ADHD IN ADULTS
Objectives

• Apply evidence-based diagnostic techniques to the identification of adult ADHD

• Differentiate the spectrum of medications available for ADHD based on pharmacokinetic and clinical profiles

• Customize ADHD medication selection to the daily functional needs of the patients

• Integrate evidence-based nonpharmacological strategies into the overall treatment plan for patients with ADHD
PCPs and Psychiatric Presentations

• 65-80% of patients with mental health problems see the primary care physician for the first visit

• 45% remaining in treatment with the PCP

Institute of Medicine, 2003.
Undertreatment of Adult ADHD

• The 2012 or 2013 National Health and Wellness Survey (NHWS), U.S. study

• Of a total of 22,397 U.S. adults who participated in the survey, 465 self-reported a diagnosis of ADHD. ADHD-like symptoms were screened using the Adult Self-Report Scale version 1.1 (ASS-v1.1)

• In patients who self-reported an ADHD diagnosis, 62.6% reported not currently using a prescription medication to treat it

Prevalence Rates of Psychiatric Disorders in Adults

Kessler RC et al. JAMA. 2003 Jan 18;278(23):3095-105;
ADHD in Adults Age >50

• Adult ADHD Prevalence
  Longitudinal Aging Study Amsterdam (LASA)

• Prevalence of syndromic ADHD in adults: 2.8%

• Prevalence of symptomatic ADHD in adults: 4.2%

• Men and women reported similar levels of symptoms

Identification and Assessment of Late-Life ADHD in U.S. Memory Clinics

• ONLY 1 of 5 clinics reported screening regularly for ADHD

• 1/2 reported seeing ADHD patients
  – 60% reported contact with previously diagnosed ADHD patients

• ADHD symptomatology may not have been considered as pre-morbid baseline cognitive functioning

Canadian Guidelines on ADHD in Older Adults

• Recognizes ADHD in older adults
• Highlights importance in evaluation of cognitive complaints in older adults
• Medication and psychotherapies as treatments
• Consideration of medical illnesses/drug interactions when considering ADHD medication
• Consider two co-existing disorders (ADHD/MCI)

Canadian ADHD Resource Alliance (CADDRA); Canadian ADHD Practice Guidelines, 4th Ed. 2018; (www.caddra.ca) DW Goodman, MD contributor.
Diagnostic Issues
Diagnostic Difference in DSM-IV and DSM 5 for Adult ADHD

<table>
<thead>
<tr>
<th></th>
<th>DSM-IV</th>
<th>DSM 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max child age threshold for symptoms</td>
<td>&lt; 7</td>
<td>&lt;12</td>
</tr>
<tr>
<td>Age for adults</td>
<td>≥18 yo</td>
<td>≥17 yo</td>
</tr>
<tr>
<td>Symptom threshold count</td>
<td>≥6 in IA and/or HI</td>
<td>Child: ≥6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adult: ≥5</td>
</tr>
<tr>
<td>Category designation</td>
<td>Subtypes</td>
<td>Presentation</td>
</tr>
<tr>
<td>Research protocol exclusion</td>
<td></td>
<td>Autism spectrum disorder</td>
</tr>
</tbody>
</table>
Age of Diagnosis

- **Symptoms**: Increasing demands of Family, Work, Social
- **Impairments**: Intelligence, Compensatory Skills, Environmental Structure

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Child Diagnosis</th>
<th>Adult Diagnosis</th>
<th>Adult Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>12</td>
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<td></td>
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<tr>
<td>18</td>
<td></td>
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<tr>
<td>25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Impairment Sources

ADHD

- Executive Dysfunction
  - Performance Impairment

- Emotional dysregulation
  - Social Impairment
Adult ADHD and Comorbidities
National Comorbidity Survey Replication: Adult ADHD in Other Psychiatric Disorders

- Major Depression: ADHD 9.4%
- Chronic Dysthymia: ADHD 22.6%
- Bipolar Disorder: ADHD 21.2%

National Comorbidity Survey Replication: Adult ADHD in Other Psychiatric Disorders

Anxiety Disorder: ADHD 8.6%
Substance Abuse: ADHD 10.8%
???: ADHD ???%
Diagnostic History

Mood Disorders

Schizophrenia

Hallucinations/Delusions
Symptomatic Overlap: Not Distinguishing Features

ADHD

Executive Dysfunction

Bipolar

Emotion Dysregulation

David W. Goodman, MD
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Bipolar</th>
<th>ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hypomanic/manic symptoms of increased talkativeness, racing thoughts, distractibility, psychomotor agitation, increase risky behavior</td>
<td>Talks too much in social situations, difficulty maintaining attention and distractible, fidgety and restless, impulsivity</td>
</tr>
<tr>
<td>Impairments</td>
<td>Social/occupational distress or impairment be present</td>
<td>Impulsive risk-taking behavior and sleep disturbance</td>
</tr>
<tr>
<td>Not Diagnostic Criteria</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Emotion Dysregulation in ADHD

- Children 25-45% (7 studies)
- Adults 34-70% (5 studies)

Emotion Dysregulation

- Persistent ADHD  n=55  42-72%
- Remitted ADHD   n=80  23-45%

**Persisters have higher rates of emotion dysregulation compared to remitters**

Emotion Regulation:
ADHD vs. Bipolar Adults

• A total of 150 adults ADHD, 335 adults BD subjects, and 48 controls

• Assessed using the Affective Lability Scale (ALS) (emotion lability) and the Affect Intensity Measure (AIM) (emotion responsiveness)

• Retrospective study; Swiss study

• ASRS, WURS, DIVA 2.0, DIGS

Conclusions

• Using two self-reports, adult ADHD patients displayed emotional dysregulation with a higher mood lability and responsiveness similar to bipolar patients in comparison to controls.

• ADHD subjects essentially differ from bipolar subjects on the perceived emotional intensity, but not on emotional instability.

• Severity of ADHD was strongly correlated to AIM and ALS scores.

Case Presentation: Diagnostic Prioritization for Pharmacotherapy

Alcohol and substance abuse
Mood disorders
Bipolar and MDD
Anxiety disorders
Obsessive-compulsive disorder, generalized anxiety disorder, panic
ADHD

Order of treatment also considers the severity of the concurrent disorders.

“In our clinical experience, consistently with other authors, patients with ADHD-BD should be treated for BD first. Based on the current level of information, we do not recommend treatment of comorbid ADHD-BD with ADHD medications in the absence of mood stabilizers.”

Bipolar Disorder: Risk of Mania With Methylphenidate

- Swedish national registries
- 2307 bipolar adults, 2006-2014
- MPH with and without mood stabilizers
- Mania defined: hospitalization or new dispensation of stabilizing medication
- 0-3 months and 3-6 months after medication start following non-treated periods
# Bipolar Disorder: Risk of Mania With Methylphenidate

<table>
<thead>
<tr>
<th></th>
<th>HAZARD RATIO 0-3 months</th>
<th>3-6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPH without mood stabilizer</td>
<td>6.7 (95%CI=2.0-22.4)</td>
<td>similar</td>
</tr>
<tr>
<td>MPH with mood stabilizer</td>
<td>0.6 (95%CI=0.4-0.9)</td>
<td>similar</td>
</tr>
</tbody>
</table>

Diagnostic Overlap

- Intelligence
- Neuropsychological Diagnoses
- Executive Function
- Learning Disabilities
- Behavioral Diagnosis
Executive Function

- Response inhibition
- Working memory
- Set shifting
- Interference control

30-50% of ADHD patients have executive dysfunction vs. 5-10% in controls

Seidman LJ. Neuropsychological functioning in people with ADHD across the lifespan. Clinical Psychology Review 2006. 26;466-485.
EF Associated With Other Disorders

- ADHD (30-50% with EF)
- Bipolar Disorder
- Schizophrenia
- Major Depression
- Neurologic Disorders (TBI, MCI, CVA, CNS tumors, Degenerative)
- Genetic Disorder (Klinefelter’s, 47, XXY)
- Chronic SUD
- Learning Disorders
- Autism

General Population: 5-10% with EF
Can EF neuropsychological tests detect ADHD?

These studies have examined male and female youth, as well as adults, and found that most measures of EFs have good positive predictive power for ADHD (characterized by adequate sensitivity), but poor negative predictive power (poor specificity).

That is, abnormal scores on measures of EFs are generally predictive of the diagnosis; however, normal scores cannot rule out the diagnosis.

In well-controlled studies using batteries, stimulant-related cognitive enhancements were more prominent on tasks without an executive function component (complex reaction time, spatial recognition memory reaction time, and delayed matching-to-sample) than on tasks with an executive function component (inhibition, working memory, strategy formation, planning, and set-shifting).
Treatment Options and Medication
Treatment Options

• Diagnoses (what’s there, what’s not)
• Education (what this is, what it’s not)
• Environmental changes (academic, occupational, social, family)
• Psychopharm/Psychotherapies
  • Behavior, social, individual, family, couples
  • Support associations (www.CHADD.org)
# Methylphenidate Preparations

<table>
<thead>
<tr>
<th>Methylphenidate Formulation</th>
<th>Duration</th>
<th>Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic methylphenidate</td>
<td>2-3 hrs</td>
<td>tablet</td>
</tr>
<tr>
<td>Methylin liquid</td>
<td>2-3 hrs</td>
<td>liquid</td>
</tr>
<tr>
<td>MPH SR</td>
<td>4 hrs</td>
<td>wax matrix</td>
</tr>
<tr>
<td>MPH LA</td>
<td>8 hrs</td>
<td>beaded</td>
</tr>
<tr>
<td>OROS MPH</td>
<td>12 hrs</td>
<td>OROS</td>
</tr>
<tr>
<td>MPH ER</td>
<td>6-8 hrs</td>
<td>beaded</td>
</tr>
<tr>
<td>MPH CD</td>
<td>8 hrs</td>
<td>beaded</td>
</tr>
<tr>
<td>DexMPH XL</td>
<td>3 hrs</td>
<td>tablet</td>
</tr>
<tr>
<td></td>
<td>10 hrs</td>
<td>beaded</td>
</tr>
<tr>
<td>MPH ER liquid</td>
<td>12 hrs</td>
<td>liquid</td>
</tr>
<tr>
<td>MPH-ODT ER</td>
<td>12 hrs</td>
<td>dissolvable tab</td>
</tr>
<tr>
<td>MPH transdermal patch</td>
<td>12 hrs</td>
<td>patch</td>
</tr>
</tbody>
</table>
## Amphetamine Preparations

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liquadd</td>
<td>2-3 hrs liquid</td>
</tr>
<tr>
<td>Dextrostat</td>
<td>2-3 hrs tablet</td>
</tr>
<tr>
<td>Dextroamphetamine spanules</td>
<td>4 hrs tablet</td>
</tr>
<tr>
<td></td>
<td>6 hrs beaded</td>
</tr>
<tr>
<td>Amphetamine (racemic)</td>
<td>6 hrs tablet</td>
</tr>
<tr>
<td>Mixed AMPH salts XR</td>
<td>6 hrs tablet</td>
</tr>
<tr>
<td></td>
<td>Up to 12 hrs beaded</td>
</tr>
<tr>
<td>d-Amphetamine-ODT ER</td>
<td>12 Dissolvable tab</td>
</tr>
<tr>
<td>d-Amphetamine ER</td>
<td>12 liquid</td>
</tr>
<tr>
<td>Lisdexamfetamine</td>
<td>Up to 14 hrs prodrug</td>
</tr>
</tbody>
</table>
Non-Stimulants

• Atomoxetine approved for children/adolescents
• Guanfacine ER
• Clonidine ER

Off-label:
• Bupropion (positive controlled adult trials)
• Desipramine (positive adult trial)
• Modafinil (child study positive, adult study negative)
## FDA-Approved Medications for Adults With ADHD

<table>
<thead>
<tr>
<th>Medication</th>
<th>Child dosing</th>
<th>Adolescent dosing</th>
<th>Adult dosing</th>
<th>U.S. trials (adult)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atomoxetine</td>
<td>0.5 mg/kg (&lt;70kg) max 1.2 mg/kg (max 100 mg)</td>
<td>40 mg max 100 mg</td>
<td>120 mg</td>
<td></td>
</tr>
<tr>
<td>Dexmethylphenidate XR</td>
<td>5 mg max 20 mg</td>
<td>10 mg max 20 mg</td>
<td>40 mg</td>
<td></td>
</tr>
<tr>
<td>Lisdexamfetamine</td>
<td>30 mg max 70 mg</td>
<td>30 mg max 70 mg</td>
<td>70 mg</td>
<td></td>
</tr>
<tr>
<td>Mixed amphetamine salts XR</td>
<td>10 mg max 30 mg</td>
<td>20 mg max-none</td>
<td>60 mg</td>
<td></td>
</tr>
<tr>
<td>OROS Methylphenidate HCL</td>
<td>18 mg max 54 mg</td>
<td>18 mg max 72 mg</td>
<td>108 mg</td>
<td></td>
</tr>
</tbody>
</table>
# CYP450 Inhibitory Effects of ADHD Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>1A2</th>
<th>2C9</th>
<th>2C19</th>
<th>2D6</th>
<th>3A4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Atomoxetine</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0*</td>
<td>0</td>
</tr>
<tr>
<td>Bupropion</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>+++</td>
<td>?</td>
</tr>
<tr>
<td>Desipramine</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

MPH-Guanfacine XR in Adults

35 healthy adult

MPH-Guanfacine XR in Adults

35 healthy adult

Side Effects With Stimulant Medication

- Insomnia
- GI upset
- Decreased appetite
- Weight loss
- Headaches
- Dry mouth
- Constipation
- Hand tremors
- Jittery

- Research on individual stimulants has generally shown no dose relationship with side effects in group data\textsuperscript{1, 2}

- Some research has shown side effects may be more likely in stimulant naïve patients\textsuperscript{3}

\textsuperscript{1}Weisler RH et al. (2006), CNS Spectr 11(8):625-639; \textsuperscript{2}Adler L et al. (2005), Presented at the 158th Meeting of the American Psychiatric Association, May 21-25; \textsuperscript{3}Goodman DW et al. (2005), CNS Spectr 10(Suppl 20):26-34.
Safety Concerns
Medical Illness Considerations

• Hypertension
• Hypo- or Hyperthyroidism
• Diabetes Mellitus
• Cardiac: Post MI, post-stent placement, arrhythmias, electrical/structural abnormalities
• Seizure disorder
• Substance Use: caffeine, alcohol, illicit drugs
• Pregnancy
Congenital Abnormalities

- In the U.S., 3% of infants are born with a major birth defect
- Risk of congenital heart defects in general population: 8.2 per 1000 births

Cardiovascular Risk: Stimulants in Pregnancy

• Cohort study of the Medicaid-insured population in the United States nested in the 2000-2013 U.S. Medicaid Analytic eXtract

• Nordic Health Registries, 2003-2013 (Denmark, Finland, Iceland, Norway, and Sweden)

• Relative risks were estimated accounting for underlying psychiatric disorders and other potential confounders

Cardiovascular Risk: Stimulants in Pregnancy

In the US data, of the 1,813,894 pregnancies evaluated

Cardiovascular Risk: Stimulants in Pregnancy

Stimulant Pregnancy Risk

• Pregnancies exposed to amphetamine-dextroamphetamine (n=3331), methylphenidate (n=1515) monotherapy in early pregnancy were compared with 1,461,493 unexposed pregnancies. Among unexposed women, the risks of the outcomes were 3.7% for preeclampsia, 1.4% for placental abruption, 2.9% for small-for-gestational age, and 11.2% for preterm birth.

• The adjusted risk ratio for stimulant use was 1.29 for preeclampsia (95% CI 1.11-1.49), 1.13 for placental abruption (0.88-1.44), 0.91 for small-for-gestational age (0.77-1.07), and 1.06 for preterm birth (0.97-1.16).

• Compared with discontinuation (n=3,527), the adjusted risk ratio for continuation of stimulant use in the latter half of pregnancy (n=1,319) was 1.26 for preeclampsia (0.94-1.67), 1.08 for placental abruption (0.67-1.74), 1.37 for small-for-gestational age (0.97-1.93), and 1.30 for preterm birth (1.10-1.55).

Pregnancy and Stimulants

• Category C
  - Amphetamines, methylphenidates, atomoxetine
  - Animal reproduction studies have shown an adverse effect on the fetus. There are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks

Breastfeeding and Amphetamines

• Amphetamine
  • Detectable in breast milk
  • In infants’ urine

• Methylphenidate
  • Detectable in breast milk

• American Academy of Pediatrics considers amphetamines and methylphenidate a contraindication for breastfeeding

Psychotherapies
Psychotherapies for ADHD

- Education
  - Patients and family members
  - Books and websites
- Cognitive behavior therapy
  - Structure routines
  - Audio and visual cues
  - Consistent consequences for behavior
- Individual
  - Self-esteem issues
  - Social skills and relationship issues
  - Academic and occupational accommodations
When to Refer

• Presenting with symptoms of a major mental illness, serious mood disorder, substance dependence, or other complex comorbid psychiatric symptoms that are beyond your level of clinical competence and/or comfort level

• Confused about the patient’s presentation, unsure about ADHD, and uncomfortable about the idea of prescribing ADHD medication for this person

• Suspect drug-seeking behavior

• Patient not responding to medications or expresses sensitivity to drug side effects

• Treatment seems to require multiple psychiatric medications
Summary

✓ ADHD is highly prevalent in both children and adults - screen regardless of age
✓ Diagnostic accuracy is enhanced by considering:
  • Presenting symptoms
  • Age of onset
  • Longitudinal course: chronic, pervasive, impairing
  • Family psychiatric history
✓ Use symptom checklists for baseline target symptoms and change with treatment
✓ Look for psychiatric comorbidities and prioritize accordingly
✓ Education, behavioral changes, and cognitive therapies are effective