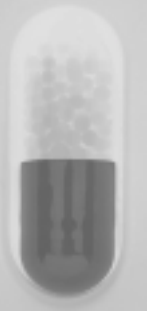


Treatment of Attention-Deficit/Hyperactivity Disorder in Adults



Stimulants

Adderall and Adderall XR (amphetamine mixture)
Concerta (methylphenidate, extended release)
Daytrana (methylphenidate topical patch)
DextroStat and Dexedrine Spansules (dextroamphetamine)
Focalin and Focalin XR (dexmethylphenidate,
immediate and extended release)
Metadate ER and Metadate CD
(methylphenidate, extended release)
Ritalin, Ritalin-SR, and Ritalin LA (methylphenidate,
immediate and extended release)
Vyvanse (lisdexamfetamine)

Nonstimulants

Catapres (clonidine)
Strattera (atomoxetine)
Tenex (guanfacine)

Attention-deficit/hyperactivity disorder (ADHD) is a common childhood or adolescent psychiatric diagnosis. Although most children outgrow symptoms of hyperactivity, many continue to have residual attention problems in their teenage years, and a significant percentage (about 25%) of childhood ADHD persists into adulthood. It is estimated that 1%–2% of men and women in United States, some 5 million adults, have ADHD. These individuals have problems sustaining attention, sitting still, and controlling their impulses. The prevalence of adulthood ADHD is almost equal among men and women, whereas in childhood ADHD the diagnosis is higher in boys than girls.

Adults with ADHD generally do not have the extent of hyperactivity seen in the childhood disorder, and the disorder in adults is diagnosed as **attention-deficit disorder** (ADD). Their principal difficulty is distractibility; they have a hard time sustaining attention and maintaining their focus. Impulse control is also lacking, and often these individuals act or speak without thinking. They may rush into misguided ventures or business deals without much forethought. Others may view their behavior and judgment as immature and impulsive. Untreated, adults with ADD are prone to abuse alcohol and drugs, get into accidents or trouble with the law, or develop other mental health disorders; sadly, they are also prone to commit suicide.

Studies show that ADHD runs in families, particularly in male relatives of ADHD children, but it is unclear exactly how the disorder is transmitted. There is no evidence that ADHD is caused by a single, identifiable genetic defect. Genetic transmission of ADHD will probably be explained by a group of genes that controls or modifies the inheritance of the disorder.

There are nongenetic explanations of ADHD as well. Recognized causes of ADHD also include brain damage, low birth weight, and prenatal factors such as inadequate maternal nutrition and alcohol and substance abuse. Brain damage may result from obstetrical complications, viral infections, and exposure to toxins. Low birth weight is correlated with ADHD, with or without birth complications. In some cases, low birth weight may be attributed to lack of prenatal care (e.g., malnutrition) and substance abuse. Fetal exposure to toxic substances, including alcohol and lead, may predispose the child to ADHD and cognitive deficits. For example, **fetal alcohol syndrome** includes hyperactivity, attention deficit, and impulsivity as well as other physical problems.

The symptoms of ADHD may be explained by aberrations of neurotransmitter systems in areas of the brain that mediate attention. ADHD is associated with the brain cells (neurons) that require **dopamine** and **norepinephrine** as their neurotransmitters (i.e., brain chemicals that facilitate transmission of impulses between neurons). Low levels of these neurotransmitters in specific and interrelated areas of the brain that regulate attention, regardless of the cause, may result in the symptoms of attention-deficit and hyperactivity. A depletion of dopamine may result in difficulties in sustaining attention, and depletion of norepinephrine may be responsible for hyperactivity. The most compelling evidence to support this hypothesis is that treatments prescribed for ADHD—medications such as dextroamphetamine and methylphenidate (e.g., Ritalin)—work by enhancing the levels of dopamine and norepinephrine in the brain.

The principal medications used in treatment of ADHD are stimulants. It may seem paradoxical that stimulants, which excite the central nervous system, are effective in blunting the symptoms of hyperactivity, inattention, and impulsivity in ADHD. The explanation may be that ADHD is a disorder of deficit caused by deficient levels of two important neurotransmitters, dopamine and norepinephrine, in the brain. Increasing the levels of these neurotransmitters with stimulants may help reduce and control the symptoms of the disorder.

Because an array of stimulants is available to treat ADHD, physicians should explain the available treatment options to their patients. Essentially there are two primary stimulants used in treating ADHD: amphetamine and methylphenidate. There are several ways to change these stimulants to enhance or alter their effects. One way is to add another chemical group to the parent molecule to enhance its effect. For example, adding another chemical group to amphetamine—the parent molecule—will change it to methamphetamine (Desoxyn) and increase its potency. Another way is to isolate the more active **isomer** of the molecule. Isomers are mirror images of the drug that are not superimposable on top of each other. Our right and left hands, for example, are mirror images that are not superimposable. Dextroamphetamine is an isomer of amphetamine, and dexmethylphenidate (Focalin) is an isomer of methylphenidate. A third way is by changing the formulation of the stimulant to alter its duration of action. For example, methylphenidate comes in several formulations, including an immediate-release tablet (Ritalin), an extended-release tablet (Ritalin-SR), and a long-acting capsule (Ritalin-LA).

Amphetamine and methylphenidate stimulants have a high potential for abuse. Chronic abuse can lead to dependence. However, if they are properly prescribed by a physician and closely monitored, the risk of dependence is minimized. For this reason, prescribing of these stimulants is tightly controlled by state and federal regulations. They are classified as Schedule II controlled substances—the most closely regulated group of controlled medications.

Other medications used in the treatment of ADHD are the so-called nonstimulants. This mixed group of medications is unlike the stimulants, and there is not the concern of abuse and dependence with these medications that there is with amphetamines and methylphenidate. The only nonstimulant approved by the U.S. Food and Drug Administration (FDA) for the treatment of ADHD is Strattera (atomoxetine). The other nonstimulants used by physicians for treatment of ADHD include Tenex (guanfacine), Catapres (clonidine), and antidepressants such as Wellbutrin (bupropion) and Effexor (venlafaxine). These medications are not approved by the FDA for treatment of ADHD, and they are prescribed “off-label.” The use of a medication for its approved indications is called its *labeled use*. In clinical practice, however, physicians often prescribe medications for *unlabeled* (“off-label”) uses when published clinical studies, case reports, or their own clinical experiences support the efficacy and safety of those treatments. The nonstimulants are not as commonly used as the amphetamines and methylphenidate for ADHD. Except for Strattera, the nonstimulants have not been widely studied for treatment of ADHD, and evidence of their effectiveness is, at best, based on limited clinical trials but mostly clinical experience.

For more information on a particular medication, refer to the handout on that medication.