Adults with Attention Deficit Disorder

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Prevalence

- 3-5% of school age children (more prevalent in boys, much more so in clinical samples)
- Estimated 80% persist into early adulthood
- Estimated 30-60% into adulthood
- Hyperactivity typically resolves – inattention is chief complaint
- 1-5% prevalence in adults

Overview

- Differential Diagnosis
- Pathophysiology
- Assessment
- Treatment

Diagnostic Criteria & Considerations

- Developmentally inappropriate symptoms
- Minimum 6 month duration
- Symptoms occur in multiple settings
- Impairment in major life activities
- Symptom onset by age 7
- Exclusion of other disorders
- 6 of 9 inattention symptoms and/or 6 of 9 hyperactive impulsive symptoms
- Subtypes

Symptoms of ADHD

Inattention Symptoms	Hyperactive Impulsive Symptoms
• Inattention to detail	• Fidgets
• Sustaining attention	• Leaves seat inappropriately
• Listening	• Runs/climbs excessively
• Follow through on instructions	• Difficulty playing quietly
• Organizing activities	• "on the go"
• Avoids sustained mental effort	• Talks excessively
• Distractibility	• Blurts out answers
• Forgetful	• Difficulty awaiting turn
• Loses things	• Interrupts

Impulsivity in adulthood often have more serious adaptive consequences

- Low frustration tolerance
- Quitting jobs
- Ending relationships
- Driving too fast
- Poor control of temper

Symptoms Manifested Differently in Adults

- Difficulty Sustaining Attention
- Paralyzing Procrastination
- Slow, inefficient, disorganized
- Poor time management
- "Inner restlessness" (hyperactivity)
- Self-selects very active jobs
- Talks excessively
- Workaholic, overscheduled, overwhelmed

Similar symptoms are present in other disorders – differential diagnosis and co-morbidities

- Major Depression (9-35%)
- Bipolar Disorder (6-15%)
- Generalized Anxiety Disorder (25-40%)
- Substance Abuse (50% self-medicating?)
- Personality Disorders
- Non-psychiatric (neurological) disorders
- Fatigue/sleep disorders
- Most adults with attention problems do not have ADHD

Pathophysiology – Brain Imaging MRI, fMRI, PET

- Decreased volume and/or activity
  - ✓ Orbital-prefrontal cortex (r > l)
  - ✓ Basal ganglia (striatum and globus pallidus)
  - ✓ Cerebellum (central vermis, r > l)
  - ✓ Dorsal anterior cingulate cortex
- Neurotransmitter abnormality
  - ✓ Catecholamine hypothesis implicates dopaminergic and noradrenergic pathways, no single system is implicated

Genetics Continued

- Associated with
  - ✓ Dopamine transporter gene (DAT1) chromosome 5
  - ✓ D4 receptor gene (DRD4) chromosome 11
  - ✓ 30-40% over-activity of Dopamine transporter binding

Pathophysiology – Genetics

- Familial Aggregation
- 25-35% of siblings
- 33% of fraternal twins
- 78-92% of identical twins
- 15-20% of mothers, 20-30% of fathers
- If parent is ADHD, 20-54% of offspring
- Correlation with maternal prenatal smoking, alcohol, drugs, and low birth weight

Challenges in Diagnosis of Attention Problems in Adults

- Non-specificity of symptoms
- Reliance on subjective report (symptoms not objectively verifiable)
- Unreliability of retrospective recall of symptoms – important related to criteria of childhood onset
- High rates of self-diagnosis (33-50% who believe they have ADHD actually meet criteria)
- Diagnosed in family member and retrofit onto themselves
- Response to stimulants cannot be used to diagnose ADHD

Diagnosis of ADHD in Adults

- Thorough history should elicit consistent pattern of symptoms dating back to childhood
- If available - collateral confirmation from parents to document behaviors during childhood (caveat about retrospective recall)
- Spouse or other significant person in patient's life important because patient may lack awareness of their symptoms
- Recent onset without evidence of symptoms during childhood challenges dx of ADHD

- Neuropsychological, brain imaging and pharmacological studies implicate frontal-subcortical systems (mediated by catecholamine systems) as the underlying pathophysiology in ADHD
- Central feature in adults is disinhibition
  - ✓ Patients unable to stop from responding, deficits in monitoring their own behavior)

Diagnosis of ADHD

- Symptom Rating Scales (self and other)
  - ✓ Easy to use, collateral forms, normed, but not diagnostic by themselves.
  - ✓ Conners Adult ADHD Rating Scale
  - ✓ Wender Utah Rating Scale
  - ✓ Adult ADHD Self-Report Scale
  - ✓ Brown Adult Attention Deficit Disorder Scale
  - ✓ Barkley Current Symptoms Scale
- Objective neuropsychological tests
  - ✓ Tests of sustained attention, response inhibition, executive function

Components of Neuropsychological Examination

- Not specific for ADHD but can provide objective evaluation of functions implicated in ADHD (executive function, response inhibition, sustained concentration-vigilance)
- Not diagnostic – requires convergence of history and symptoms, and consideration of other possible etiologies
- Simple mental status tasks (digit span, serial sevens not sensitive)

Neuropsychological Measures

- Continuous Performance Test
  - ✓ Sustained concentration, vigilance, response consistency
- Wisconsin Card Sorting Test
  - ✓ Perseveration, distractibility
- Stroop Word Color Association Test
  - ✓ Response inhibition
  - ✓ Red, red, red
- Working Memory Tests
  - ✓ Letter Number Sequencing

Social, Personal, Economic Impact

- Decreased educational achievement leads to reduced vocational options
- Persistent symptoms disrupt job performance, frequent termination, impulsive quitting
- Difficulty maintaining relationships

Importance of careful diagnosis (co-morbidities) in selection of appropriate pharmacotherapy

Daily Function Implications of ADHD

- 32-40% drop out of HS, 5-10% complete college, not up to potential
- Lower SES
- Increased absenteeism and tardiness
- Inadequate work performance, inefficient, takes longer
- Acts before considering consequences
- Poor driving – increased incidence of accidents
- Risk taking – 4x accidental injury, > ER visits
- 10x unwanted pregnancy, 4x STDs

Treatment

- I: Psychosocial Strategies
- II: Biological (medication) Strategies

I: Psychosocial Strategies

- **A. Education about their condition.**
- **B. Behavioral Change and Providing Structure.**

Behavioral Changes and Providing Structure

- **Wilens and Mcdermot[1,2] acronym, SPEAR to aid with impulsivity:**

S – stop
P – pull-back
E – evaluate
A – act
R – reassess

- **Individual CBT referral – targeting executive self management tools; Marital Therapy as needed**
- **Daily lists and reminders, especially personal digital assistants (PDA's)[3]**
- **Develop routines: early to work, breaking tasks into manageable parts[4]**
- **Organization "A place for everything… and everything in its place."[2]**
- **Enlist a family member to remind important dates/events[3]**

Education

- **Recognition that ADHD is a problem that something can be done about.[3]**
- **Reading Materials and Support Groups: www.CHADD.org. (Children & Adults w/Attention Def/Hyp. Disorder)**

II: Biological (medication) Strategies

A. FDA Indicated Medications
- **i. Stimulants**
  - **a. Methylphenidate based**
  - **b. Dextroamphetamine/amphetamine salt preparations**
- **ii. Non-stimulant (Atomoxetine)**

B. Off label Medication Interventions
- **i. Antidepressants**
- **ii. Modafinil**

Stimulants: Methylphenidate

- Variations include:
  - ✓ Ritalin (SR/LA)
  - ✓ Methylin (ER)
  - ✓ Metadate (ER/CD)
  - ✓ Concerta
  - ✓ Focalin (XR)
  - ✓ Daytrana (Methylphenidate Transdermal System)

Stimulants: D-Amphetamine

- Variations include:
  - ✓ Adderall (XR)
  - ✓ Dexedrine (ER)
  - ✓ Vyvanse (dextroamphetamine prodrug, requires 1st pass metabolism – essentially makes it an ER formulation, potential benefit when concerned about substance abuse)

Stimulants: Methylphenidate (cont'd)

- Example dosing:
  - ✓ Methylphenidate/Ritalin:
    - Can initiate once or twice daily 5 - 10 mg total
    - 20 - 80 mg daily max total
    - ~3-4hr duration
    - Concerta ~10 - 12hr duration, initiate at 18 – 26 mg daily, weekly increases with max dose of 72 mg

Stimulants: D-Amphetamine (cont'd)

- Example dosing:
  - ✓ Adderall/D-amphetamine salts:
    - Initiate 5 – 10 mg once daily or divided
    - Typical doses 20-40 mg, occasionally higher
    - ~5hr duration.[8]
  - ✓ Adderall XR:
    - Initiate as above as single dose
    - If transition from immed. release dose is 1:1
    - ~9 -12hr duration.[8]
    - Vyvanse ~8hr duration[7], starting dose 30mg, max 70mg, increase 10-20mg weekly

Stimulant Considerations

- Contraindications include[5,6]:
  - ✓ Advanced arteriosclerosis, symptomatic heart dz, mod/sev hypertension, hyperthyroidism, known sensitivity, glaucoma, recent MAOI, *h/o substance abuse, anxiety*.
- Adverse effects[5,6]:
  - ✓ High abuse potential – extended release forms considered to have less abuse potential.[9]
  - ✓ Risk of sudden death, stroke, and heart attack in patients with pre-existing heart conditions and risk of seizures in patients with a history of seizures.
  - ✓ Decrease appetite in some people, leading to weight loss. Insomnia/HA common, potentially time limited. Changes in vision (blurring/accommodation difficulties) have been reported.
  - ✓ Psychiatric adverse effects: bipolar switching, psychosis, agitation.

Stimulant Considerations

- **Prescription Issues:**
  - ✓ **Schedule II = written script required, no refills, no post-dating, but up to 90 days worth of medication is acceptable unless otherwise specified by the prescriber's state medical board, e.g. "do not fill until.."**
  - ✓ **Consider UDS prior and periodically during treatment.**

Stimulant Considerations

- **Prolonged use:**
  - ✓ Cardiovascular effects of *long-term* (24 month study) MAS XR (Adderall XR ≤60 mg/day) were minimal in otherwise healthy adults with ADHD. Nevertheless, vital signs should be monitored prior to and during treatment with any stimulant.
  - ✓ *Small number of cases with borderline blood pressure or pulse measures at baseline who experienced clinically significant increases in such values with MAS XR therapy highlights the importance of evaluating blood pressure and pulse at baseline and periodically during therapy so treatment regimen can be adjusted in a timely manner.* [11]
  - ✓ Tolerance, extreme psychological dependence can occur. Abrupt cessation can result in extreme fatigue and mental depression. Chronic abuse of amphetamines can result in the manifestation of amphetamine psychosis. [5,6]

Screening for Cardiac Risk[9]

- Medical History, including:
  - Personal, congenital, or acquired cardiac disease history
  - Family history of, or premature, cardiac disease (<30years of age)
  - History of palpitations, chest pain, syncope, seizures, post-exercise symptoms
  - Medication history (including OTC formulations)
- Screening Physical Exam
  - Monitor BP and pulse pre- and post-treatment
  - No established guidelines for work-up
  - Many adults get routine baseline EKGs
  - Careful attention to baseline pulse and BP
- Subspecialty evaluation for:
  - Suspicion of cardiovascular defect (eg, idiopathic hypertrophic sub aortic stenosis)
  - Individual or family history suggesting elevated risk

Non-Stimulant: Atomoxetine[10]

- "Strattera" is an FDA approved norepinephrine reuptake inhibitor.
- Shown to be effective for inattention as well as impulsivity.
- Initiate at 20 - 40 mg dose, can be increased no sooner than 3 days to 80 mg in either single or divided doses, in 2 - 4 weeks can target max 100-120 mg daily.
- Peak plasma levels 2 hr, half life 5hr, CYP 2D6 (i.e., interactions with antidepressants, etc.)

Off Label Medication Strategies

- Antidepressants with Norepinephrine effects:
  1. Bupropion (Wellbutrin SR/XL)
  2. TCA's (desipramine, imipramine, nortryptiline)
  3. SNRI's (Venlafaxine/ Effexor XR/ Cymbalta).
  4. MAOI's anyone? (Parnate)

Atomoxetine Considerations

- For patients reluctant to consider controlled substances.
- Contraindication to stimulant trials - substance abuse concerns, significant cardiac hx, etc.
- Side-effect profile of atomoxetine is not very different than it is with psychostimulants. Dry mouth, HA, Insomnia, N, constipation, decr appetite, urinary hesitancy and sexual side effects most common adverse events.
- Atomoxetine has a black box warning for suicidal ideation in children and adolescents.
- Atomoxetine can be used alone or in combination with other effective medications, although there is little empirical evidence to guide combined medication treatment.

Off Label Medication Strategies

- Modafinil/Provigil
  - ✓ An atypical Schedule IV stimulant approved for narcolepsy and disorders of arousal, was studied extensively in children with ADHD. However, despite solid efficacy data in clinical trials,[11] there were questions about whether a drug rash that was seen in several cases might indicate increased risk for Stevens-Johnson syndrome. Consequently, further study was recommended.
  - ✓ Can initiate at 100mg daily, titrate to 200-300mg once daily over a few weeks or slower.
  - ✓ Be aware of interactions, common and catastrophic SE's (SJS). *Lexicomp or Micromedex* are good resources for researching interactions.

Off Label Considerations

- Comorbid depression/anxiety symptoms.
- Substance abuse/diversion concerns.
- Poor response or inability to tolerate Stimulants or Atomoxetine.

Sample Case 2

- 49 y.o. man saw a television special on Adult ADHD and presents to his physician to report he has been experiencing several symptoms. He reports disorganization, inattentiveness both at work and at home to a level affecting his job and his relationships. He also cites frequently locking his keys in his car. He does not recall childhood symptoms and was a good student. He has difficulty spelling 'world' in reverse order and with serial 7's.

Sample Case 1

- 24 y.o. man c/o poor attention, distractibility, feelings of restlessness. He endorses 7 inattentive and 9 hyperactive, impulsive ADHD symptoms during childhood. Though a bright student, received average grades and was frequently sent to principal for misbehavior. No college, did well with activity/structure of military. Recently honorably discharged, now attending community college. Current impairment noted with 6 inattentive and 3 hyperactive, impulsive symptoms.

Psychiatric Differential/Comorbidities

- Developmental Disorders (MR, learning d/o)[9]
- Major Depression – *distinguished by* enduring dysphoric mood/anhedonia/sleep/appetite disturbance.[4]
- Bipolar Disorder – enduring dysphoric/euphoric mood, lack of need for sleep, delusions. [4]
- Generalized Anxiety – exaggerated apprehension and worry; somatic symptoms of anxiety. [4]
- Substance abuse/dependence – social consequences, physiologic/psychologic tolerance and withdrawal. [4]
- Personality Disorders (esp. borderline/antisocial) – repeated self injurious behavior/arrest history – lack of recognition that behavior is self defeating. [4]

Medical Mimics[9]

- Medical Disorders (chronic disease, hearing impairment, sleep disorder)
- Medications (steroids, anticonvulsants, antihistamines, caffeine, nicotine, sedatives, analgesics)
- Neurologic disorder (brain injury, seizures)
- Endocrine/metabolic/genetic disorders (obesity, metabolic syndrome, thyroid dz)

Sample Case 2 cont'd

- No evidence of coexisting psychopathology.
- Neuropsych testing validated concerns: his memory was indeed poor.
- Physical exam revealed swollen lymph glands and leukoplakia.
- Further testing (Serum, CSF, Imaging) revealed HIV encephalopathy, thus symptoms of ADHD turned out to be AIDS encephalopathy.

Sample Case 1 cont'd

- No evidence of coexisting psychopathology or medical etiology.
- Diagnosed with Adult ADHD, combined type in partial remission vs. inattentive type.
- Initiated on once-a-day stimulant, titrated and optimized over several weeks.
- Academic function improved, eventually transferred to 4 year university.

Useful Online Resource

- http://www.cnsspectrums.com/

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