FORWARD FOCUS: TRANSITIONING FROM ADOLESCENCE TO ADULTHOOD WITH ADHD
Learning Objectives

• Identify the different challenges in the management of ADHD in child and adolescent patients

• Differentiate the spectrum of medication options available for use in pediatric ADHD based on formulation and pharmacokinetic profile

• Optimize treatment of pediatric ADHD to fit the specific needs of the patient and their caregivers
ADHD Overview

• Most common presenting neurobehavioral disorder in children and adolescents
  • ADHD prevalence among 8- to 15-year-olds: 8.7%
  • ADHD prevalence among 18- to 44-year-olds: 4.4%

• Highly familial, high level of genetic accountability (>75%)

• Associated with Impairment in multiple domains

• Associated with high degrees of psychiatric comorbidity

• Chronic course
  • 50% of children continue with ADHD in adulthood
  • 75% of adolescents continue with ADHD into adulthood

Adler, Spencer, Wilens (eds) ADHD in Children and Adults, Cambridge Press 2015
Childhood Symptoms of ADHD Decline With Time…

…but most patients are still impaired at age 20

**DSM-III-R ADHD**

![Graph showing the percentage of patients in remission over age ranges](image)

- N = 128
- Patients in remission (%)
- Age
Presenting *DSM-IV* Symptoms in Adults With ADHD

- Easily distracted
- Difficulty sustaining attention
- Difficulty with sustained attention
- Difficulty following instructions
- Difficulty organizing
- Doesn’t listen
- Forgetful in daily activities
- Loses things
- Careless/sloppy
- Blurts out answers
- Interrupts or intrudes
- Fidgets
- Difficulty waiting turn
- Driven by a motor
- Talks excessively
- Runs/climbs excessively
- Difficulty remaining seated
- Difficulty playing quietly
- Difficulty with sustained attention
- Difficulty following instructions
- Difficulty organizing
- Doesn’t listen
- Forgetful in daily activities
- Loses things
- Careless/sloppy
- Blurts out answers
- Interrupts or intrudes
- Fidgets
- Difficulty waiting turn
- Driven by a motor
- Talks excessively
- Runs/climbs excessively
- Difficulty remaining seated
- Difficulty playing quietly

Proportion of patients with ADHD presenting with symptom

Main Changes To ADHD DSM-5 (vs IV)

- Change: less emphasis on defined subtypes
- Similar symptoms (e.g., symptoms of inattention and/or hyperactive-impulsivity) – more prompts added
- Change in symptom requirements:
  - <17 years: 6/9 Hyperactivity-impulsivity and/or 6/9 of inattention
  - >17 years: 5/9 Hyperactivity-impulsivity and/or 5/9 of inattention
- Change in symptom onset: prior to age 12 years
- Change in “clinically significant impairment” to relative impairment
- Change in exclusion: diagnosis can be made in autism spectrum disorder
Significant brain growth and development occurs during adolescence, and continues into the twenties. Some studies show that this growth and development extends to the age of 30!

(Sowell et al., 1999; Sowell et al., 2001)
Grey matter develops quickly during childhood, but slows during adolescence.

Grey matter volume peaks at age 11 in **girls** and at age 13 in **boys**.

Then, the volume of grey matter begins to decline.
Conclusions: Despite the inherent limitations and heterogeneity of the extant MRI literature, our review suggests that therapeutic oral doses of stimulants decrease alterations in brain structure and function in subjects with ADHD relative to unmedicated subjects and controls. These medication-associated brain effects parallel, and may underlie, the well-established clinical benefits.
Differential Brain Development May Explain Observable Problems in ADHD Adolescents and Young Adults
So how does the brain mature after adolescence?

In a study of young adults, the frontal lobes showed large changes up to the age of 30!

This suggests that frontal lobe maturation is important for adult cognition.

There is evidence that these changes continue WELL after the teenage years.
Transitional Aged Youth Behavior?

Dysregulated Mood (e.g., frustration, irritability, temper tantrums)

Exaggerated in SUD, ADHD, or Mood dysregulation?
Emotional Impulsiveness & Impairment in Life Activities in Hyperactive Children as Adults

Percentage of Each Group Endorsing Each Symptom of Emotional Impulsiveness as Occurring Often or More Frequently:

ADHD-P = Persistent ADHD (N = 55)
ADHD-NP = Nonpersistent ADHD (N = 80)
Community (N = 75)
Emotional Dysregulation Increases Substance Abuse (N=308)

HR = 5; p=0.001; Association remained significant when controlling for bipolar, ADHD, and conduct disorders

Emotional Dysregulation

More Substance Abuse

CBCL = Child Behavior Checklist

Wilens et al. Drug Alcohol Dependence 2013
Challenges for the Transitioning Adolescent With ADHD

- Increasing demands in school
  - Tests/examinations
  - More homework
  - Missing assignments
  - College applications, board examinations
- Occupational independence
- Substance abuse
- Medication diversion

- Increasing demands in sports
  - Increasing complexity of “playbook”
  - Higher level of play
  - Self-imposed practice
  - Extended training
  - Diet
- Social impairment
- Driving responsibilities
- Autonomy
- Comorbidities

Social Impairment in Adolescents and Young Adults with ADHD

- Less socially competent than peers\(^1\)
- Involved in fewer social activities\(^2\)
- Fewer friends\(^2\)
- Delinquent friends\(^3\)
- Social isolation\(^3\)

Adolescents with ADHD report an overly optimistic appraisal of their social adjustment; they are not good sources for assessing social functioning\(^1\)
## Impact of ADHD on Driving

### Frequency of Accidents and Violations for Teenage Drivers With ADHD Compared With Other Adolescents

<table>
<thead>
<tr>
<th>Times Greater than Adolescents without ADHD</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Automobile Accidents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 to 4 times</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associated Injuries</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3 times</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At Fault for Accidents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4 times</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speeding Tickets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 to 6 times</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspended Licenses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6 to 8 times</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Parent management strategies (driver education, restricting driving with teen passengers, limiting driving at night, close monitoring) should be enforced.
## Long Term Studies of ADHD: Periods On versus Off ADHD Medication and Motor Vehicle Accidents

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>ADHD: N</th>
<th>Age</th>
<th>Main Findings Tx vs UnTx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chang et al 2017*</td>
<td>USA</td>
<td>2,319,450</td>
<td>Mean 32.5 yrs</td>
<td>↓</td>
</tr>
<tr>
<td>Chang et al 2014*</td>
<td>Sweden</td>
<td>17,408</td>
<td>18 – 46 yrs</td>
<td>↓</td>
</tr>
</tbody>
</table>

* Included atomoxetine
ADHD and Sexual Behavior

• Ongoing Milwaukee follow-up study of boys with ADHD vs controls:
  • Sexual intercourse at earlier age (15 yrs vs 16 yrs)
  • More sexual partners (19 vs 7)
  • More pregnancies (38% vs 4%)
  • More sexually transmitted diseases (17% vs 4%)
New Diagnosis of ADHD in College Students

• Clinical interview with student and others
• Self-report questionnaires of ADHD and related symptomatology
• Behavioral questionnaires completed by parents (regarding childhood and current symptoms)
• Review of school records
• ± Psychoeducational testing (may be necessary for accommodations)
Educational Level of Adults with ADHD

% of Subjects

- Observed
- Expected

z = -7.98, p < 0.001

“To do good things is noble, to tell other people to do good things is nobler... and a lot easier.”

MARK TWAIN
Developing a Treatment Plan: Education and Support

- Educate about ADHD and the individual’s strengths and weaknesses
- Use local and online resources for education and support
- Aid in implementation of home, work, school, lifestyle accommodations (e.g., quiet work space, extra time for tests)
- Consider vocational assessment/career counseling
- Set reasonable expectations of pharmacologic and psychosocial treatment
How to Cope With ADHD in College

- Understand ADHD and accept the need to seek out help
- Seek accommodations such as extended time for tests, a scribe for note taking, writing/math tutoring centers
- Develop positive self-care habits (adequate sleep and nutrition, exercise, stress-management techniques)
- Create structure (regular study periods)
- Take a reduced load, especially during the first semester
- Make use of available study skills/time management classes and support groups
- Take medication regularly (not just as needed/PRN)
Attention-Deficit/Hyperactivity Disorder

Pharmacological Treatment

**Stimulants**
- Methylphenidate
- Amphetamines
- Atomoxetine

**Antihypertensives (+/- stimulants)**
- Guanfacine (XR)
- Clonidine (XR)

**Antidepressants**
- Bupropion
- Tricyclics

**Miscellaneous**
- Modafinil / Memantine
- Combined pharmacology

*FDA Approved*
Cognitive Therapy for Adult ADHD

• **Group** \(^{a}\): \(N = 88\); 12-week manualized meta-cognitive therapy group intervention designed to enhance time management, organization, and planning in adults with attention deficit hyperactivity disorder (ADHD).

  Treatment yielded significantly greater improvements in dimensional and categorical estimates of severity of ADHD symptoms compared with supportive therapy.

• **Individual** \(^{b}\): \(N = 86\) symptomatic adults with ADHD already being treated with medication. Subjects randomized to 12 individual sessions of CBT or relaxation with educational support.

  CBT resulted in improved ADHD symptoms, compared to relaxation with educational support. Improvement in ADHD symptoms maintained at 6 and 12 months.
Barriers to Adherence

• Poor adherence is the rule: only 20% continue meds at 1 year
• Forgetting to take medication, especially multiple doses
• Unreasonable expectations: medication helps, not curative
• Uncomfortable side effects or dislike of medication effects (e.g., emotional blunting)
• Denial: patients may not recognize the serious effects of ADHD
• Stigma: embarrassment, feeling “defective”

• Belief system: patients may feel that it is better to overcome problems without resorting to medication, or they just “don’t like the idea”
• Difficulty obtaining medication: cost or insurance problems
• Therapeutic alliance helpful
• Text-messaging helpful

Most Other Psychiatric Disorder Onset in Child & Young-Adult Years

Adapted from Burke et al. 2000, Archives of General Psychiatry; Wilens and Rosenbaum, JAACAP, 2013
High Rates of Psychiatric Disorders Exist in Young Men With ADHD

Cumulative Morbidity Risk of Disorder by Age 21

10-year Follow-Up of Males with ADHD (n=112) and Case Controls (n=105)
Mean Age at Follow-up: 22 years

- ADHD vs Control, p < .001
- *p = .004

Bar chart showing the cumulative morbidity risk of various disorders:
- Depression
- Bipolar
- OCD
- Tic disorders
- Oppositional
- Conduct

Mean Age at Follow-up: 22 years
10-Year Follow-Up Data:

N=140 boys with ADHD at entry;
N=82 subjects receiving stimulants [mean duration of 6 yrs]
N=30 not on stimulants
ADHD Increases the Risk for Substance Use Disorders:
(SUD) in Young Adults (10-Year Follow-up of ADHD)


Controls (N=417)

ADHD (N=361)
Figure 2.4 Past Month Illicit Drug Use among Persons Aged 12 or Older, by Age: 2008 and 2009

* Difference between this estimate and the 2009 estimate is statistically significant at the .05 level.
Executive Function Deficits in Mid-Adolescence Do Not Predict Substance Abuse 5 Years Later (N=412)


- Executive Function Deficits
- ADHD

More Likely to Use

<table>
<thead>
<tr>
<th>Condition</th>
<th>Executive Function Deficits</th>
<th>ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any SUD</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td>Alcohol Use Disorders</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Drug Use Disorders (ADHD +)</td>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>Drug Use Disorders (ADHD -)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Cigarette Smoking</td>
<td>0.5</td>
<td>3.5</td>
</tr>
</tbody>
</table>
HOWEVER, Cigarette Smoking is Related to the Development of Later Executive Function Deficits

Subjects With Current Executive Dysfunction

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control</strong></td>
<td>147</td>
<td>2</td>
</tr>
<tr>
<td><strong>ADHD</strong></td>
<td>88</td>
<td>2</td>
</tr>
<tr>
<td><strong>Control+Use</strong></td>
<td>9</td>
<td>22</td>
</tr>
<tr>
<td><strong>ADHD+Use</strong></td>
<td>14</td>
<td>29</td>
</tr>
</tbody>
</table>

Pairwise Comparisons:
- a p < 0.05 vs. Controls
- b p < 0.05 vs. ADHD
- c p < 0.05 vs. both ADHD and Use

Early ADHD Treatment Reduces Marijuana Use

10 Cohorts of Senior Years 2005 to 2014
(N=40,358; ca. 10% with ADHD)

- Population risk
- Stimulant use started prior to 9 years of age*
- Stimulant use started between 10-14 years*
P<0.001 vs controls
- Stimulant use started after 15 years of age**
P<0.001 vs controls

Past Year Use

20% 30% 40% 50% 60%
### Long Term Studies of ADHD: Stimulant Treated vs Untreated and Subsequent Substance Use Disorders

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Total: N</th>
<th>ADHD: N</th>
<th>Age</th>
<th>Main Findings Tx vs UnTx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinn et al. 2017</td>
<td>USA</td>
<td>146,000,000</td>
<td>2,993,887</td>
<td>15–42 yrs</td>
<td>Within group</td>
</tr>
<tr>
<td>Sundquist et al. 2015</td>
<td>Sweden</td>
<td>551,164</td>
<td>9,424</td>
<td>Mean 15 yrs</td>
<td>Between group</td>
</tr>
<tr>
<td>Chang et al. 2014</td>
<td>Sweden</td>
<td>38,753</td>
<td></td>
<td>8–46 yrs</td>
<td>Between group</td>
</tr>
<tr>
<td>Steinhausen et al. 2014</td>
<td>Denmark</td>
<td>20,742</td>
<td></td>
<td>11–20 yrs</td>
<td>Between &amp; Within groups</td>
</tr>
</tbody>
</table>
# Amphetamine in ADHD

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting Dose</th>
<th>Maximum Dose*</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adderall®</td>
<td>2.5–5 mg QD</td>
<td>1.5 mg/kg/day</td>
<td>6 hr / BID</td>
</tr>
<tr>
<td>Adderall XR®</td>
<td>2.5–5 mg QD</td>
<td>12 hr / QD</td>
<td></td>
</tr>
<tr>
<td>Vyvanse®</td>
<td>30 mg QD</td>
<td>12–14 hr / QD</td>
<td></td>
</tr>
<tr>
<td>Mydayis®</td>
<td>12.5 mg QD</td>
<td>50/25 mg (adults/adolescents)</td>
<td>To 16 hr/QD</td>
</tr>
<tr>
<td>Dexedrine Tablets®</td>
<td>2.5–5 mg BID</td>
<td>1.5 mg/kg/day</td>
<td>3–5 hr / BID–QID</td>
</tr>
<tr>
<td>Evekeo®</td>
<td>2.5–5 mg BID</td>
<td>3–5 hr / BID–QID</td>
<td></td>
</tr>
<tr>
<td>Dexedrine Spansule®</td>
<td>5 mg QD</td>
<td>6 hr / QD–BID</td>
<td></td>
</tr>
<tr>
<td>Dyanavel XR™ (suspension)</td>
<td>2.5–5 mg QD</td>
<td>1.5 mg/kg/day</td>
<td>12 hr / QD</td>
</tr>
<tr>
<td>Adzenys XR™ (disintegrating tab)</td>
<td>6.3–12.5 mg QD</td>
<td>12.5 mg (adolescents)</td>
<td>12 hr / QD</td>
</tr>
</tbody>
</table>

*May exceed FDA approved dose (e.g., > 20 to 30 mg/day).
# Methylphenidate in ADHD

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting Dose</th>
<th>Maximum Dose*</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritalin IR®</td>
<td>5 mg QD/BID</td>
<td>2 mg/kg/day</td>
<td>4 hr /BID</td>
</tr>
<tr>
<td>Focalin®</td>
<td>2.5 mg QD/BID</td>
<td>1 mg/kg/day</td>
<td>4–5 hr / BID–TID</td>
</tr>
<tr>
<td>Focalin XR®</td>
<td>5 mg QD</td>
<td>1 mg/kg/day</td>
<td>10–12 hr QD</td>
</tr>
<tr>
<td>Daytrana®</td>
<td>10 mg</td>
<td></td>
<td>6–16 hr</td>
</tr>
<tr>
<td>Concerta®</td>
<td>18 mg QD</td>
<td>2 mg/kg/day</td>
<td>12 hr / once</td>
</tr>
<tr>
<td>Metadate CD®</td>
<td>20 mg QD</td>
<td></td>
<td>8 hr / once</td>
</tr>
<tr>
<td>Ritalin LA®</td>
<td>20 mg QD</td>
<td></td>
<td>8 hr / once</td>
</tr>
<tr>
<td>Quillivant®</td>
<td>&lt;10 mg QD</td>
<td></td>
<td>12 hr /once</td>
</tr>
<tr>
<td>Quillichew™</td>
<td>&lt;10 mg QD</td>
<td></td>
<td>8 hr / once</td>
</tr>
<tr>
<td>Aptensio XR</td>
<td>10 mg QD</td>
<td></td>
<td>12 hr/once</td>
</tr>
<tr>
<td>Contempla XR</td>
<td>8.6 mg QD</td>
<td>51.8 mg</td>
<td>12 hr/once</td>
</tr>
<tr>
<td>(disintegrating tab)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jornay®</td>
<td>20 mg QD</td>
<td>100 mg</td>
<td>12 hr/once</td>
</tr>
<tr>
<td>Adhansia XR</td>
<td>25 mg QD</td>
<td>100 mg</td>
<td>Up to 16 hr/once</td>
</tr>
</tbody>
</table>
ADHD and Substance Use Disorder: Pharmacotherapy

- Treat through cannabis use/misuse
- Use disorder ➔ sequence treatment to address substance use, then restart ADHD treatment
- In refractory SUD cases ➔ Treat ADHD
- Nonstimulants
  - Atomoxetine
  - Guanfacine XR/Clonidine XR
  - Bupropion
- Stimulants (use extended release; avoid immediate release)
  - Methylphenidate (e.g., Concerta® and equivalent)
  - Amphetamine (e.g., Vyvanse®, add XR and equivalent)
Stimulant Misuse and Diversion
Stimulant Misuse and Diversion

• 10-20% prevalence of non medical use of stimulants
• 65-85% of stimulants diverted from “friends”
  • Majority *not* “scamming” local docs
  • Not seen as potentially dangerous
  • No ethical or moral issues: “Responsible misuse”
Rates of Substance Use Disorders are Higher in Boston-area College Students who Misuse Stimulants


Hazard Ratio (HR): 2.7; 95% Confidence Interval (CI): 1.7, 4.2; p<0.001
Reasons for Prescription Drug Misuse/Abuse in Teens & Young Adults

Teen/Young Adult’s Perception

• Not dangerous
• Not addictive (vs street drugs)
• No ethical or moral issues: “Responsible misuse”
• Less stigma
• Not illegal
• Worth money
• Available
• Easily shared with others: social
• Parents generally unaware
Stimulant Misuse and Diversion

• High rates of ADHD and neuropsychological dysfunction in stimulant misusers

• More misuse of immediate vs extended release stimulant preparations

• Almost one-third misuse stimulants intranasally

• Stimulant misuse linked to SUD and dysfunction in adulthood (16 years later)
Stimulants Mainly Misused for Focus/Energy in College Students


<table>
<thead>
<tr>
<th>Reasons for Using Stimulants Nonmedically</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>To help concentrate or focus better</td>
<td>77 (79%)</td>
</tr>
<tr>
<td>To stay awake</td>
<td>61 (62%)</td>
</tr>
<tr>
<td>To reduce distraction</td>
<td>55 (56%)</td>
</tr>
<tr>
<td>To get more energy</td>
<td>47 (48%)</td>
</tr>
<tr>
<td>To experiment – to see what it’s like</td>
<td>42 (42%)</td>
</tr>
<tr>
<td>To have a good time with my friends</td>
<td>22 (22%)</td>
</tr>
<tr>
<td>To feel good or get high</td>
<td>21 (21%)</td>
</tr>
<tr>
<td>To get through the day</td>
<td>12 (12%)</td>
</tr>
</tbody>
</table>
Things Practitioners Can Do to Curtail Prescription Drug Misuse

• Educate adolescents, young adults, and yourself about prescription drug abuse

• Communicate with your patient about the medical, psychological, addictive, legal issues of prescription drug abuse

• Safe storage (not in medicine cabinets)

• Confidentiality: “don’t advertise you are on stimulants”

• Don’t overprescribe quantity (e.g., stockpile)

• Safeguard—recommend to dispense of old medications, monitor active prescriptions (pain killers, stimulants, benzodiazepines)
Summary: Adolescents and Young Adults with ADHD

- Critical time for independence and development
- Strong neurobiological underpinnings suggesting continued brain development through adolescence into young adulthood—may be delayed in ADHD
- Work with youth to monitor their ADHD, activities (e.g., driving, relationships), study habits, cigarette and substance use
- Treatment should be maintained and encouraged on regular basis
- Monitor for stimulant misuse and diversion

*Rewarding time to see your patients grow and flourish!*