



The Pathophysiology, Medical Management, and Dental Implications of Children and Young Adults Having Attention-Deficit Hyperactivity Disorder

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ABSTRACT

Attention-deficit hyperactivity disorder is considered to be the most common neurobehavioral disorder among school-aged children. Children who have ADHD exhibit symptoms of inattention, hyperactivity, and impulsivity that are extreme for their age. These symptoms adversely affect academic performance, vocational success, and social-emotional development. The disorder is usually treated with stimulant medications, but on occasion antidepressants and certain antihypertensive agents are used. Dentists caring for individuals with ADHD must be familiar with the manifestations of the disease and its associated features so they can garner the maximum level of cooperation from the patient. They must also be familiar with the drugs used to treat the disorder because many of these pharmaceuticals cause adverse orofacial and systemic reactions and may interact with dental therapeutic agents.

Attention-deficit hyperactivity disorder is a lifelong behavioral illness that often becomes apparent before age 7. Classified innumerable ways (mental illness, neurodevelopment disorder, neuropsychological disorder, behavioral illness), ADHD is characterized by a persistent pattern of inattention and/or hyperactivity and impulsivity that impairs school and occupational activities and social interactions.¹

Inattention is evident in preschoolers with ADHD when they appear to

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be daydreaming and when they seem not to listen or hear what was just said. As they get older and enter school, class work is done carelessly, and homework is performed without considered thought. Homework may also go uncompleted because of their inability to persist with the task and their easy distractibility by such things as a car honking outside or students talking in the next room. As teenagers and young adults, they avoid tasks requiring sustained mental effort and organizational skills and are often forgetful (e.g., missing appointments). In social situations, inattention is expressed as they appear distracted during conversations or do not follow the rules of games and activities.

Hyperactivity is evident in preschoolers when they appear to run continually back and forth, jump or climb on furniture, and have difficulty participating in sedentary group activities such as listening to a story. As they get older and enter school, they have difficulty remaining seated, fidget with objects, tap their hands, and shake their feet or legs excessively. They also often get up from the table when doing homework, walk around, and talk excessively. As teenagers and young adults, they have difficulty engaging in quiet activities and complain of feeling restless.

Impulsivity manifests in young children as impatience and difficulty in waiting their turn. In school, children with ADHD blurt out answers before questions have been completed, frequently interrupt their classmates, and fail to listen to directions. As teenagers and young adults they interrupt others excessively, grab objects from others, and engage in potentially dangerous activities without consideration of possible consequences (e.g., repeatedly climb to precarious positions or ride a skateboard over extremely rough terrain).

In addition to the behavioral problems encountered at school, these children also often have learning disabilities in reading, spelling, and math.² Some also have problems verbally expressing themselves and understanding what others have said. This deficit often results in their having a low scholastic average, being held back in school, and graduating from high school at a rate (68 per-

They are only aware that their teachers and/or classmates are always yelling at them and ascribe it to meanness, not realizing that what they do elicits the yelling.

cent) far below the national average (95 percent).³ Speech problems, reduced stamina and strength in physical fitness tests, motor incoordination, and a predisposition for accidental injury are also more prevalent in these children than in those without the disorder. Academic failures and skill deficits often lead to demoralization and poor self-esteem.^{4,5}

Symptoms of ADHD are usually exacerbated by stress, by unstructured situations, by group situations, and by demands for complex performance. Many children with ADHD are not cognizant of their deficits and have little insight; they are only aware that their teachers and/or classmates are al-

ways yelling at them and ascribe it to meanness, not realizing that what they do elicits the yelling. Similarly, family relationships suffer because others believe that the behaviors associated with ADHD are deliberate or merely signs of laziness.^{6,7}

The diagnosis of ADHD is based on a behavioral history obtained from parents/caretakers and teachers, and medical, psychological, and educational tests.⁸ To assist parents and other responsible parties in identifying the aforementioned symptoms, they are often asked to fill out symptom check lists or standardized rating scales, such as the Achenbach Child Behavior Check List.⁹ The clinician then weighs the reliability and validity of the historians, elicits information about modifying circumstances, explores alternative explanations for the presence of the symptoms (i.e., bipolar disorder, learning disabilities, anxiety, Gilles de la Tourette's syndrome), and then arrives at the diagnosis. There are no specific medical or laboratory tests available to confirm the diagnosis.¹⁰

Epidemiology

The prevalence of ADHD is estimated to be between 3 percent and 5 percent in school-aged children, with boys outnumbering girls by a 3:1 ratio.^{11,12} Most children (60 percent) exhibit symptoms of both inattention and hyperactivity-impulsivity. However, in approximately 25 percent of individuals, inattention is the predominant symptom; and it is often accompanied by reduced speed in cognitive processing and responding.^{13,14} In the remaining 15 percent of individuals, hyperactivity and impulsivity are the predominant symptoms; and they are accompanied on occasion (usually in middle school or high school) by abuse of alcohol and illicit substances.¹⁵

Associated Disorders and Risk Factors

A substantial portion (greater than 40 percent) of children with the combined form of ADHD and the type whose predominate symptom is hyperactivity-impulsivity also suffer from oppositional defiant disorder. ODD is characterized by a recurrent pattern of negativistic (resentful), defiant (argues with adults), disobedient (refuses to comply with adults' requests), and hostile (spiteful and vindictive) behavior toward authority figures. Large numbers (25 percent) of children with the combined form of ADHD and the type whose predominant symptom is hyperactivity-impulsive also suffer from conduct disorder. CD manifests as a repetitive and persistent pattern of behavior in which the basic rights of others or major societal rules are violated (e.g., aggression to people and animals, and destruction or theft of property). ADHD and CD may also interact to afford a higher risk for substance abuse than either disorder alone.¹⁶ Boys are twice as likely as girls to suffer either ODD or CD.¹⁷ The behaviors seen in both of these accompanying disorders probably arise because ADHD impairs the ability of these individuals to self-regulate mood states like anger and hostility. Approximately 18 percent of individuals with ADHD also develop depression (seen more commonly in the combined and inattentive types), 25 percent have an anxiety disorder (seen mainly in the inattentive type), and 30 percent have a learning disorder (also most common in the inattentive type).¹⁸

Genetics and Etiology

The exact cause of ADHD remains unknown, although most hypotheses focus on abnormal brain function of genetic origin.¹⁹ The monozygotic (identical) twin of a child with ADHD

(with essentially identical genes) has a greater than 90 percent chance of having the disorder. The dizygotic (fraternal) twin of a child with ADHD (who shares half of the genes) has a 33 percent chance of developing ADHD.²⁰ Siblings and first-degree relatives of children with ADHD are five times more likely to suffer the disorder than are nonrelatives.

Many of the mechanisms believed responsible for the symptoms of ADHD have recently been identified by brain imaging studies and responses to medication.

The fathers of children with ADHD have high rates of alcoholism, antisocial personalities, mood disorders, and anxiety disorders, and they likely suffered as children from ADHD, ODD, or CD.²¹ In fact, approximately one-third of these men still suffer from ADHD, with the most prominent symptoms being restlessness, distractibility, and impulsivity. The mothers of children with ADHD often exhibit Briquet's syndrome, which is characterized by alcoholism and multiple somatic complaints seemingly related to anxiety or other psychological factors. Other anxiety disorders and depression are also rife within these families.

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ADHD



ADHD have recently been identified by brain imaging studies and responses to medication. Anatomic brain imaging studies have shown that most youngsters with the disorder have smaller total cerebral volumes and specific significant reductions in both gray and white matter in the frontal lobes.²² Functional brain imaging studies also demonstrate that these children exhibit reduced global activation and reduced local activation of the basal ganglia and anterior frontal lobe.^{23,24} These areas of the brain are involved with executive functions, such as impulse control (self-regulation), organization and planning, sustained goal directed activities, and socially responsive behavior.²⁵ The administration of stimulant medications activates these areas.²⁶ An imbalance of the neurotransmitters dopamine and norepinephrine in the prefrontal cortex of the brain is also believed by some to be responsible for such symptoms as inattention, lack of alertness, and impaired planning and working memory.²⁷ The administration of stimulants and certain tricyclic antidepressants appears to increase the activities of these neurotransmitters in the brain, thereby ameliorating these symptoms.^{28,29}

Medical Management

Management of ADHD almost always includes pharmacotherapy and may also include behavior therapy.^{30,31} Stimulant medications (methylphenidate, amphetamine and dextroamphetamine^a) are most commonly used (75 percent) to treat ADHD in children.³² In fact, it is estimated that 3 million children (including 1.2 percent of the preschool population) and adolescents in the United States take these medications daily.^{33,34}

Stimulant medications increase the active concentrations of dopamine

and norepinephrine in the brain stem, midbrain, and frontal cortex, thereby increasing the child's attention span and concentration ability and reducing hyperactivity and impulsivity.³⁵⁻³⁸ These medications also improve academic performance (short-term memory, reaction time, math computation, problem-solving, task persistence, handwriting), fine motor speed, coordination, parent-child interactions, social and classroom behaviors, aggression, oppositionality, mood, and peer relations.^{39,40} In addition, children with ADHD who are treated with stimulants are less likely to abuse sub-

These medications are particularly effective in relieving inattention and hyperactivity but may not address impulsivity.

stances (tobacco, other stimulants, glue inhalants, opioids) and alcohol than are peers who have the disorder but remain unmedicated.^{41,42} Some researchers have also postulated that stimulant control of the core ADHD symptoms permits behavioral and psychological treatments to address more effectively the learning problems, reduced social skills, and low self-esteem that are refractory to medication. Stimulant medications are effective in 75 percent to 95 percent of patients and often lead to improvements that permit normal behavior.⁴³ Side effects are usually mild and consist of slight elevations in diastolic and systolic blood pressure and pulse rate, anorexia and weight loss, sleep disturbances, and transient motor tics.

Antidepressants are prescribed for children with ADHD who respond poorly to stimulants, experience unacceptable side effects, or have severe concomitant disorders such as depression, anxiety, or a tic disorder.⁴⁴ The tricyclic antidepressants have proved most effective, specifically those TCAs (e.g., desipramine and imipramine) that increase concentrations of norepinephrine in the synaptic cleft. These medications are particularly effective in relieving inattention and hyperactivity but may not address impulsivity. Use of TCAs (especially imipramine) is associated with significant anticholinergic effects (e.g., dry mouth and constipation) and postural hypotension. The atypical antidepressant bupropion is also used to treat ADHD and is also especially effective in relieving inattention and hyperactivity but not impulsivity. Bupropion's therapeutic effect derives from its ability to increase the concentrations of norepinephrine and dopamine in the synaptic cleft.⁴⁵ The principal dose-dependent toxic effect of bupropion is stimulation, which may lead to anxiety, agitation, and seizures. Other side effects from bupropion therapy include fatigue, dry mouth, insomnia, headache, nausea, vomiting, constipation, and skin rash.

When either a TCA or bupropion is prescribed for ADHD, it is often accompanied by clonidine or guanfacine — centrally acting α_2 -adrenergic agonists used to control hypertension — which are specifically effective in controlling impulsivity and aggressivity.^{46,47} These agents may be effective in ADHD because they alter the activity of norepinephrine in the locus ceruleus.⁴⁸ Systemic side effects include sedation, depression, and possibly hypotension.

Atomoxetine, an antidepressant medication that selectively raises the concentration of norepinephrine in the synaptic cleft, was approved in

Table 1

Drugs Commonly Used to Treat ADHD and Their Adverse Systemic Side Effects and Interactions With Dental Therapeutics

Drug (trade name)	Other common usage	Side effects and interactions
Amphetamine and dextroamphetamine (Adderall)	Narcolepsy	Do not use or prescribe meperidine; danger of hypotension and respiratory collapse. Use vasoconstrictors with caution, in low doses and with careful aspiration. May potentiate central nervous system stimulation caused by large doses of propoxyphene. Anorexia and reduced weight gain in children. Potentiates arrhythmogenic effects of tricyclic antidepressants.
Atomoxetine (Strattera)	None	Use associated with elevated blood pressure and pulse. Avoid levonordefrin; use epinephrine with caution, in low doses, and with careful aspiration. Propoxyphene increases the stimulant effect of atomoxetine.
Bupropion (Wellbutrin, Zyban)	Antidepressant, smoking cessation	May cause central nervous system stimulation, including agitation, anxiety, and seizures. Increased seizure activity when concurrently administered with tricyclic antidepressants.
Clonidine (Catapres)	Antihypertensive	Increases sedation of other central nervous system depressants. May cause cardiac arrhythmias and orthostatic hypotension.
Desipramine (Norpramin)	Antidepressant	Avoid levonordefrin; use epinephrine with caution, in low doses, and with careful aspiration. Increases sedation of other central nervous system depressants. May cause orthostatic hypotension. Causes antimuscarinic effects.
Dextroamphetamine (Dexedrine)	Narcolepsy	Do not prescribe meperidine; danger of hypotension and respiratory collapse. Use vasoconstrictors with caution, in low doses, and with careful aspiration. May potentiate central nervous system stimulation caused by large doses of propoxyphene. Anorexia and reduced weight gain in children. Potentiates arrhythmogenic effects of tricyclic antidepressants.
Guanfacine (Tenex)	Antihypertensive	Increases sedation of other central nervous system depressants. May cause orthostatic hypotension.
Imipramine (Tofranil)	Antidepressant	Avoid levonordefrin; use epinephrine with caution, in low doses, and with careful aspiration. Increases sedation of other central nervous system depressants. May cause cardiac arrhythmias and orthostatic hypotension. Causes antimuscarinic effects.
Methylphenidate (Ritalin, Concerta, Methylin, Metadate)	Central nervous system stimulant	May rarely cause thrombocytopenia, leukopenia, and anemia. Use vasoconstrictors with caution, in low doses, and with careful aspiration. Anorexia and reduced weight gain in children. Potentiates arrhythmogenic effects of tricyclic antidepressants.

ADHD



November 2002 by the United States Food and Drug Administration for the treatment of ADHD in children. It appears to improve all three of the core symptoms of ADHD, namely inattention, hyperactivity, and impulsivity. Its use is associated with an increase in blood pressure and pulse, decreased appetite, weight loss, tiredness, fatigue, and sleep disturbance.^{49,50}

Behavior therapy involves providing rewards (positive reinforcement) for demonstrating desired behaviors (e.g., improving relationships with parents and siblings, improving volume of completed school work) or consequences (negative reinforcement) for failure to meet the goals. Repetitive application of the rewards and consequences has been shown by a few investigators to promote positive behavior of children with ADHD.⁵¹ To maximize the effectiveness of behavior therapy, it is often combined with parental training and family therapy. Parents are taught how to give the child clear instructions, to positively reinforce good behavior, to ignore some behaviors, and to use punishment (such as “time-outs”) effectively. Family therapy involves teaching the family how to negotiate and solve as a cohesive unit the problems of raising and managing the child.

Specialized education techniques are often required to assist children with ADHD, because more than one-third of them have a co-occurring learning disorder. These techniques include increased structure, predictable routine, learning aids, resource room time, and homework checked by parents and teachers.⁵²

The parents of children with ADHD often (60 percent) turn to “complementary” (used in addition to traditional therapy) or “alternative” (used as a replacement for traditional therapy) medicine because they perceive it

Table 2

Adverse Orofacial Reactions to Drugs Used to Treat ADHD

Drug (trade name)	Xerostomia	Sialorrhea	Dysphagia	Sialadenitis	Dysgeusia	Stomatitis
Amphetamine and dextroamphetamine (Adderall)	yes	no	no	no	yes	no
Atomoxetine (Strattera)	yes	no	no	no	no	no
Bupropion (Wellbutrin, Zyban)	yes	no	no	no	yes	yes
Clonidine (Catapres)	yes	no	yes	yes	no	no
Desipramine (Norpramin)	yes	no	no	yes	yes	no
Dextroamphetamine (Dexedrine)	yes	no	no	no	yes	no
Guanfacine (Tenex)	yes	no	no	no	yes	no
Imipramine (Tofranil)	yes	no	no	yes	yes	yes
Methylphenidate (Ritalin, Concerta, Methylin, Metadate)	yes	no	no	no	no	no

to be more “natural” and free of the stigma associated with stimulants and antidepressants. Practitioners of these arts often recommend additive-free diets and low- or no-sugar diets (e.g., Kaiser-Permanente diet, Feingold diet). They also recommend supplementing the diet with chamomile, kava kava, and valerian for their sedative effects, or ginkgo biloba and ginseng to improve learning, memory, and cognition. Megavitamin therapy (specifically iron, pyridoxine, zinc, and magnesium), guided imagery, biofeedback, and massage are also used by these complementary/alternative medicine practitioners to treat the disorder. These interventions are not supported by evidence-based studies.⁵³⁻⁵⁵

Orofacial Findings and Dental Management Implications

Minor physical anomalies of the orofacial region are the most frequently reported biological abnormality in ADHD. These anomalies are termed “minor” because they rarely present a cosmetic concern. Prevalence rates have not been determined, but hyper-telorism (wide spacing of the eyes), highly arched palate and low-set ears are most commonly reported.⁵⁶

Orofacial injury is also common because children with the disorder are constantly running and climbing, and occasionally falling.⁵⁷ However, injuries to children with ADHD are not always accidental. A hyperactive child is five to seven times more likely to suffer physical abuse from a parent than is a child

Gingivitis	Glossitis	Tongue edema	Discolored tongue	Bruxism	Miscellaneous
no	no	no	no	yes	Loss of smell and taste acuity
no	no	no	no	no	Angioneurotic edema, vomiting, ear infection, sinusitis, sinus headache
yes	yes	no	no	yes	Toothache, oral edema, dysphagia
no	no	no	no	no	Parotid gland swelling and pain
no	no	yes	yes	no	Facial edema
no	no	no	no	yes	Loss of smell and taste acuity
no	no	no	no	no	Rhinitis, tinnitus
no	no	yes	yes	no	Facial edema
no	no	no	no	no	Erythema multiforme

ing the parents reward (small amounts of money) the child each time he or she initiates and completes a tooth brushing episode.⁶⁸

Many of the medications used to treat ADHD have adverse orofacial side effects (**Table 1**).^{69,70} The stimulants methylphenidate, amphetamine, and dextroamphetamine may cause xerostomia; and use of the latter two medications is also associated, on occasion, with loss of smell and taste acuity. The antidepressants desipramine, imipramine, and bupropion may cause xerostomia and dysgeusia (altered taste sensation). The α_2 -adrenergic agonists clonidine and guanfacine may cause xerostomia, with the former medication also being occasionally implicated in parotid gland swelling and pain. Atomoxetine has also been shown to cause xerostomia and sinusitis.

The medications used to treat ADHD also cause adverse interactions with drugs used in dentistry (**Table 2**).⁷¹⁻⁷⁴ As previously mentioned, methylphenidate, amphetamine, and dextroamphetamine are associated with elevations in systolic and diastolic blood pressure and a more rapid heart rate. Prudent care necessitates taking and recording the patient's preoperative vital signs and intraoperative values as deemed clinically necessary. Obtaining profound local anesthesia, and thus limiting pain and the endogenous production of catecholamines that might interact with these agents, is mandatory. Moreover, an aspirating syringe must be used to avoid intravascular injection and the possibility of summation of drug effects with the pressor agents (epinephrine, levonordefrin) used in local anesthesia. It is also prudent to administer no more than 1 $\mu\text{g}/\text{kg}$ of epinephrine up to a maximum of 40 μg (as is found in two cartridges of 2

in the general population.⁵⁸⁻⁶³ A good history obtained from the parent/caretaker and a separate informal one obtained from the child is vital for the correct diagnosis.

Provision of comprehensive dental care to children under treatment for ADHD usually requires only minimal modification because their behavior in the dental office often does not differ significantly from peers free of the disease. The standard "tell-show-do" technique is very effective for young children with ADHD. The technique instills trust, focuses the child's attention on the procedures, and stimulates cooperative behavior.⁶⁴ Dental appointments should be scheduled in the morning, when these children are least fatigued, most

attentive, and best able to remain seated in the dental chair. Morning appointments are also appropriate because most medication regimens are designed for the maximum drug effect (enhanced cognition and behavior) to occur during the early part of the school day.

Compliance with an age-appropriate home care regimen is difficult for some of these children.⁶⁵ Understanding and adherence are enhanced when colorful or highly stimulating educational materials are employed, and instructions are simplified and repeated numerous times during the dental treatment visit.⁶⁶ Emphasis should be placed upon the brushing of teeth rather than the specifics of a brushing technique.⁶⁷ Compliance may be enhanced by hav-



percent lidocaine with 1:100,000 epinephrine) initially. If vital signs remain stable, additional anesthetic may be administered. The stimulants amphetamine and dextroamphetamine adversely interact with meperidine and may cause hypotension and respiratory collapse. These same two stimulants may likewise interact with large doses of propoxyphene, producing excessive central nervous system stimulation and seizure activity.

The TCAs desipramine and imipramine block the uptake of adrenergic vasoconstrictors (i.e., levonordefrin and epinephrine) compounded with many local anesthetic agents. They also block muscarinic and α_1 -adrenergic receptors, actions that can, respectively, increase the heart rate and relax the peripheral vasculature. Although no adverse reports have been published for children, prudence dictates that patients receiving either of these two TCAs should not be administered a local anesthetic agent containing levonordefrin because cardiac arrhythmias and a dramatic increase in systolic blood pressure may follow, especially after an accidental intravascular injection. Epinephrine more modestly interacts with TCAs so that it can be used in reduced doses (e.g., one-half cartridge of 1:100,000 epinephrine per 10 kg body weight per half hour up to an adult maximum of three cartridges per half hour) and with careful aspiration to avoid intravascular administration.⁷⁵ Because atomoxetine also blocks the reuptake of norepinephrine, this same restriction on vasoconstrictors used for the TCAs should be followed for it until more is known about the drug's potential for this interaction.

Patients receiving TCAs should not be prescribed Zyban, the brand name of bupropion promoted for

smoking cessation, because in tandem these medications decrease the seizure threshold. Counseling and other nonpharmacologic approaches are best instituted in these highly vulnerable patients, who smoke cigarettes at a rate twice that of individuals free of ADHD.⁷⁷

Other adverse drug interactions between TCAs and medications used in dentistry may also produce significant morbid reactions. Sedative-hypnotics, anti-anxiety drugs, and opioids may have their depressant effects potentiated by TCAs, and respiratory depression may ensue. The administration of drugs with anticholinergic properties, such as atropine or scopolamine, can cause an increase in intraocular pressure and worsen occult or known narrow-angle glaucoma. Lastly, care should be observed when prescribing acetaminophen because of its ability to increase TCA concentrations.⁷⁶

Patients receiving a centrally acting antihypertensive agent (clonidine or guanfacine) should have their preoperative vital signs obtained and recorded because of the propensity of these agents to cause hypotension. Opioids should be avoided or prescribed in reduced dosage because they may interact with these agents and potentiate their sedative and hypotensive effects.

Final Comment

Dentists caring for patients with ADHD must exhibit compassion. They must not misconstrue inattention, motor restlessness, and an inability to complete home care tasks with simple noncompliance but rather as a component of a disease requiring special techniques to manage. In consultation with the physician or psychologist treating the patient's ADHD, the full range of dental procedures can be provided to these individuals. **CDA**

Notes / a. Pemoline, another stimulant, is rarely used, as it is less effective than alternative drugs and has caused fatal hepatic failure.

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