

# Attention-Deficit Hyperactivity Disorder

by

Frank Minirth, M.D., Ph.D.

Radio 08/25/09

- Introduction
- Bible verses
  - I Corinthians 12
- ADHD (attention-deficit hyperactivity disorder) medications
 

Medication is one of the most successful treatments for the person with ADHD. Children (3-5% of school-aged children) often become organized, calmer, and less stubborn. Benefits include:

  - more control over impulsiveness, conduct, social behavior, and aggressive behavior
  - improvement in attention span and in completion of work
  - healthier relationships with peers and family members

Medications on-label and off-label include:

- psychostimulants (sympathomimetics)
 

These drugs stimulate the nervous system in the areas of the brain that determine the attention, impulses, and self-regulation of behavior. These medications are helpful for at least seventy to eighty percent of patients. These drugs work by inducing the release of dopamine and/or norepinephrine. They also work by blocking the reuptake of dopamine and norepinephrine. These neurotransmitters are important in attention. Some salient features among the various stimulants are as follows: Amphetamine is twice as potent as methylphenidate; this can be either helpful or detrimental. These types of medications include dextroamphetamine + amphetamine (Adderall), dextroamphetamine (Dexadrine), lisdexamfetamine dimesylate (Vyvanse), methylphenidate (Concerta, Metadate, Methylin, Ritalin, Focalin), and Pemoline (Cylert). Methylphenidate is also available in a skin patch (Daytrana). It is worth noting that methylphenidate products have different durations of action (for example, Concerta has a 22 percent release the first hour and the remainder four hours later, with the drug lasting 10 to 12 hours). Also Adderall XR has a 50 percent release the first hour and the rest four hours later, with the drug lasting about 12 hours. Incidentally, Vyvanse is the first prodrug stimulant; after ingestion Vyvanse is converted to l-lysine (an amino acid) and d-amphetamine. It has an extended duration of action (13 hours), reduced addiction potential, and less GI complications. Adderall XR is approved down to age three years. Vyvanse and Adderall XR are often not given with patients who have CV disease, severe ASHD (arteriosclerotic heart disease), severe hypertension, hyperthyroidism, glaucoma, severe agitation, and in those on an MAOI. Side effects of

Vyvanse include, decreased appetite, insomnia, upper abdominal pain, headaches, and irritability. Sympathomimetics used for appetite suppression include Adipex-P and Ionamin (phentermine), and Bontril (phendimetrazine). Pemoline (Cylert), formerly for ADHD, has been associated with liver failure; it was withdrawn from the market in December 2005.

- atomoxetine (Strattera)
 

Atomoxetine blocks the reuptake and therefore the degradation of norepinephrine. As norepinephrine increases in the synapse, ADHD symptoms can decrease. Atomoxetine was the first non-stimulant in history approved for ADHD treatment. Although Strattera is sometimes used when depression is present, antidepressant effects are sometimes in doubt.
- antidepressants
 

This classification of medication is often utilized if the individual is depressed and also has ADHD. There are several types of antidepressants used off-label in the treatment of depression and ADHD: bupropion (Wellbutrin), venlafaxine (Effexor), tricyclic antidepressants (imipramine, desipramine, and nortriptyline). Mood disorders in ADHD patients is 30%. Desipramine can cause QT prolongation so it is often not used in children.
- other medications
 

Clonidine [Catapres (off-label)] and guanfacine (on-label) have been used for ADHD. Guanfacine extended release at 2 mg, 3 mg, 4 mg has been used. Modafinil (Provigil), a histamine agonist and DAT blocker is being used off-label for ADHD. The sympathomimetics and modafinil have also been used for narcolepsy, hypersomnolence, fatigue, and obesity.
- natural products
 

Natural products that have been tried in ADHD include, caffeine (increases dopamine), acetyl-L-carnitine (a precursor of acetylcholine), fish oil, SAmE (increases biogenic amines), ginseng, and guarana.
- A triple-beaded mixed amphetamine salt (MAS) with a duration of 16 hours has been developed. It should improve executive functioning in adults resulting in:
  - ↑ focus
  - ↑ prioritizing
  - ↑ organizing
  - ↑ working memory
  - ↓ frustration

The above in adults may:

  - ↑ healthier relationships
  - ↑ parenting skills
  - ↑ driving safety
  - ↑ financial management
  - ↑ domestic obligations
  - ↑ planning for future goals

It contains the same 4 salts in the same ratio (3:1) as the MAS immediate release and MAS extended release:

- dextroamphetamine saccharate
- amphetamine aspartate monohydrate
- dextroamphetamine sulfate USP
- amphetamine sulfate USP

The triple-bead MAS capsule has 3 types of beads:

- 33% immediate pulse-release
- 33% delayed pulse-release
- 33% delayed extended-release

- ***ADHD in adults***

ADHD continues into adulthood 60% of the time. An estimated 4.4% of adults have ADHD.

Below are screening questions for adult ADHD (Grade 0 to 10 with 0 meaning nonexistent and 10 meaning horrible).

**0 to 10 on 10 questions**

I am hyperactive.  
 I feel like I am driven by a motor.  
 I have trouble sitting down for a long time.  
 I fidget.  
 I delay work that requires intense thought.  
 I forget appointments.  
 I have trouble organizing for a task.  
 I have trouble getting closure on a project.  
 I am impulsive.  
 My life has been filled with difficulties.

Many medications are used on-label and off-label for ADHD. FDA-approved medications include:

- Adderall XR (extended-release mixed with amphetamine)
- Concerta (extended-release OROS methylphenidate)
- Focalin XR (extended-release dexmethylphenidate)
- Strattera (atomoxetine)
- Vyvanse (lisdexamfetamine)

- ***ADHD and behavior tips***

The treatment of ADHD is not all medical. Behavior tips can help including:

- Look for and emphasize success. For younger children a point system with rewards is excellent for rewarding success.
- Have fun; be playful; be enthusiastic. Children respond to heightened focus.
- Encourage the child that individual differences are acceptable; Einstein and Edison had trouble with focus.

- Simplify instructions and choices. Write down rules and directions and repeat them as often as needed. Tutors are helpful.
- Minimize learning distractions. Use eye contact, slow speech, and short sentences. Divide lessons into small segments.
- Seat the child near the front of the class. When possible provide a learning space for the child that is free from distractions.
- Increase stimulus level in work such as visual aids with instructions, animated learning activities, color coding, eye catching materials of large size or odd shapes, flash cards, outlines, mutual story telling techniques.
- Anticipate variability in the child's day to day performance. Check on the child's progress often and offer feedback.
- Be able to manage apparent "catastrophic" reactions such as bursting into tears when a task seems unbearable.
- If the child is persistently repeating an activity, substitute another topic or task and suggest returning to the previous activity later.
- Allow the use of learning helps as needed such as a finger, eraser tip, or underliner. With older children suggest reminder notes.
- Social skills training may be helpful. Show children how their behavior affects others and teach them appropriate behaviors.
- Encourage the ample use of computers. Children with ADHD symptoms often do well with computer work.

- ***ADHD, brain circuits, and neurotransmitters***

ADHD individuals have deficits in several brain circuits and neurotransmitters. The brain circuits include deficits in the dorsolateral prefrontal cortex with resulting decreased sustained attention, decreased working memory, and decreased organizational skills; deficits in the orbital frontal cortex with increased impulsivity, increased distractibility, and increased disordered behavior; and deficits in the anterior cingulate cortex with decreased selective attention. Neurotransmitters involved in ADHD include dopamine (D), norepinephrine (NE), acetylcholine (Ach), and histamine (H). The D deficits are treated with stimulants (Adderall, Ritalin), modafinil (Provigil) and amphetamines; the NE deficits are treated with atomoxetine (Strattera), bupropion (Wellbutrin). Guanfacine (Tenex), and clonidine (Catapres) are NE alpha 2 agonists that through a feedback system decreases norepinephrine and thereby decreases agitation. The H deficits are treated with modafinil (Provigil). The Ach deficits have been treated with nicotine and by reducing anticholinergics. Difficult cases of mania plus ADHD have been treated by D2 antagonists of neuroleptics and D1 agonists of stimulants.

- ***ADHD and the brain***

Brain circuits that may be malfunctioning in ADHD include the prefrontal cortex, the striatum, and the thalamus. The frontal-subcortical circuits involved include:

- the dorsolateral prefrontal cortex (↓ sustained attention)
- the orbitalfrontal cortex (↑ impulsivity)

- the anterior cingulate cortex (↓ focused attention)

Neurotransmitters involved in ADHD and ADHD treatments include:

- dopamine
- norepinephrine
- acetylcholine
- histamine

Methylphenidate blocks DAT (dopamine transport); amphetamine blocks DAT and VMATs (vesicular monoamine transporters). In summary, in ADHD:

- DLPC: ↓ sustained attention
- OFC: ↑ impulsivity
- ACC: ↓ focused attention
- ↓ D: ↓ focus (↑ D with treatment from stimulants causes ↑ focus)
- ↓ NE: ↓ focus (↑ NE with treatment from stimulants causes ↑ focus and ↓ distractibility)
- ↓ Ach: ↓ focus (↑ Ach for ↑ focus treatment has been tried by giving acetyl-L-carnitine, a precursor of Ach)
- H<sub>1</sub>: H<sub>1</sub> involvement (↑ H with modafinil or Provigil causes ↑ focus)

- ***ADHD comorbidities***

- child
  - poor academics
  - ↓ self-esteem
  - impaired peer interactions
  - disciplining issues at school and home
- adolescents
  - substance abuse
  - truancy
  - delinquency
  - academic failure
  - car accidents
  - dangerous sexual activity
- adults
  - divorce
  - substance abuse
  - job loss
  - legal issues
- ODD/CD – 50%
- anxiety disorder – 30% of children, 50% of adults
- depression – 30%
- bipolar disorder – 10% of adults
- SUDs – 15%

- ***ADHD and depression***

Thirty percent of those with ADHD have a mood disorder; bupropion (Wellbutrin) seems to help both disorders; atomoxetine (Strattera) helps ADHD but not comorbid depression as much.

- **ADHD diagnosis**

DSM IV R is ultimately a book of categories of symptoms that are used to make a diagnosis. DSM IV R is the authority in psychiatry and psychology. It is based on symptoms. Thus, reliable historians are the most help in making most diagnoses. Psychological testing can of course help. Neuroimaging can also at times be of help, but it often remains more at a research level. Symptoms from reliable historians are invaluable.

- **ADHD drugs and FDA approvals**

Drug	Approval		
	children (age/yrs)	teens 13-17 yrs	adult 18-65 yrs
Vyvanse (lisdexamfetamine)	✓ 6-12		✓
Adderall (mixed amphetamine IR)	✓ 6-12		
Adderall XR (mixed amphetamine salt)	✓ 3-12	✓	✓
Ritalin (methylphenidate MPH)	✓ 6-12		
Medadate ER (long-acting MPH)	✓ 6-12		
Medadate CD (long-acting MPH)	✓ 6-12		
Methylin ER (long-acting MPH)	✓ 6-12		
Ritalin SR (long-acting MPH)	✓ 6-12		
Ritalin LA (long-acting MPH)	✓ 6-12		
Concerta (long-acting MPH)	✓ 6-12	✓	✓
dexmethylphenidate (Focalin)	✓ 6-12		
dexmethylphenidate (Focalin XR)	✓ 6-12	✓	✓
dextroamphetamine (Dexadrine, Dexrostat)	✓ 6-12		
Dexadrine Spansule	✓ 6-12		
Daytrana (methylphenidate patch)	✓ 6-12		
atomoxetine (Strattera)—has been tried for comorbid anxiety and tics	✓ 6-12	✓	✓
modafinil (Provigil)			
bupropion (Wellbutrin)			
guanfacine (Tenex)			
imipramine (Tofranil)—has been tried with comorbid bed wetting			
methylphenidate comes in a chewable tablet as Methylin Chewable tablets 2.5 mg, 5 mg, and 10 mg. It also comes in a liquid as Methylin Oral Solution in 5 mg/5 ml or 10 mg/5 ml.			
ProCentra (dextroamphetamine sulfate) Oral Solution for down to 3 years of age, 5 mg/5 ml, 43% of children have trouble swallowing tablets; half-life is 11.7 hrs; approved for ages 3 to 16 years			
methamphetamine hydrochloride (Desoxyn) for ADHD (ages > 6 years at 2.5-5 mg, 1-2			

times/day); also used for obesity in adults at 2.5-5 mg, 1-3 times/day 30 minutes before meals; 5-15 mg/day is long-acting			
--	--	--	--

- ***ADHD evaluation considerations***

ADHD evaluations vary considerably; considerations include:

- blood pressure, pulse
- history of cardiac risk factors such as cardiac murmur in patient or family history of coronary artery disease (wide QT, arrhythmias, MI, hypertrophy) at a young age
- drug information
- risks of the ADHD drug
- risks such as cardiac event risks in the general population (the occurrence of sudden death does not seem to occur more frequently in patients treated with stimulants, although sudden deaths have occurred with concurrent ADHD stimulant treatment)
- EKG screening is not essential in no suspicion of significant risk, but a consideration in some
- stimulant use is associated with decreased substance abuse on average

- ***ADHD and the genomic era***

Various genes contribute to ADHD including:

- dopamine genes—receptors DRD4, DRD5, DRD2
- dopamine transporter (DAT)
- dopamine  $\beta$ -hydroxylase
- serotonin genes

Various brain regions contribute to ADHD including:

- prefrontal cortex—DLPC
- anterior cingulate
- limbic structures—hippocampus, amygdale
- basal ganglia
- right/left hemisphere asymmetries

Various strengths can manifest in ADHD including:

- creativity from right brain dominance
- intuition from right brain dominance
- insight problem solving from right brain dominance
- self-transcendence with increased survival after illness
- daydreaming with increased creativity

- ***ADHD: nuances of interest***

- ADHD continues into adulthood 60% of the time
- Prevalence of ADHD overall is 3-7% and 5-8% of youths
- ADHD is the most common neurobehavioral disorder in children

- Costs of ADHD often include:
  - inattentiveness and/or impulsivity and/or hyperactivity
  - poor grades
  - repeat grades
  - ↓ graduation from high school and college
  - ↑ behavioral problems
  - ↑ medical costs
  - ↑ criminality
  - ↑ accidents
  - ↑ lost days at work and school
  - ↑ tutoring
  - ↑ problems in workplace
  - ↑ unemployment
  - ↑ job changes and loss
  - ↑ impairment in relationships
  - ↑ difficulties making friends
  - once rejected, ↓ difficulty regaining peer status even after treatment
  - ↑ disruptive behavior
  - ↓ social skills
  - ↓ note-taking skills
  - ↓ homework completion
  - ↓ educational achievement
  - ↑ failed marriages
  - ↑ divorce
  - ↑ speeding violations
  - ↑ motor accidents
  - ↑ driver's license suspensions
  - ↓ life satisfaction
  - ↓ socioeconomic status
  - ↑ substance abuse
  - ↑ conduct problems
  - ↓ participation in social activities
  - ↓ time with friends and family
  - ↓ work performance
  - ↓ maintaining work
- Most effective treatments include:
  - stimulants
  - social skills training with behavioral contingency management
- Comorbidities include:
  - depression—Atomoxetine (Strattera) might help some
  - conduct problems
  - substance abuse—treatment with ADHD medicines may help
- Compliance with medication helps include:
  - extended release formulations
  - topical formulations (Daytrana)

- liquid and chewable formulations (Methylin)
  - improved patient and family education
  - improved coping skills
  - behavioral medications
  - school accommodations
  - compliance tools
- Neurobiology of ADHD includes:
  - catecholamergic dysfunction (D and NE)
  - frontal cortex dysfunction
  - frontal-striatal dysfunction
  - ↑ DAT binding potential
  - Ach dysfunction
  - D dysfunction (D2 and D4 receptor subtypes)
  - vesicular
  - movement protein
  - dysfunction
  - 5HT receptor dysfunction
- ***ADHD in adults: points of interest***
  - 4.4% of college students and adults have ADHD 8% of children have ADHD
  - 90%-95% of adult ADHDs have inattentive type
  - Adults with ADHD often have:
    - inattention
    - inner restlessness
    - poor concentration
    - forgetfulness
    - daydreaming
    - low frustration tolerance
    - explosive emotional episodes
    - reckless driving
    - a short temper
    - poor self-discipline
    - difficulty keeping a routine
    - difficulty thinking clearly
- ***ADHD resources***
  - ADHD video game – Supercharged
  - [www.addhealthandwellness.com](http://www.addhealthandwellness.com) for organization and time management
  - [www.addconsults.com](http://www.addconsults.com) – a site for children and adults with ADHD
  - [www.add.org](http://www.add.org) – National Attention Deficit Disorder Association
  - [www.additude.com](http://www.additude.com) – ADDitude Magazine
  - *Girls with ADHD* by Patricia Quinn, Kathleen Nadeau, and Ellen Litman
  - *Driven to Distraction: Recognizing and Coping with Attention Deficit Disorder from Childhood through Adulthood* by Edward M. Hallowell
  - *Delivered from Distraction* by Edward M. Hallowell and John J. Ratey

- *ADHD and the Nature of Self-Control* by Russell Barkley
- *Teach Your Child How to Think* by Edward Bono
- ***ADHD treatment options***

ADHD treatment options with positives and negatives are:

  - Do nothing. The brain does develop until we are almost 30 years old; some do improve without treatment. The concern here is the fear of the development of psychological conditions such as low self-image. One may never reach their potential.
  - Take a conservative approach. Use fish oil, caffeine, Focus Factor, behavior tools, and/or special schools for ADHD. Some of the special schools are excellent. The concern is whether this approach will be enough.
  - Take a more conservative medical approach such as Strattera (atomoxetine). This helps perhaps seven to ten percent. The concern here is whether the approach is too weak; also any drug, even Strattera, can have side effects.
  - Treat a comorbid condition such as depression with Wellbutrin (bupropion), an antidepressant, and hope the ADHD gets better. The concern here is again over weakness of the approach and possible side effects. I must hasten to add that children with ADHD are less likely to get into drug abuse if they are treated.
  - Treat with a stimulant (methylphenidate, amphetamine). Effectiveness is high but side effects, although rare overall, are possible. Stimulant drugs are narcotics.

There is not a right or wrong choice in general; there may be a right or wrong answer for a specific child. The parents will decide. Timing is also important and one option now does not preclude a different one later. Finally it should be mentioned that sometimes two strong comorbid conditions (ADHD + bipolar) may need to be treated concurrently.

- resources
  - Hope Line – 1-888-789-HOPE (4673)
  - Minirth Clinic – 1-888-MINIRTH (646-4784) / [www.minirthclinic.com](http://www.minirthclinic.com)
  - AACC – American Association of Christian Counselors/ [www.aacc.net](http://www.aacc.net)
  - [www.2ndfiddleentertainment.com/margiespassage](http://www.2ndfiddleentertainment.com/margiespassage)
- Conclusion
- Bible verses
  - I Corinthians 12