Diagnosing and Managing ADHD in Primary Care

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1

Learning Objectives

- Describe ADHD symptoms and common presentations in primary care
- Assess symptoms of ADHD using evidence-based tools/scales
- Implement appropriate and individualized treatment for patients with ADHD

2

Case Study - Emily

- A 19-year-old female sophomore college student presents to you upon advice from the school psychologist that she might need medication for mood
- She has been anxious and a bit depressed that her grades are falling, and she is losing sleep over it. She feels tired during the day
- She has always done well in school, with an A/B average, but has gone down to a C average in college, and now she is failing one course
- It has always been a struggle to get good grades, spending much more time on schoolwork than others, and now she is finding it impossible to keep up
- She has a history of hypothyroidism, but has responded well to treatment and is currently stable on levothyroxine
- Case-appropriate physical exam is normal

3

Case Study - Emily *(continued)*

- PCP orders blood tests, and they all come back normal
- PHQ-9 = 6; SAS = 12
- ASRS v 1.1 scores 5 out of 6 for part A, and 10 out of 12 for part B
- Urine drug test is negative
- Patient reads and signs scheduled drug agreement form
- Patient is started on methylphenidate ER 27 mg once daily, and asked to return in 1-2 weeks

PHQ-9: Patient Health Questionnaire-9
SAS: Zung Self-Rating Anxiety Scale
ASRS: Adult ADHD Rating Scale

4

What is ADHD?

5

ADHD (Attention-Deficit/Hyperactivity Disorder)

- Complex and heterogeneous neurodevelopmental disorder that often persists into adulthood
- Symptoms marked by persistent pattern of hyperactivity-impulsivity and/or inattention, which hinders executive functioning skills (attention, concentration, memory, organization, motivation, emotional control)

Faraone SV, et al. *Neurosci Beiobehav Rev.* 2021;128:789-818. Polanczyk GV, et al. *Child Psychol Psychiatry*. 2015;56:345-365. Xu G, et al. *JAMA* Network Open. 2018;1:e181471.

6

Epidemiology

- Prevalence is increasing in most developed countries
  - US prevalence among children and adolescents increased from 6.1% in 1998 to 10.2% in 2016
  - Increases mainly reflect changes in diagnostic criteria and awareness of ADHD
- Frequent comorbidities with other psychiatric disorders (~50%)
- Most patients first diagnosed by a primary care provider
- Adequate detection is important; when left untreated, ADHD is associated with driving accidents, worse academic and employment outcomes, criminality, and risk for other mental health conditions

Faraone SV, et al. *Neurosci Beiobehav Rev*. 2021;128:789-818. Polanczyk GV, et al. *Child Psychol Psychiatry*. 2015;56:345-365. Xu G, et al. *JAMA* Network Open. 2018;1:e181471.

7

Co-existing Conditions in Children

Coexisting Disorder	Children with ADHD	Children without ADHD
Learning Disability	45%	5%
Conduct Disorder	27%	2%
Anxiety	18%	2%
Depression	15%	1%
Speech Problems	12%	3%

https://chadd.org/about-adhd/co-occuring-conditions/

8

Co-existing Conditions in Adults

Coexisting Condition	Adults with ADHD	Adults without ADHD
Any mood disorder	**38.3%**	**11.1%**
Major depressive disorder	18.6%	7.8%
Dysthymia (mild, chronic depression)	12.3%	1.9%
Bipolar disorder	19.4%	3.1%
Any anxiety disorder	**47.1%**	**19.5%**
Generalized anxiety disorder	8.0%	2.6%
PTSD	11.9%	3.3%
Panic disorder	8.9%	3.1%
Agoraphobia	4.0%	0.7%
Specific phobia	22.7%	9.5%
Social phobia	29.3%	7.8%
Obsessive-compulsive disorder (OCD)	2.7%	1.3%
Any substance abuse disorder	**15.2%**	**5.6%**
Alcohol abuse	5.9%	2.4%
Alcohol dependence	5.8%	2.0%
Drug abuse	2.4%	1.4%
Drug dependence	4.4%	0.6%
Intermittent explosive disorder	**19.6%**	**6.1%**

https://chadd.org/about-adhd/co-occuring-conditions/

9

Etiology and Risk Factors

- ADHD is highly heritable
  - Most estimates range between 70% and 80%; several genome-wide risk loci have been identified
  - Gene-environment interactions are being studied
- Environmental exposures are likely factors, but causality difficult to determine
  - Prematurity and low birthweight
  - Intrauterine exposure to tobacco, maternal stress, obesity,
  - Inconclusive evidence for the role of intrauterine exposure to alcohol and drugs and prenatal and perinatal birth-related complications
  - Acetaminophen
- Parenting style as cause is questionable

Faraone SV, et al. *Biol Psychiatry*. 2005;57:1313-1323.

10

Neuropathology of ADHD

- Emerging idea that ADHD is not the result of a fixed deficit that affects performance across all settings, but varies from setting to setting
  - Symptoms are more common on tasks with low amount of stimulation than on interesting tasks
- ADHD is associated with developmental delays in the prefrontal cortex (PFC)
  - Attention, reasoning, judgment, problem solving, creativity, emotional regulation, impulse control and awareness of aspects of one's and others' functioning
- Dopamine and norepinephrine mediate PFC function and regulate executive function
- ADHD brains lack the dopamine and norepinephrine they need to initiate and maintain tasks
- Patients with ADHD are more likely to use illicit substances because those substances provide the neurotransmitters they need to function

Functional MRI Images

No ADHD | Active ADHD | ADHD in Remission

Posner J, et al. *Lancet*. 2020;395(10222):450-462. Mattfeld A, Gabrieli J, Biederman J, et al. Brain differences between persistent and remitted attention deficit hyperactivity disorder. *Brain*, 2014;137(9): 2423-2428. https://doi.org/10.1093/brain/awu137

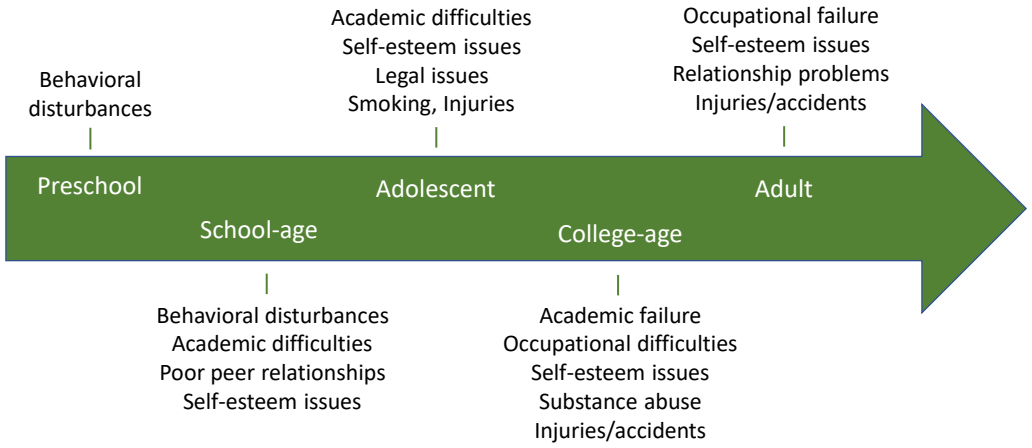
11

ADHD is a Dysfunction of Executive Function

- Patients with executive dysfunction often have difficulty…
  - Monitoring and self-regulating actions
  - Utilizing working memory and accessing recall
  - Managing frustration and modulating emotions
  - Regulating alertness, sustained effort, and speed
  - Focusing, sustaining, and shifting attention to tasks
  - Organizing, prioritizing, and activating to work
- Other disorders, such as depression, anxiety, and PTSD include executive dysfunction as a symptom, but **executive dysfunction is the primary feature of ADHD**

12

Impairments Occur Across the Lifespan



Jain R, Jain S, Montano CB. Addressing diagnosis and treatment gaps in adults with attention-deficit/hyperactivity Disorder. *Prim Care Companion CNS Disord*. 2017;19(5):17nr02153.

13

Gender Disparities in Diagnosis

- Women are less likely to be diagnosed; tend to be diagnosed later in life than men
- Women are more likely to internalize their symptoms, so people around them are less likely to notice that they're struggling
  - Often manifests as depression and anxiety
- Diagnostic criteria are written with hyperactive male patients in mind, so women and primarily inattentive men are more likely to slide under the radar

Ramtekkar UP, et al. *J Am Acad Child Adolesc Psychiatry*. 2010;49(3):217-228.e1-3.

14

Gender Disparities in Diagnosis *(continued)*

- Boys' symptoms are more obvious and external
  - Impulsivity or acting out
  - Hyperactivity: running and climbing
  - Lack of focus, inattentiveness
  - Physical aggression such as hitting
- Girls' symptoms are less obvious and often more internal
  - Being withdrawn
  - Low self-esteem and anxiety
  - Impairment in attention
  - Inattentiveness: a tendency to daydream
  - Verbal aggression: teasing, taunting, or name-calling

Ramtekkar UP, et al. *J Am Acad Child Adolesc Psychiatry*. 2010;49(3):217-228.e1-3.

15

Racial Disparities in Diagnosis

- Black and Hispanic patients are less likely to be diagnosed with ADHD than white patients and less likely to be taking stimulant medications
- More research is needed to determine the cause of the diagnostic gap, but economic resources, cultural attitudes towards ADHD, and clinician bias may play a role

Morgan PJ, et al. *Pediatrics.* 2013;132:85-93.

16

How is ADHD Diagnosed?

17

Inattentive, Hyperactive, and Combined Presentations

Three possible presentations:

1. Predominantly Inattentive (ADHD-PI): Meets inattentive type diagnostic criteria only
2. Predominantly Hyperactive-Impulsive (ADHD-PH): Meets hyperactive/ impulsive type diagnostic criteria only
3. Combined (ADHD-C): Meets diagnostic criteria for both presentations

- Presentation may change over patient lifetime
- Presentation differences do not affect treatment outcomes
- Most adults who met diagnostic criteria as children will ***not*** grow out of the disorder – 15% still meet full criteria; 40-60% partial remitters
- Patients who do grow out of the disorder may still experience functional impairments

American Psychiatric Association. DSM-5; 2013. Faraone SV, et al. *Psychol Med.* 2006;36:159-165.

18

DSM-V Criteria: Inattentive Symptoms

- Inattentive Symptoms
  - Displays poor listening skills
  - Loses and/or misplaces items needed to complete activities or tasks
  - Sidetracked by external or unimportant stimuli
  - Forgets daily activities
  - Diminished attention span
  - Lacks ability to complete schoolwork and other assignments or to follow instructions
  - Avoids or is disinclined to begin homework or activities requiring concentration
  - Fails to focus on details and/or makes thoughtless mistakes in schoolwork or assignments

American Psychiatric Association. DSM-5; 2013.

19

DSM-V Criteria: Hyperactive/Impulsive Symptoms

- Hyperactive Symptoms
  - Squirms when seated or fidgets with feet/hands
  - Marked restlessness that is difficult to control
  - Appears driven by “a motor” or is often “on the go”
  - Lacks ability to play and engage in leisure activities in a quiet manner
  - Incapable of staying seated in class
  - Overly talkative
- Impulsive Symptoms
  - Difficulty waiting turn
  - Interrupts or intrudes into conversations and activities of others
  - Impulsively blurts out answers before questions completed

American Psychiatric Association. DSM-5; 2013.

20

Diagnostic Criteria - Additional Requirements

- The presence of six or more symptoms in either the inattentive or hyperactive/impulsive domains, or both
- Symptoms must persist for at least 6 months, be inconsistent with the child's development level, and have a negative effect on more than one social and academic activity
- Symptoms must be present prior to age 12 years and not be better accounted for by a different psychiatric disorder
- Symptoms are not exclusively a manifestation of oppositional behavior
- Differential diagnosis: Rule out learning disabilities, oppositional defiant disorder, bipolar and depressive disorders, conduct disorder, anxiety disorder, Tourette's syndrome

American Psychiatric Association. 2013

21

Making the ADHD Diagnosis

- Requires detailed evaluation of current and previous symptoms and functional impairment
- Take a detailed family, gestational, and developmental history
- In children <17 years, 6 or more symptoms in either inattentive or hyperactive/impulsive domains, or both are required (DSM-5)
- For adults, at least 5 symptoms overall are required
- Physical examination
- Behavior rating scale and further testing, if needed

Posner J, et al. *Lancet.* 2020;395:450-462. Tran T. *Pediatr Nurs.* 2021;47:202-207.

22

Differential Diagnosis of ADHD in Children

- ADHD symptoms often overlap with developmental and behavioral conditions and medical problems
- Screen for learning disabilities, language disorder, autism spectrum disorder, sleep disorders, depression, anxiety, substance disorder, behavioral disorders
- To differentiate from other medical conditions, assess vision and hearing, measure lead levels and thyroid function, and check other medications for side effects mimicking ADHD

Pearl PI, et al. *Ann NY Acad Sci.* 2001;931:97-112. Tran T. *Pediatr Nurs*. 2021;47:202-207.

23

Indications for Referral in Children

- Intellectual disabilities
- Developmental disorders
- Learning disabilities
- Visual or hearing impairments
- Abuse history
- Severe aggression levels
- Seizure disorder
- Coexisting learning and/or emotional problems
- First presentation at age 12 or older
- Failure of both stimulant classes

Referral Possibilities: Psychologists, Psychiatrists, Neurologists, Educational Specialists, Developmental-Behavioral Pediatricians

Brahmbhatt K, et al. *J Adolescent Health*. 2016;59:135-143.

24

Diagnostic Criteria for Adult ADHD

Four Key Features:

1. Early childhood onset, possibly undiagnosed ADHD
2. Documentation of 5 current symptoms of inattention or hyperactivity/ impulsivity
3. Significant behavioral or functional impairment in 2 settings: home, work/ school, social, that have resulted from ADHD symptoms
4. Symptoms are best explained by ADHD and not another disorder

- Symptoms must have begun in childhood before age 12 years and continued into adulthood
- Clinicians should screen patients presenting with a history of concentration difficulties, or poor organization or planning
- Other suspicious symptoms are complaints of poor memory, forgetfulness, trouble with mood lability, low self-esteem, and poor self-discipline

American Psychiatric Association. 2013

25

Common Challenges

Children

- Diagnosis often relies on the participation of teachers and caregivers who can present challenges
- Trauma in childhood and adolescence can mask as or exacerbate ADHD symptoms; taking a trauma history is important for this group
- Parents may be resistant to diagnosing or treating their child due to stigma
- Parents may have undiagnosed ADHD as well, so they may struggle to build the structure that they and their child need

Adults

- Symptoms as listed are geared towards children and adolescents, so diagnosing adults can be difficult
- Report cards from elementary or middle school may be helpful, but can be difficult to produce for patients who already struggle with organization
- Both diagnosis and treatment are expensive and often only minimally covered by insurance

Brown NM, et al. *Acad Pediatrics*. 2017;17:349-355. Spencer AE, et al. *Pediatrics*. 2021;148(4):e2021051261. Pynoos RS, et al. *J Traum Stress*. 2009;22:391-398.

26

Diagnostic Gap Between Children and Adults

- Shortage of professionals with ADHD expertise
- High frequency of comorbid disorders
- Adults show different expression of core symptoms
  - Inner restlessness, excessive talkativeness, need to move
  - Impulsiveness, impatience, acting without thinking
  - Difficulty holding a job or maintaining personal relationships
  - Feeling bored, unable to make decisions, procrastinating, being disorganized and distracted

Kooij SJJ, et al. *BMC Psychiatry*. 2010;1067.

27

Rating Scales for ADHD

- ASRS v1.1 Part A (Adult ADHD Self-Report Scale) is most widely used in adults
  - Useful as a screening test when there is high clinical suspicion of ADHD
- Other scales include
  - Vanderbilt ADHD Diagnostic Rating Scale (VADRS)
  - Conners' ADHD Rating Scales
  - Test of Variables of Attention (TOVA)
  - ADHD Rating Scale-5
  - Adult ADHD Clinical Diagnostic Scale (ACDS)
  - Brown Attention-Deficit Disorder Symptom Assessment Scale (BADDS)

Kessler RC, et al. *Psychol Med*. 2005;35(2):245-256. Chamberlain SR, et al. *Compr Psychiatry*. 2021;106:152224.

28

Adult ADHD Self-Report Scale for DSM V (ASRS-DSM-5)

- Updated ASRS v1.1 in 2017 to reflect DSM-5 changes
- Recognizes that adult ADHD is characterized by executive function deficits not shown in DSM-5 criteria
- Not designed to be a stand-alone diagnostic tool

Kessler RC, et al. *Psychol Med*. 2005;35:245-256.

Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist

Patient Name _____ Today's Date _____

Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X in the box that best describes how you have felt and conducted yourself over the past 6 months. Please give this completed checklist to your healthcare professional to discuss during today's appointment.

	Never	Rarely	Sometimes	Often	Very Often
1. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?					
2. How often do you have difficulty getting things in order when you have to do a task that requires organization?					
3. How often do you have problems remembering appointments or obligations?					
4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					
5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?					
6. How often do you feel overly active and compelled to do things, like you were driven by a motor?					

Part A

7. How often do you make careless mistakes when you have to work on a boring or difficult project?					
8. How often do you have difficulty keeping your attention when you are doing boring or repetitive work?					
9. How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?					
10. How often do you misplace or have difficulty finding things at home or at work?					
11. How often are you distracted by activity or noise around you?					
12. How often do you leave your seat in meetings or other situations in which you are expected to remain seated?					
13. How often do you feel restless or fidgety?					
14. How often do you have difficulty unwinding and relaxing when you have time to yourself?					
15. How often do you find yourself talking too much when you are in social situations?					
16. When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to, before they can finish them themselves?					
17. How often do you have difficulty waiting your turn in situations when turn taking is required?					
18. How often do you interrupt others when they are busy?					

Part B

29

Adult ADHD Self-Report Screening Scale for DSM V (ASRS-DSM-5)

- 6 items are most predictive for ADHD and identify adults who need comprehensive evaluation
- 4 or more marks in darkly shaded area are considered suspicious for ADHD and warrant further investigation

Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist

Patient Name _____ Today's Date _____

Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X in the box that best describes how you have felt and conducted yourself over the past 6 months. Please give this completed checklist to your healthcare professional to discuss during today's appointment.

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4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					
5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?					
6. How often do you feel overly active and compelled to do things, like you were driven by a motor?					

Part A

Kessler RC, et al. *Psychol Med.* 2005;35:245-256.

30

Vanderbilt ADHD Diagnostic Rating Scale

- Psychological assessment tool for parents and teachers of children aged 6 to 12 years
- Toolkit includes assessment and follow-up scales
- Two components
  1. Symptom frequency assessment
  2. Degree of performance impairment
- Allows calculation of symptom score that can be followed over time to monitor response to treatment

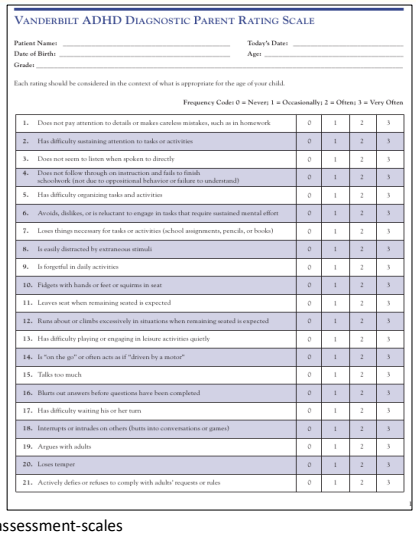
Wolraich M, et al. *J Pediatr Psychology*. 2003;28:559-568.
https://www.nichq.org/resource/nichq-vanderbilt-assessment-scales

31

Vanderbilt ADHD Diagnostic Rating Scale

Scoring instructions for parents and teachers

- Predominately inattentive subtype requires 6 or 9 behaviors, (scores of 2 or 3 are positive) on items 1 through 9, and a performance problem (scores of 1 or 2) in any of the items on the performance section
- Predominately hyperactive/impulsive subtype requires 6 or 9 behaviors (scores of 2 or 3 are positive) on items 10 through 18 and a problem (scores of 1 or 2) in any of the items on the performance section
- The combined subtype requires the above criteria on both inattention and hyperactivity/impulsivity



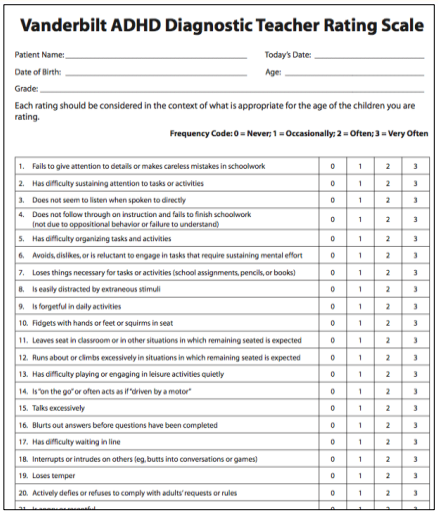
VANDERBILT ADHD DIAGNOSTIC PARENT RATING SCALE

Patient Name: _____ Today's Date: _____
Date of Birth: _____ Age: _____
Grade: _____

Each rating should be considered in the context of what is appropriate for the age of your child.

Frequency Code: 0 = Never; 1 = Occasionally; 2 = Often; 3 = Very Often

1. Does not pay attention to details or makes careless mistakes, such as in homework	0	1	2	3
2. Has difficulty sustaining attention to tasks or activities	0	1	2	3
3. Does not seem to listen when spoken to directly	0	1	2	3
4. Does not follow through on instruction and fails to finish schoolwork (not due to oppositional behavior or failure to understand)	0	1	2	3
5. Has difficulty organizing tasks and activities	0	1	2	3
6. Avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort	0	1	2	3
7. Loses things necessary for tasks or activities (school assignments, pencils, or books)	0	1	2	3
8. Is easily distracted by extraneous stimuli	0	1	2	3
9. Is forgetful in daily activities	0	1	2	3
10. Fidgets with hands or feet or squirms in seat	0	1	2	3
11. Leaves seat when remaining seated is expected	0	1	2	3
12. Runs about or climbs excessively in situations when remaining seated is expected	0	1	2	3
13. Has difficulty playing or engaging in leisure activities quietly	0	1	2	3
14. Is "on the go" or often acts as if "driven by a motor"	0	1	2	3
15. Talks too much	0	1	2	3
16. Blurts out answers before questions have been completed	0	1	2	3
17. Has difficulty waiting his or her turn	0	1	2	3
18. Interrupts or intrudes on others (butts into conversations or games)	0	1	2	3
19. Argues with adults	0	1	2	3
20. Loses temper	0	1	2	3
21. Actively defies or refuses to comply with adults' requests or rules	0	1	2	3



Vanderbilt ADHD Diagnostic Teacher Rating Scale

Patient Name: _____ Today's Date: _____
Date of Birth: _____ Age: _____
Grade: _____

Each rating should be considered in the context of what is appropriate for the age of the children you are rating.

Frequency Code: 0 = Never; 1 = Occasionally; 2 = Often; 3 = Very Often

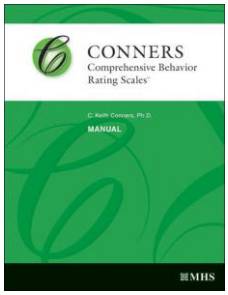
1. Fails to give attention to details or makes careless mistakes in schoolwork	0	1	2	3
2. Has difficulty sustaining attention to tasks or activities	0	1	2	3
3. Does not seem to listen when spoken to directly	0	1	2	3
4. Does not follow through on instruction and fails to finish schoolwork (not due to oppositional behavior or failure to understand)	0	1	2	3
5. Has difficulty organizing tasks and activities	0	1	2	3
6. Avoids, dislikes, or is reluctant to engage in tasks that require sustaining mental effort	0	1	2	3
7. Loses things necessary for tasks or activities (school assignments, pencils, or books)	0	1	2	3
8. Is easily distracted by extraneous stimuli	0	1	2	3
9. Is forgetful in daily activities	0	1	2	3
10. Fidgets with hands or feet or squirms in seat	0	1	2	3
11. Leaves seat in classroom or in other situations in which remaining seated is expected	0	1	2	3
12. Runs about or climbs excessively in situations in which remaining seated is expected	0	1	2	3
13. Has difficulty playing or engaging in leisure activities quietly	0	1	2	3
14. Is "on the go" or often acts as if "driven by a motor"	0	1	2	3
15. Talks excessively	0	1	2	3
16. Blurts out answers before questions have been completed	0	1	2	3
17. Has difficulty waiting in line	0	1	2	3
18. Interrupts or intrudes on others (eg, butts into conversations or games)	0	1	2	3
19. Loses temper	0	1	2	3
20. Actively defies or refuses to comply with adults' requests or rules	0	1	2	3

https://www.nichq.org/resource/nichq-vanderbilt-assessment-scales

32

Conners' ADHD Rating Scales

- Short and long versions for children 6 - 18 years
  - Long version – initial evaluation
  - Short version (25 questions) – follow-up on child's behavioral patterns
  - Each includes 3 forms – for parents, teachers, and child
- Used to understand behavioral, social, and academic issues and help diagnose ADHD
- Results developed into standardized T-scores and displayed visually
- T-score > 60 may indicate ADHD
- T-score > 70 indicates more serious ADHD symptoms



Conners CK. Multihealth Systems; 1997.

33

Additional ADHD Screening Tools

- Test of Variables of Attention (TOVA®)[1]
  - A Continuous Performance Test that measures a person's inattention and impulsivity using a simple, yet boring, computer game
- ADHD Rating Scale-5[2]
  - Parent and teacher questionnaires on child's behaviors are keyed to DSM-5 criteria
- Adult ADHD Clinical Diagnostic Scale (ACDS)[3]
  - Based on a semi-structured clinical interview
  - 18 items assessing DSM and non-DSM adult symptoms of ADHD
- Brown Attention-Deficit Disorder Symptom Assessment Scale (BADDS)[4]
  - 40 items in 5 symptom areas: activation, attention, effort, affect, and memory

1. About the TOVA®. https://www.tovatest.com/about-the-t-o-v-a/. 2. DuPaul GJ, et al. Guilford Press, 2016.
3. Kessler RC, et al. *Arch Gen Psychiatry*. 2010;67:1168-1178. 4. Rucklidge JJ, Tannock R. *J Atten Disord*. 2002;5:155-164.

34

Screening Heuristics for PCPs

- Ask patients about their academic history – particularly whether they struggle to complete assignments to a degree that is disproportionate to the difficulty of the work
  - "She's so smart; if only she would do her homework."
- Consider caffeine use – many undiagnosed patients self-medicate with caffeine as it is a readily available stimulant drug. Some patients may find that caffeine calms them down or even makes them drowsy
- Does the patient struggle with starting tasks – even tasks they find enjoyable?
- Is the patient on time to their appointment? Do they have a history of missing appointments?
- Consider using screening tests like the Adult ADHD Self-Report Scale Screener

35

Comorbidities May Hinder Diagnosis in Adults

- High frequency of comorbidities, particularly mood, anxiety, personality, and substance use disorders as well as obesity, sleep disorders, asthma, and migraines
- Self-medication with illicit substances to deal with ADHD symptoms
- Some depression is the result of demoralization, decreased pleasure, sleep disorders, irritability due to ADHD functional impairments
- Women more likely to develop comorbidities with depression and eating disorders
- Men more likely to have comorbid substance use disorders

36

ADHD Treatment

37

Adult ADHD Requires Treatment Throughout the Day

24 Hours

Go to bed on time
Plan logistics for next day
Balance checkbook
Interact with significant other
Help kids with homework
Drive carefully home
Finish work accurately & on time

Sleep soundly
Wake-up
Organize kids for school
Organize themselves for work
Drive carefully to work
Pay attention at work

Jain R, Jain S, Montano CB. Addressing diagnosis and treatment gaps in adults with attention-deficit/hyperactivity Disorder. *Prim Care Companion CNS Disord*. 2017;19(5):17nr02153. This Photo by Unknown Author is licensed under CC BY-SA-NC.

38

Treatment Considerations

- Treatment should incorporate multiple components and evolve as patient matures
  - Behavioral therapy and parental practices are first-line treatment for children < 6 years
  - Medication therapy is indicated for patients ≥ 6 years
  - Academic support and behavioral therapy are adjuncts to medication therapy
  - Psychoeducation more important in adolescents (driving and substance use)
  - Assessment and treatment of associated disorders
- US guidelines suggest medication as initial treatment
  - Meta-analysis of 9,952 adults showed that pharmacologic treatment more effective than placebo; psychostimulants have larger effect size than nonstimulants

Partners for Kids. Prescribing Guidelines for ADHD. 2021. Cunill R, et al. *Psychopharmacology (Berl)*. 2016;233:187-197.

39

Pharmacologic Treatment of ADHD

- Amphetamines and methylphenidate and, less often, nonstimulants (atomoxetine, clonidine, and guanfacine) are used to treat ADHD
- Inattentiveness and restlessness are improved more than quality-of-life measures in short-term trials
- Short-term beneficial effects of medication on injuries, motor vehicle accidents, education, substance use disorder
  - Relative risk reductions of 9–58%
- Considering stimulant effects is vital when treating ADHD with comorbidities

Cortese S. *N Engl J Med*. 2020;383:1050-1056.

40

Psychostimulants Are First-line Medications

- Methylphenidate (MPH), amphetamine and dextroamphetamine combination, lisdexamfetamine are mainstays of pharmacotherapy
- Primary effect is to increase central dopamine and norepinephrine activity, which impacts executive and attentional function
  - Available in various formulations including chewable, oral solution, and transdermal patch
  - Long-acting/dual release capsules combine immediate-release (IR) and extended-release (ER) formulations in varying proportions
  - Rapid clearance with no accumulation results in “on/off” mode with daily rebound symptoms rather than stable plateau
- Must obtain agreement from patient not to misuse prior to initiation

Faraone SV. *Neurosci Biobehav Rev*. 2018;87:255-270. Jaeschke RR, et al. *Psychopharmacology (Berl)*. 2021;238:2667-2691.

41

ADHD Psychostimulants: Methylphenidate

Formulation	Dosage Strengths	Duration
Methylphenidate short-acting tablet, liquid	Tablets: 2.5 mg to 20 mg Liquid: 5 mg/5 ml – 10 mg/5 ml	3 – 5 hours
Methylphenidate extended-release tablet, capsule, liquid, transdermal patch	Tablets: 18 mg – 40 mg Capsules: 10 mg – 100 mg Liquid: 25 mg/5 ml Transdermal patch: 10 – 30 mg	7 – 12 hours 7 – 16 hours 8 – 12 hours 10 – 12 hours
Serdexmethylphenidate and dexmethylphenidate capsule	26.1 mg/5.2 mg 39.2 mg/7.8 mg 52.3 mg/10.4 mg	10+ hours
Dexmethylphenidate short-acting tablet	2.5 mg – 10 mg	3 – 5 hours
Dexmethylphenidate extended-release capsule	5 mg – 40 mg	12 hours

Medications Used in the Treatment of ADHD. Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD). 2022. https://chadd.org/for-parents/medications-used-in-the-treatment-of-adhd/. Nationwide Children's Hospital. Prescribing Guidelines for Attention Deficit/Hyperactivity Disorder (ADHD). 2021. Partners for Kids in conjunction with Nationwide Children's Hospital. 2022. https://www.nationwidechildrens.org/-/media/nch/for-medical-professionals/practice-tools-new/prescribing-guidelines-for-adhd.ashx

42

ADHD Psychostimulants: Amphetamine

Formulation	Dosage Strengths	Duration
Amphetamine, methamphetamine short-acting tablet	5 mg – 20 mg	4 – 8 hours
Amphetamine extended-release tablet, capsule, liquid	Tablets: 3.1 mg – 18.8 mg Capsules: 2.5 mg – 50 mg Liquid: 3.1 mg/2.5 ml; 18.8 mg/15 ml	9 – 12 hours 8 – 16 hours 9 – 12 hours
Amphetamine and dextroamphetamine mixed salts tablet	5 mg – 30 mg	4 – 8 hours
Amphetamine and dextroamphetamine mixed salts extended-release capsule	5 mg – 30 mg	8 – 12 hours
Dextroamphetamine extended-release tablet	5 mg – 15 mg	6 - 9 hours
Lisdexamfetamine tablet	10 mg – 60 mg	8 – 12 hours
Lisdexamfetamine capsule	10 mg – 70 mg	10 – 12 hours

Medications Used in the Treatment of ADHD. Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD). 2022. https://chadd.org/for-parents/medications-used-in-the-treatment-of-adhd/. Nationwide Children's Hospital. Prescribing Guidelines for Attention Deficit/Hyperactivity Disorder (ADHD). 2021. Partners for Kids in conjunction with Nationwide Children's Hospital. 2022. https://www.nationwidechildrens.org/-/media/nch/for-medical-professionals/practice-tools-new/prescribing-guidelines-for-adhd.ashx

43

ADHD Non-Stimulants

Formulation	Dosage Strengths	Duration
Atomoxetine capsules (norepinephrine reuptake inhibitor)	10 mg – 100 mg	24 hours
Viloxazine extended-release capsules (norepinephrine reuptake inhibitor)	100 mg – 200 mg	24 hours
Clonidine extended-release tablet (alpha agonist)	0.1 mg – 0.2 mg	12 – 24 hours
Guanfacine extended-release tablet (alpha agonist)	1 mg – 4 mg	12 – 24 hours

Medications Used in the Treatment of ADHD. Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD). 2022. https://chadd.org/for-parents/medications-used-in-the-treatment-of-adhd/. Nationwide Children's Hospital. Prescribing Guidelines for Attention Deficit/Hyperactivity Disorder (ADHD). 2021. Partners for Kids in conjunction with Nationwide Children's Hospital. 2022. https://www.nationwidechildrens.org/-/media/nch/for-medical-professionals/practice-tools-new/prescribing-guidelines-for-adhd.ashx

44

Psychosocial and Nonpharmacologic Approaches

- For children: psychosocial treatments combined with medication is preferable to medication alone
- For adults: cognitive behavioral therapy and occupational coaching may be helpful
- Neurofeedback and computer-based attentional/executive function training may be effective, but may not translate to ADHD symptom improvement
- Dietary treatments: excluding additives or supplementing with free fatty acids have shown modest effects
- Physical exercise and meditation may be helpful

Posner J, et al. *Lancet.* 2020;395(10222):450-462.

45

Case Study - Emily *(continued)*

- The patient started therapy with methylphenidate 27 mg once daily
- She returns in 10 days stating her symptoms are much less, with better ability to concentrate, focus and maintain tasks
- The medication seems to last 10 hours or so, so she has concerns about what to do in the later hours of the day
- No side effects
- She continues to see the therapist for support, and is also directed to campus disability services for possible accommodations

46

Summary

- ADHD is associated with developmental delays in the prefrontal cortex (PFC)
- Dopamine and norepinephrine mediate PFC function and regulate executive function
- Children show a persistent pattern of behavioral problems and school difficulties resulting from problems with inattention and/or hyperactivity
- Adults have a high frequency of comorbid disorders and show a different expression of core symptoms
- Psychostimulants are first-line medications
- Their primary effect is to increase central dopamine and norepinephrine activity, which impacts executive and attentional function

47