diagnostic.¹

Thus, the overall approach to diagnosis may involve (1) a comprehensive interview with the child's adult caregivers; (2) a mental status examination of the child; (3) a medical evaluation for general health and neurologic status; (4) a cognitive assessment of ability and achievement; (5) use of ADHD-focused parent and teacher rating scales; and (6) school reports and other adjunctive evaluations if necessary (speech, language assessment, etc) depending on clinical findings.^{1,14,15} An evaluation can be performed by a clinician with the skills and knowledge to carry out those components.

Attempts to clarify the pathophysiology of ADHD have been made on several fronts. Genetic studies have revealed up to 92% concordance in monozygotic twins and 33% in dizygotics.¹⁶⁻¹⁸ Abnormalities have been noted in mag-

netic resonance imaging studies of the brains of those with ADHD,¹⁹ single photon emission computed tomography,^{20,21} and neurophysiological studies (heart rate deceleration, electroencephalogram amplitude of response to stimulation, habituation on evoked responses).¹ These findings and others, when taken together, provide increasing support for the concept of ADHD as a neuropsychiatric condition or set of conditions.

Even with the use of carefully applied diagnostic criteria, there remains the issue of the validity of ADHD as a discrete condition.²² With regard to unitary etiology, many medical conditions (eg, heart failure, seizures) are syndromes representing a final common presentation of a number of pathophysiological disturbances. Thus, the absence of a single cause would be a weak argument against the validity of ADHD as a discrete syndrome. The familial, genetic, neuroanatomical, and neurophysiological studies are mounting evidence to date for postdictive validity. Findings with regard to concurrent validity are mixed: there is clearly a great deal of overlap between ADHD and a number of learning conditions and conduct disorder, among other conditions. The strongest evidence of validity has been for course prediction and treatment re-

sponse. Overall, ADHD is one of the best-researched disorders in medicine, and the overall data on its validity are far more compelling than for many medical conditions.^{15,23,24}

EPIDEMIOLOGY OF ADHD

A number of studies have examined the prevalence of ADHD in various populations. The patient sample used is critical because of variations in different settings: at least 10% of behavior problems seen in general pediatrics settings are due to ADHD, while children with ADHD make up to 50% of some child psychiatric populations.¹⁵ In general, most ADHD patients in the United States are cared for by pediatricians and family practitioners, while child psychiatrists, neurologists, and behavioral pediatricians tend to see refractory patients and those with significant comorbidity. Community studies have yielded prevalences between 1.7% and 16%, depending on the population and the diagnostic methods. These studies are summarized in Table 2.

These results suggest that across fairly diverse populations (geographically, racially, socioeconomically) there exists a sizable percentage of school-aged children with ADHD. The evolution of criteria from *DSM-III* to *DSM-IV*, although based on a progressively larger empirical base,³⁶ has broadened the case definition, so that more children appear to be affected. This is largely a function of the increased emphasis on attentional problems as opposed to a more narrow focus on hyperactivity in earlier diagnostic sets. As a result, girls have been diagnosed as having ADHD more frequently than they were in the past.³⁷

ILLNESS COURSE AND COMORBIDITY OF ADHD

Longer-term follow-up studies of children with ADHD as well as "lookback" studies of symptomatic adults who can be retrospectively diagnosed as having had childhood ADHD show that there is symptomatic persistence into adulthood in many cases. On average, symptoms diminish by about 50% every 5 years between the ages of 10 and 25 years. Hyperactivity itself declines more quickly than impulsivity or inattentiveness.^{38,39}

A number of psychiatric conditions co-occur with ADHD. Between 10% and 20% of children with ADHD in both community and clinical samples have mood disorders, 20% have conduct disorders, and up to 40% may have oppositional defiant disorder.⁴⁰ Bipolar disorder is being increasingly recognized.⁴¹ Only about 7% of those with ADHD have tics or Tourette syndrome, but 60% of those with Tourette syndrome have ADHD,

raising questions about common etiologic mechanisms. Learning disorders (especially reading disorder) and subnormal intelligence also are increased in the total population of those with ADHD and vice versa.^{42,43} Overall, perhaps as many as 65% of children with ADHD will have 1 or more comorbid conditions, although their presence will not be recognized without appropriate questioning and evaluation.⁴⁴ In general, when ADHD is untreated there is a gradual accumulation of adverse processes and events that increase the risk of serious psychopathology later in life.⁴⁵ Whether this can be reversed by long-term treatment remains unknown.

The relationship between substance use disorders and ADHD is complex. Children with ADHD who do not have comorbid conditions have a risk of substance use disorders that is no different from children without ADHD up to the age of about 14 years. The risk of developing substance use disorders in those with ADHD is increased in adolescents, and the risk ratio increases further in adulthood, regardless of whether there is comorbidity. Persistence of ADHD symptoms and family history of both ADHD and substance use disorders are risk factors for their development. Highly potent risk factors are the presence of comorbid conduct disorder or bipolar disorder. There is debate about whether long-term treatment of ADHD may decrease the risk of subsequent development of substance use disorders.⁴⁶

One prospective study, which followed an ADHD cohort over an average of 16 years along with a matched control group, found an 11-fold increase in ongoing ADHD symptoms (11% vs 1%), a 9-fold increase in antisocial personality disorder (18% vs 2%), and a 4-fold higher rate of drug use disorder (16% vs 4%).⁴⁷ The strongest predictors of persistence of psychopathology are psychiatric comorbidity and family history of ADHD.⁴⁸

TREATMENT OF ADHD

Methylphenidate, created in 1955, now accounts for more than 90% of the stimulant use in ADHD in the United States. A racemic mixture of amphetamines (Adderall), dextroamphetamine sulfate (Dexedrine and others), and pemoline (Cylert) are also used. Methylphenidate is strongly favored by US physicians, perhaps because the overuse of amphetamines for treatment of obesity and their misuse in the 1960s gave that class of drugs a reputation as more problematic than methylphenidate.

There have been more than 170 studies involving more than 6000 school-aged children using stimulant medication for ADHD. The response rate for any single

Table 2.—Prevalence Studies of Attention-Deficit/Hyperactivity Disorder

Site	Source, y	Criteria*	Prevalence, %
New Zealand	Anderson et al, ²⁵ 1987	DSM-III	6.7
New York, NY	Cohen, ²⁶ 1988	DSM-III	3-6
Ontario	Szatmari et al, ²⁷ 1989	DSM-III	6.3
Puerto Rico	Bird et al, ²⁸ 1988	DSM-III	9.5-16.1
US inner city	Newcorn et al, ²⁹ 1989	DSM-III†	12.9
Pittsburgh, Pa	Costello et al, ³⁰ 1988	DSM-III-R	2.6
Iowa	Lindgren et al, ³¹ 1990	DSM-III‡	2.8
Germany	Baumgaertel et al, ³² 1995	DSM-III§	9.6
London, England	Esser et al, ³³ 1990	DSM-III-R	1.7
Mannheim, Germany	Esser et al, ³³ 1990	DSM-III-R	4.2
United States	Pelham et al, ³⁴ 1992	DSM-III-R	2.5-4.0
Tennessee	Wolraich et al, ³⁵ 1996	DSM-III-R	7.3
United States	Shaffer et al, ¹¹ 1996	DSM-III-R	4.1

*DSM-III indicates *Diagnostic and Statistical Manual of Mental Disorders, Third Edition*⁹; DSM-III-R, *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition*⁹; and DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.¹⁰

†Prevalence of 18.9% using DSM-III-R.

‡Prevalence of 6.1% using DSM-III-R.

§Prevalence of 9.0% primarily inattentive, 3.9% primarily hyperactive, 4.8% combined (17.8% total) using DSM-IV, 10.9% using DSM-III-R.

||Prevalence of 5.4% primarily inattentive, 2.4% primarily hyperactive, 3.6% combined (total 11.4%) using DSM-IV.

stimulant drug in ADHD is approximately 70%, and up to 90% of children will respond to at least 1 stimulant without major adverse events if drug titration is done carefully. A “response” in this context means a statistically or clinically significant reduction in hyperactivity or increase in attention as rated by parents, teachers, and/or research raters. There have been only about a half-dozen studies in adolescents.^{49,50}

Medications have been unequivocally shown (ie, by double-blind, placebo-controlled studies) to reduce core symptoms of hyperactivity, impulsivity, and inattentiveness. They improve classroom behavior and academic performance; diminish oppositional and aggressive behaviors; promote increased interaction with teachers, family, and others; and increase participation in leisure time activities. Finally, stimulants have demonstrated improvement in irritability, anxiety, and nail biting.⁵¹ A recent meta-analysis found that the effect of stimulants on behavior and cognition may be severalfold greater than the effects on academic achievement.⁵²

Contrary to earlier assertions, the response to stimulant medications in those with ADHD is not “paradoxical”: the direction of changes in behavioral measures in those with ADHD, those with conditions other than ADHD (eg, learning disabilities, depression), and normal controls is the same. Thus, a favorable response to stimulants does not confirm a diagnosis of ADHD (nor, of course, does a nonresponse refute the diagnosis). A nonspecific performance-enhancing effect may mask other problems and delay use of other interventions.^{53,54}

In addition to their value in childhood and adult ADHD, methylphenidate and other stimulants may play a role in the treatment of other medical conditions,

including narcolepsy, as a short-term treatment for depression in the medically ill, as potentiating agents with conventional antidepressants for major depressive disorder, as potentiating agents with opiates for pain control, and to reduce apathy in dementia and some other brain diseases.⁵⁵⁻⁵⁷ The number of patients receiving these drugs for these indications probably represents no more than a small percentage of all stimulant use in the United States.

For patients with ADHD who are intolerant of or unresponsive to stimulants, a number of other drugs have proven useful in clinical practice, including tricyclic antidepressants⁵⁰ and bupropion hydrochloride, a newer antidepressant that blocks the reuptake of norepinephrine and dopamine.⁵⁸ Serotonin-specific reuptake inhibitors have not been effective to date.⁵⁰ Centrally acting α -blocking drugs (clonidine, guanfacine hydrochloride) have been helpful in some children, but data are still limited.^{59,60} Subsets of children seem to have some response to lithium carbonate.⁶¹ Neuroleptic medication is occasionally effective, but the risk of tardive dyskinesia makes this a problematic long-term approach.¹⁴ By contrast, some 20 studies have refuted the efficacy of dietary manipulations (eg, the Feingold diet) in ADHD.⁶²

It is important to emphasize that pharmacotherapy alone, while highly effective for short-term symptomatic improvement, has not yet been shown to improve the long-term outcome for any domain of functioning (classroom behavior, learning, impulsivity, etc). This may be a function of several factors: most studies have been carried out only for a short term, there may have been inadequate dosage titration to maximize the number of responders, and dose-re-

sponse relationships may be different for different domains.^{63,65}

Swanson⁵² published a careful review of all review studies of stimulant use in children in 1993. He found overwhelming evidence for temporary improvement of core symptoms (hyperactivity, inattention, and impulsivity) as well as the associated features of defiance, aggression, and negative social skills. On the other hand, changes that point toward longer-term improvement (eg, in academic outcome, antisocial behavior, or arrest rate) were not found, and only small effects were observed on learning and achievement.

Children should be reevaluated periodically while not taking medications to see if the medications are still appropriate and necessary.

Multimodal therapy, ie, integrating pharmacotherapy with a number of environmental, educational, psychotherapeutic, and school-based approaches, is a tailored approach that seems intuitively powerful, matching the child's particular problems to selections from a menu of focused treatment interventions. In a few studies, multimodal therapy has affected long-term results, although how applicable these findings are beyond research settings remains unclear.^{65,66} While three quarters of treatment review articles assert that multimodal therapy is superior to medication or psychosocial interventions separately, there is in fact little empirical evidence to support such a conclusion.⁵²

Nonmedication approaches include parent education; parent management training (contingency management in individual or group setting; this technique decreases disruptive behavior, increases parents' self-confidence, and decreases family stress); classroom environmental manipulations (special class, seating in class, etc); contingency management and daily report cards by teacher; individual psychotherapy for depression, anxiety, and low self-esteem; impulse and social skills control training; support groups such as Children and Adults With Attention Deficit Disorder and Attention Deficit Disorder Association for families; and summer treatment programs.^{15,67}

Some experts feel that stimulants alone may be adequate for cases of ADHD without comorbidity, but that additional treatments are necessary where there are co-occurring conditions. Behavioral therapy has not proved effective alone, although it has been when combined with pharmacotherapy.¹ Since psychosocial treatments may be labor intensive and expensive, it is important to establish when and which treatments are indicated. A large multisite study is

currently being carried out by the National Institute of Mental Health to clarify the role of multimodal treatment: carefully evaluated children will be randomized to receive standard community care, medication alone, psychosocial treatments alone, or multimodal therapy (medication and psychosocial treatments together).^{65,68}

A number of textbooks^{1,14} and many review articles^{50,69,70} are available to practitioners. The Academy of Child and Adolescent Psychiatry's practice parameters⁷¹ have recently been released. A recent American Academy of Pediatrics position paper emphasizes the need for careful evaluation and monitoring of children with ADHD, and it stresses that drugs be used as part of an overall care plan.⁷²

ADVERSE EFFECTS OF STIMULANTS

Adverse effects from stimulants are generally mild, short lived, and responsive to dosing or timing adjustments. The most common effects are insomnia, decreased appetite, stomach ache, headache, and jitteriness. Some children will exhibit motor tics while on stimulants: whether this reflects a true drug effect or an "unmasking" of a latent tic disorder is unknown. A small percentage of children experience cognitive impairment that responds to dosage reduction or drug cessation. Rare cases of psychosis have occurred. Pemoline has been infrequently associated with hepatic toxic effects, so periodic monitoring of liver enzymes is necessary.^{14,49}

Concerns had been raised about the effects of chronic stimulant ingestion on growth and development. It is unclear whether children's heights are affected by long-term use of these medications.⁷³⁻⁷⁵

A great deal of concern has been raised by the DEA and others about the potential for abuse or diversion of stimulant medication: production (and use) of methylphenidate in the United States has risen from less than 2000 kg in 1986 to 9000 kg in 1995, with a tripling between 1990 and 1995 alone. By contrast, amphetamine production rose from 400 to 1000 kg in the same period. More than 90% of US-produced methylphenidate is used in the United States.

The reasoning for the concern about possible overproduction of methylphenidate has been expressed as follows: Stimulants at times are abused by adolescents and adults; those with ADHD are at increased risk of developing a substance use disorder; methylphenidate and other stimulants may either become the drug abused by those with ADHD, or they may serve as a "gateway" to other drug use; and even if they do not

abuse their medication themselves, children and adolescents with access to stimulants will be under pressure to divert their medication to those who will.

There is little disagreement that stimulants as a class have marked abuse potential, and their misuse can have severe adverse medical and social consequences. However, stimulants differ in their ability to induce euphoria and thus liability to abuse. Almost all of the reports of abuse of methylphenidate itself have been of polysubstance-abusing adults who have tried to solubilize the tablets and inject them (with disastrous results from talc granulomatosis in some cases).⁷⁰ This last problem in particular led Sweden to withdraw methylphenidate from the market in that country entirely in 1968.⁷⁶

It is clear that there is a fair amount of use of stimulants by adolescents. The annual school survey of drug use conducted by the University of Michigan has shown an increase from 6.2% to 9.9% of eighth-graders reporting nonmedical stimulant use in the preceding year between 1991 and 1994. However, lifetime nonmedical methylphenidate use has remained essentially constant around 1% during the same period. Sixty percent of students who used any stimulants reported using them fewer than 6 times in their lifetime, and 80%, fewer than 20 times. Only 4% reported any injection use of stimulants.⁷⁷ Thus, while nonmedical stimulant use may be somewhat more common among adolescents in recent years, little use is of methylphenidate itself, and the pattern of use for the vast majority appears to be experimental and not of the type (regular, heavy, injecting, etc) likely to lead to serious adverse consequences.

Drug Abuse Warning Network data on emergency department visit monitoring show a 6-fold increase between 1990 and 1995 in mentions of methylphenidate. A "mention" simply indicates that the patient listed the drug as one taken: it is not necessarily the drug leading to the emergency department visit, nor is there any medical confirmation. The rate of cocaine mentions, by contrast, is 40 to 50 times higher. The methylphenidate cases are overwhelmingly young women, not the population (ie, male adolescents) felt to be at highest risk for abusing prescription methylphenidate. The DEA has had reports of thefts of methylphenidate, street sales, drug rings, illegal importation from outside the United States, and illegal sales by health professionals. There have also been reports of theft of school supplies of methylphenidate.⁷⁷

On the other hand, abuse of methylphenidate by patients with ADHD or

their family members has been reported rarely. Only 2 cases of methylphenidate abuse by adolescents with ADHD have been described,^{78,79} and only 2 cases of methylphenidate abuse by parents of children taking it for ADHD have been reported.⁸⁰ While there is no way to know how many cases may have been unrecognized or unreported, such a minimal published experience is quite remarkable in light of the population exposed.

Under Section 306(a) of the Controlled Substances Act, production limitations of methylphenidate, a Schedule II drug, are established by the attorney general (using information developed by the DEA). The attorney general also receives input from the secretary of health and human services (using information provided by the Food and Drug Administration [FDA]). In 1988 a DEA administrative law judge ruled that the method used by the DEA in 1986 to calculate methylphenidate production quotas failed to provide for legitimate medical need, leading to several policy changes. In 1993 there were some methylphenidate shortages because of a delay in publishing proposed quotas in the *Federal Register*, leading to a streamlining of the procedures for final quota notice approval.⁷⁷ American Medical Association (AMA) policy was adopted at the 1993 Interim Meeting (100.975, *AMA Policy Compendium*) calling on the AMA to work with the DEA and the FDA to ensure adequate supplies of methylphenidate and other Schedule II drugs.⁸¹

CURRENT PRACTICE

It is clear from the discussion of diagnostic assessment that ADHD simply cannot be diagnosed in a typical 15-minute primary care office visit. Taking the necessary multiple histories, performing a careful examination, and obtaining appropriate testing will require several visits and may require a multidisciplinary team approach, specialty consultation, or both in some cases. Nonetheless, there have been descriptions of such assessments in typical pediatric settings.^{12,82} Few data exist on actual practice habits in terms of what diagnostic criteria (if any) are used by clinicians, how they are applied, or exactly what a minimally satisfactory level of investigation entails.

A national survey of physicians⁸³ found that 5.3% of elementary school children in pediatrics practices were diagnosed as having ADHD, and 4.2% were diagnosed by family practitioners. When explicit *DSM-III-R* criteria were used, however, only 72% of those assigned a diagnosis of ADHD by their physicians would have received the di-

agnosis based on a structured interview. Only 53% of the physician diagnoses included teachers' reports. Eighty-eight percent of the physician-diagnosed children were prescribed methylphenidate, and 85% of the parents reported that the medication was helpful. Only 22% of the parents reported treatment with behavioral modification, and in 70% of those cases that modality was recommended by someone other than the treating physician. Eleven percent received counseling from the physician, and no parents queried judged it effective. The authors of this survey drew attention to the mismatch between physician diagnosis from a single source, often an unreliable one, and the use of stimulant medication. They also stressed the low rates of use of nonpharmacological treatment by their physician sample.

Safer and Krager⁸⁴ conducted regular surveys of school nurses in Baltimore County, Maryland, to look for methylphenidate prescribing. They found that 6% of the school-aged children received this treatment and that methylphenidate accounted for over 90% of the pharmacological treatment provided for ADHD.

There is evidence to suggest that stimulants in ADHD populations are simply being used more broadly, for longer periods, and without interruptions in recent years than was done previously. Overall, there has been a 2.5-fold increase in the prevalence of child and adolescent methylphenidate treatment from 1990 to 1995, so that some 2.8% of US youth between the ages of 5 and 18 years were taking this medication in mid 1995. A recent national study found no evidence of overdiagnosis of ADHD or overprescription of methylphenidate.⁸⁵

Several of the community studies cited in Table 2 also looked at which children diagnosed as having ADHD by researchers had been so diagnosed by clinicians or were receiving treatment. In the New Zealand sample, 43% of the children found to have ADHD by the researchers had been referred for medical care for this problem.²⁵ In the Tennessee study, only 15% to 40% of the children diagnosed by researchers with ADHD had been so diagnosed clinically, and only 21% to 32% were receiving pharmacotherapy.³⁵

Swanson et al⁸⁶ addressed the increase in US methylphenidate usage by showing that from 1990 to 1993 the number of patients diagnosed as having ADHD increased from 900 000 to 2 million, and the number of outpatient visits for the condition rose from 1.7 million to 4.2 million. The percentage of patients given methylphenidate remained around 70%. Thus,

the amount of methylphenidate produced per 1 million patients increased from 1.98 g to 2.53 g, a 27% increase.

There are several important clinical reasons for the increased diagnosis and stimulant treatment of ADHD. These include increased public and physician awareness and acceptance of the condition; acceptance of a broader case definition as appropriate; greater knowledge of the illness course, justifying lengthier treatment (eg, of adolescents); fewer interruptions in treatment because of diminished concerns about growth retardation; and increased treatment of adults.

Finally, with regard to cross-national data, there is some consensus that most non-US clinicians are more likely to rely on older, more stringent diagnostic criteria, reserve the diagnosis for only the most obvious or severe cases, or even be reluctant to diagnose ADHD at all. Physicians from countries with strong psychoanalytic traditions may be particularly reluctant to use discrete diagnostic criteria at all. Physicians in the United Kingdom, for example, tend to use a *DSM-II* approach, so they place more emphasis on hyperactivity and therefore diagnose ADHD far less frequently than their US counterparts. When physicians in the United Kingdom are instructed in applying US criteria, however, they diagnose ADHD as often as their US counterparts do in US children. Thus, the apparent discrepancy is more a matter of case recognition than actual prevalence. Canadian physicians, who tend to use later *DSM* criteria, diagnose and treat children at rates similar to those seen in the United States.⁴⁰

CONCLUSIONS

1. ADHD is a childhood neuropsychiatric syndrome that has been studied thoroughly over the past 40 years. Available diagnostic criteria for ADHD are based on extensive empirical research and, if applied appropriately, lead to the diagnosis of a syndrome with high inter-rater reliability, good face validity, and high predictability of course and medication responsiveness. ADHD is one of the best-researched disorders in medicine, and the overall data on its validity are far more compelling than for most mental disorders and even for many medical conditions. Nonetheless, the pathophysiology of ADHD remains unknown, although a number of neurophysiological theories are under investigation. ADHD demonstrates a very high heritability.

2. The diagnostic criteria for ADHD are designed to be used by a clinician familiar with childhood development and behavioral disorders. Application of

the diagnostic criteria requires time and effort to obtain a careful history from parents, teachers, and the child. As with almost all mental disorders, there is as yet no confirmatory genetic, radiologic, biochemical, neurophysiological, or neuropsychological test for ADHD, but such examinations may be helpful at times in evaluating presenting complaints suggestive of ADHD.

3. ADHD is associated with significant potential comorbidity and functional impairment, and its presence at any age increases the risk of behavioral and emotional problems at subsequent stages of life. It is thus a chronic illness with persistence common into adolescence and beyond.

4. Epidemiologic studies using standardized diagnostic criteria suggest that 3% to 6% of the school-aged population may have ADHD. A few studies have suggested a somewhat lower prevalence, but others, particularly those using newer, broader criteria, yield prevalences well above 6%. These studies have been conducted in a number of different countries and encompass a range of racial and socioeconomic backgrounds in the populations examined.

5. The percentage of US youth being treated for ADHD is at most at the lower end of this prevalence range. More cases of ADHD are being recognized and treated, and the duration of treatment is increasing. However, ADHD is also diagnosed inappropriately at times because of failure to do a thorough enough evaluation or to use established diagnostic criteria.

6. Pharmacotherapy, particularly stimulants, has been extensively studied. Medication alone generally provides significant short-term symptomatic and academic improvement, but response to stimulant medication is not specific to ADHD, and it is currently unknown whether long-term outcomes will be altered. The risk-benefit ratio of stimulant treatment in ADHD must be evaluated and monitored on an ongoing basis in each case, but in general is highly favorable.

7. Optimal treatment of ADHD involves an individualized plan based on any comorbidity as well as child and family preferences. This treatment generally will include pharmacotherapy (usually with stimulant medication) along with adjunctive psychoeducation, behavioral therapy, environmental changes, and, at times, supportive psychotherapy of the child, the family, or both. Nonpharmacological treatment modalities are well accepted by parents and probably significantly underused in primary care settings.

8. There should be documentation in the medical record showing evidence that appropriate diagnostic criteria for

ADHD have been met, that common comorbid conditions have been assessed, that there is a clear treatment plan, and that there is appropriate follow-up, including medication monitoring for efficacy, adverse effects, and ongoing need.

9. There is little evidence to suggest that stimulant abuse or diversion is currently a major problem, particularly among those with ADHD, although recent trends suggest that this could increase with the expanding production and use of stimulants. Clinicians need to be mindful of the risk of abuse and diversion: in addition to keeping careful records of medication prescribed, they may consider alternatives to stimulant use in patients at high risk (eg, patient or family members with substance use disorders or bipolar or conduct disorder co-occurring in the patient).

RECOMMENDATIONS

The following statements, recommended by the Council on Scientific Affairs, were adopted as AMA policy at the 1997 Annual AMA Meeting.

1. The AMA encourages physicians to use standardized diagnostic criteria in making the diagnosis of ADHD, such as the American Psychiatric Association's *DSM-IV*, as part of a comprehensive evaluation of children and adolescents presenting with attentional or hyperactivity complaints.

2. The AMA encourages the creation and dissemination of practice guidelines for ADHD by appropriate specialty societies and their use by practicing physicians and will assist in making physicians aware of their availability.

3. The AMA encourages efforts by medical schools, residency programs, medical societies, and continuing medical education programs to increase physician knowledge about ADHD and its treatment.

4. The AMA encourages the use of individualized therapeutic approaches for children diagnosed as having ADHD, which may include pharmacotherapy, psychoeducation, behavioral therapy, school-based and other environmental interventions, and psychotherapy as indicated by clinical circumstances and family preferences.

5. The AMA encourages physicians and medical groups to work with schools to improve teachers' abilities to recognize ADHD and appropriately recommend that parents seek medical evaluation of potentially affected children.

6. The AMA reaffirms Policy 100.975, to work with the FDA and the DEA to help ensure that appropriate amounts of methylphenidate and other Schedule II drugs are available for clinically warranted patient use.

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