Attention Deficit Hyperactivity Disorder
— Overview and New Perspectives —

Thomas B. Henry, MD
Board Certified Child & Adolescent Psychiatrist
Assistant Professor, Department of Psychiatry
CMU Medical Education Partners
Preceptor, Child & Adolescent Outpatient Program
Janes Street Clinic
Great Lakes Bay Health Centers, Saginaw
Learning Objectives

- Brief overview of the epidemiology, prevalence, heritability, impact, and the developmental course of ADHD over the lifespan.
- Overview of psychopathology findings in ADHD.
- Identify the primary comorbidities.
- Learn the differential diagnoses of ADHD.
- Overview of assessment and diagnosis.
- Overview of the various evidenced-based treatment interventions.
I have no financial relationships or affiliations to disclose.
Epidemiology

- Most commonly diagnosed behavioral disorder of childhood (1 in 20 worldwide).
- 3-7% of school children are affected in the U.S.
- Males to Females: DSM-5 states 2:1
- Worldwide prevalence ranges ~3% - 7%.
- Pooled world prevalence 5.29% (Polanczyk, et al, 2007)

- Pooled world prevalence 5.29% (Polanczyk, et al, 2007)

![Graph showing prevalence rates across different countries and years, with DSM versions indicated.](image-url)
ADHD is Familial

Twin Studies Show ADHD Is a Genetic Disorder

ADHD is a heterogeneous neurodevelopmental disorder with many possible etiological factors.

- Genes
- Brain Imaging
- Other neuro-biologic factors
  - Maternal-fetal/Perinatal stress
  - Maternal smoking
  - Low birth weight
  - Traumatic brain injury
  - Early life adversity
Psychopathology: Executive Function

Executive Dysfunction

- Trouble getting started
- Difficulty with organizing work
- Misunderstand directions
- Lose focus when trying to listen
- Forget what has been read, need to re-read
- Easily distracted
- Hard to sit still or be quiet
- Rushing
- Often interrupt
- Inpatient
- Forget planned tasks
- Trouble following sequential directions
- Quickly lose thoughts put on hold
- Easily frustrated
- Feelings hurt easily
- Sensitive to criticism
- Emotional reactivity
- Excessive daytime drowsiness
- Trouble completing tasks on time
- Slow processing speed
A Model of ADHD

(TG Dias et al, 2013)
Course and Outcome

- Inattention
- Hyperactivity
- Impulsivity

---

Age
Potential Areas of Impairment

ADHD

- Academic Limitations
- Relationships
- Low Self-Esteem
- Injuries
- Smoking & SUDs
- Motor Vehicle Accidents
- Legal Difficulties
- Occupation/Vocation

Adulthood

Children

Adolescents
Course and Outcome

Increased Traffic Violations and Motor Vehicle Accidents in Adolescents and Adults with ADHD

ADHD Is Associated with Increased Medical Costs

Increased Lifetime Substance Abuse in Untreated Adults with ADHD

Comorbidities

- 2/3 of children with ADHD present with one or more comorbid conditions.

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety disorder</td>
<td>8% – 30%</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>8% – 25%</td>
</tr>
<tr>
<td>Oppositional-defiant disorder</td>
<td>45% – 64%</td>
</tr>
<tr>
<td>Affective disorder</td>
<td>15% – 75%</td>
</tr>
<tr>
<td>Tic disorder</td>
<td>8% – 34%</td>
</tr>
<tr>
<td>Mania/hypomania</td>
<td>0% – 22%</td>
</tr>
<tr>
<td>Learning/academic problems</td>
<td>10% – 92%</td>
</tr>
</tbody>
</table>

DSM-5 Diagnostic Criteria

Inattention: Six or more symptoms of inattention for children up to age 16, or five or more for adolescents 17 and older and adults; symptoms of inattention have been present for at least 6 months, and they are inappropriate for developmental level:
- Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or with other activities.
- Often has trouble holding attention on tasks or play activities.
- Often does not seem to listen when spoken to directly.
- Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., loses focus, side-tracked).
- Often has trouble organizing tasks and activities.
- Often avoids, dislikes, or is reluctant to do tasks that require mental effort over a long period of time (such as schoolwork or homework).
- Often loses things necessary for tasks and activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).
- Is often easily distracted
- Is often forgetful in daily activities.

Hyperactivity and impulsivity: Six or more symptoms of hyperactivity-impulsivity for children up to age 16, or five or more for adolescents 17 and older and adults; symptoms of hyperactivity-impulsivity have been present for at least 6 months to an extent that is disruptive and inappropriate for the person’s developmental level:
- Often fidgets with or taps hands or feet, or squirms in seat.
- Often leaves seat in situations when remaining seated is expected.
- Often runs about or climbs in situations where it is not appropriate (adolescents or adults may be limited to feeling restless).
- Often unable to play or take part in leisure activities quietly.
- Is often “on the go” acting as if “driven by a motor”.
- Often talks excessively.
- Often blurts out an answer before a question has been completed.
- Often has trouble waiting his/her turn.
- Often interrupts or intrudes on others (e.g., butts into conversations or games)

In addition, the following may be noted:
- Several inattentive age 12 years or older
- Several hyperactive-impulsive symptoms
- There is clear evidence of onset before age 12 years
- The symptoms are not better explained by another Pervasive Developmental Disorder or another Pervasive Developmental Disorder

Specify if
- In Partial Remission: Fewer than the full criteria are met for the past 6 months.
  - Symptom impairment remains in social, academic, or occupational functioning.
Establishing a Convincing Diagnosis

- Medical history review: cardiac, neurology
- Comprehensive assessment with school-aged youth and parent(s); include self-report for adolescents.
- Collateral information (classroom, observation, school assessments, extracurricular activities).
- Teacher- and Parent-completed Questionnaires.
- Psychological testing may assist if:
  - Concerns about low cognitive ability
  - Concerns about low achievement
Differential Diagnosis

- General Medical Conditions
  - Severe Anemia
  - Lead Poisoning
  - Chronic illness
  - Hearing or vision impairment
  - Obstructive Sleep Apnea in Children

- Neurological
  - Seizure disorder (eg, Absence Seizure)
  - Head injury/Concussion

- Psychiatric

- Psychosocial/Environmental
Treatment

- Multimodal in approach.
- Treatment is dependent on duration of symptoms; and severity & impact of symptoms in day-to-function across of life domains.
- Identification and treatment of comorbid symptoms/conditions is essential.
Treatment

- Medication

- Behavioral Therapies
  - Parent Management Training approaches
  - Cognitive/Behavioral treatment(s)
  - Social skills

- Educational Supports
  - Individualized Education Plan (IEP)
  - 504 Plan

- Summer Treatment Programs
Stimulants: Response Rates

- About 70% response rate with single stimulant, and up to 90% response rate if both medication classes are tried.
- No significant differences between amphetamine-related and methylphenidate products.
Stimulants: MPH Optimizing Dosing

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting Dose</th>
<th>Maximum Dose*</th>
<th>Duration Usual Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritalin IR®</td>
<td>5mg QD/BID</td>
<td>2mg/kg/day</td>
<td>4 hour/BID-</td>
</tr>
<tr>
<td>Focalin</td>
<td>2.5mg QD/BID</td>
<td>1mg/kg/day</td>
<td>4-5 hour/BID-TID</td>
</tr>
<tr>
<td>Focalin XR</td>
<td>5mg QD</td>
<td>1mg/kg/day</td>
<td>10-12 hour QD</td>
</tr>
<tr>
<td>Daytrana</td>
<td>10mg</td>
<td></td>
<td>6-16 hour</td>
</tr>
<tr>
<td>Concerta®</td>
<td>18mg QD</td>
<td>2mg/kg/day</td>
<td>12 hour/once</td>
</tr>
<tr>
<td>Metadate CD®</td>
<td>20mg QD</td>
<td></td>
<td>8 hour/once</td>
</tr>
<tr>
<td>Ritalin LA</td>
<td>20mg QD</td>
<td></td>
<td>8 hour/once</td>
</tr>
<tr>
<td>Quillivant®</td>
<td>&lt;10mg QD</td>
<td></td>
<td>12 hour/once</td>
</tr>
<tr>
<td>Qullichew</td>
<td>&lt;10mg QD</td>
<td></td>
<td>8 hour/once</td>
</tr>
</tbody>
</table>

**BID:** Twice daily  
**QD:** Once daily  

*May exceed FDA approved dose  
Adapted from Postgrad Med. 2010;122(5):97-109. www.drugs.com
## Amphetamine (AMPH) in ADHD: Optimizing Dosing

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting Dose</th>
<th>Maximum Dose*</th>
<th>Duration Usual Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adderall®</td>
<td>2.5 to 5mg QD</td>
<td>1.5mg/kg/day</td>
<td>6 hour/BID</td>
</tr>
<tr>
<td>Adderall XR</td>
<td>2.5 to 5mg QD</td>
<td></td>
<td>12 hour/QD</td>
</tr>
<tr>
<td>Vyvanse</td>
<td>30mg QD</td>
<td></td>
<td>12-14 hour/QD</td>
</tr>
<tr>
<td>Dextroamphetamine tab®</td>
<td>2.5 to 5mg BID</td>
<td>1.5mg/kg/day</td>
<td>3-5 hour BID-QID</td>
</tr>
<tr>
<td>Evekeo</td>
<td>2.5 to 5mg BID</td>
<td></td>
<td>3-5 hour BID-QID</td>
</tr>
<tr>
<td>Dexedrine span</td>
<td>5mg QD</td>
<td></td>
<td>6 hour/QD-BID</td>
</tr>
<tr>
<td>Dynavel XR® (suspension)</td>
<td>2.5 to 5mg QD</td>
<td>1.5mg/kg/day</td>
<td>12 hour/QD</td>
</tr>
<tr>
<td>Adzenys XR (disintegrating tab)</td>
<td>6.3 to 12.5mg QD</td>
<td>Not established</td>
<td>12 hour/QD</td>
</tr>
</tbody>
</table>

*May exceed FDA approved dose (e.g. > 20 to 30 mg/day)

Stimulants: Stopping Rx & Relapse

Discontinuing Treatment Leads to ADHD Relapse

Treatment failure was defined as a 50% or greater increase in ADHD-RS-IV total score and a 2 point or greater increase in CGI-S score at any double-blind visit relative to the start of the randomized withdrawal period.

LDX=lisdexamfetamine

Atomoxetineine (Stattera®)

Atomoxetine

Uses
• Uncomplicated ADHD
• Refractory ADHD
• Comorbid ADHD
  o Anxiety or depressive disorders
  o Tic disorders
  o Disruptive disorders
  o Substance use disorders

Safety
• Rare hepatitis reported
  o Rare possibility-NO liver function tests (LFT) necessary
• Slight increase in irritability and suicidal ideation reported in clinical trials
  o 0.037% Atomoxetine vs. 0.0% placebo
  o One suicide attempt/1,357 cases; no suicides
Alpha Agonists: When to Use

Guanfacine or Clonidine: When to Use

- Monotherapy
- Stimulant or nonstimulant nonresponders
- Medication partial responders (adjunctive therapy)
  - Improved ADHD in majority of subjects
  - Tolerable adverse effect (AE): abdominal pain, fatigue and irritability most common
  - Cardiovascular (CV): typically BP/HR dose dependent decreases; no CV symptoms reported
- Adverse effects to stimulants or nonstimulants
- Comorbid ADHD plus
  - Oppositional disorder/ “Emotional dysregulation”
  - Anxiety
  - Tics
- Potentially younger children (needs to be studied)

Guanfacine ER (Intuniv®) and ADHD

Guanfacine Extended-Release (XR) in ADHD

(n=324 [51 sites]; 6 weeks active*, Mean Age 11±3 yrs)

Effect size: 0.41-0.89

*3 weeks titration
3 weeks maintenance (endpoint)
3 weeks taper

Extended-Release Guanfacine Has Similar Efficacy with AM or PM Administration

(6-12 years, dosing 1-4mg/day; samples size of GXR AM (107), GXR PM (114), or placebo (112))

**Figure 2**: Mean change from baseline in attention-deficit/hyperactivity disorder (ADHD) Rating Scale-IV (ADHD- RS-IV) scores by visit. Note: (A) Total score; (B) Hyperactivity/Impulsivity subscale; (C) Inattention subscale. All p values were based on type III sum of squares from an analysis of covariance (ANCOVA) model. GXR = guanfacine extended release; LOCF = last observation carried forward; LS = least squares; SEM = standard error of the mean. *p* < .05 versus placebo based on changes from baseline (visit 2); **p** < .01 versus placebo based on change from baseline (visit 2); ***p*** < .001 versus placebo based on changes from baseline (visit 2).

Treatment: Less Functional Impairment

Normalizing ADHD Symptoms Requires Significant Reductions in the ADHD RS-IV

ADHD Diagnosis
At diagnosis patients score up to 54 on the ADHD RS-IV

Standard Reduction
A score reduction of 16-18 points was accompanied by a detectable functional improvement

Achieving Normalization
A score reduction of 20-27 points was accompanied by pronounced functional improvement

ADHD Summary

- ADHD is a heterogeneous condition with variable presentations with respect to symptoms, neuropsychological profiles, and neurobiological and genetic features.
- ADHD is commonly co-morbid with other neuro-psychiatric conditions.
- ADHD is associated with significant impact to individuals, families, communities & society.
- Treatment is multimodal.
- Medications are effective and reduce functional impairment.
Thank You

Questions