Attention Deficit/Hyperactivity Disorder: Latest in Recommendations for Children and Adults

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Disclosures

- Speaker Bureau:
  - Sanofi-Pasteur, Abbott, Merck, Pfizer
- Consultant:
  - Sanofi, Merck, Pfizer, Arbor

Objectives

- Upon completion of this lecture, the participant will able to:
  1. Discuss statistics pertaining to ADHD
  2. Identify diagnostic criteria for ADHD
  3. Review latest pharmacologic treatment options for adults and children with ADHD

From a Clinician's Perspective

- The number of children, adolescents and adults with mental health issues is increasing
- The severity of the mental health illnesses appear to be increasing
- There is a severe shortage of psychologists, social workers, psychiatrists, nurses and nurse practitioners who specialize in children
- Many primary care providers are uncomfortable with the treatment of mental health issues, particularly ADD/ADHD
- Budget cuts within schools are severely impacting services and staff

Unable to Keep Up With Demands

- The healthcare system and the educational system is not keeping up with the mental health needs of our children
  - 6 – 9 million youth will go without services for his/her mental health needs
  - 1 in 4 of these children is at risk for school drop out due to unmet needs
- The demands today are ever evolving and are different than they were just 10 – 20 years ago
  - More children are living in single parent homes
  - More drugs are being abused
  - Pressures of society are different for children today
  - Bullying continues to occur but now, in more public and vast ways

The Tragedy….

- 1 in 5 children has a mental health issue
- Only 1 in 3 children is getting comprehensive care

Magnitude of the Childhood Mental Illness

- **Attention Deficit Hyperactivity Disorder** (ADHD)
  - 3 and 5 percent of children have ADHD
  - Approximately 2 million children in the United States
- **Autism Spectrum Disorder**
  - 3.4 of every 1,000 children 3-10 years old had autism
- **Bipolar Disorder**,
  - About 5.7 million American adults or about 2.6 percent of the population
- **Conduct disorder**
  - 1 to 4 percent of 9- to 17-year-olds
- **Depression**
  - 1 in every 10 children and adolescents are affected by serious emotional disturbances.
- **Eating Disorders**

http://www.aacap.org/cs/root/resources_for_families/child_and_adolescent_mental_illness_statistics accessed 02-01-2011

Magnitude of the Childhood Mental Illness

- **Oppositional Defiant Disorder**
  - 1 to 6 percent of the school-age population is affected
- **Post-Traumatic Stress Disorder**
  - Each year, 5.2 million Americans (including children and adolescents) suffer from PTSD
- **Risk-Taking Behavior**
  - 72% of all deaths among 10-24 year-olds result from four causes: motor-vehicle crashes, other unintentional injuries, homicide, and suicide
- **Schizophrenia**
  - It affects about 1% of Americans. usually appear in males during their late teens and early 20s and in females in their mid-20s to early 30s
- **Suicide**
  - Third leading cause of death for 15-to-24-year-olds, among this age group, suicide accounts for 12.3% of all deaths.

http://www.aacap.org/cs/root/resources_for_families/child_and_adolescent_mental_illness_statistics accessed 02-01-2011

"Attention Deficit Hyperactivity Disorder is the most common chronic psychiatric disorder in childhood that presents to primary care providers….."

http://www.addrc.org/the-multimodal-treatment-of-adhd-study-mtaquestions-and-answers/ accessed 02-02-2011

Smaller Frontal Lobe: Disruption in Frontal Lobe Function

- CEO of the brain
  - Inhibiting
  - Organizing
  - Prioritizing
  - Shifting or Stopping
  - Sustaining
  - Strategizing

Although We Often Think of It As A Childhood Disorder, Don't Forget…

- For many – it is a lifespan disorder characterized by multiple behavioral, cognitive and emotional implications that affect relationships and impair academic and occupational functioning

Prevalence

- 3 – 17 % of children and adolescents are affected by ADHD[1]
  - 22 percent increase in number of 4 – 17 year old with ADHD symptoms[2]
- In 2007, 5.4 million children have received diagnosis of ADHD from healthcare provider[2]
  - Up from 4.4 million in 2003[2]
- Typical age of onset of symptoms
  - 3 years of age

[1]Rappley MD: Attention deficit-hyperactivity disorder. N Eng J Med; 2005;352(2):165-72.
[2]http://www.medscape.com/viewarticle/735440 accessed 02-18-2011

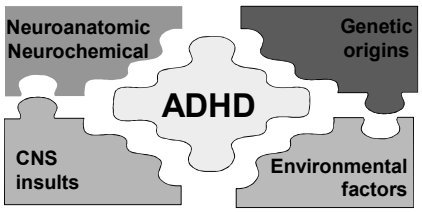
Prevalence

- Mean age of onset
  - 8 – 9 years of age
  - More common in males: 3:1 ratio
- Adulthood
  - Approximately, 60% persist into adulthood

[1]Rappley MD: Attention deficit-hyperactivity disorder. N Eng J Med; 2005;352(2):165-72.
[2]http://www.medscape.com/viewarticle/735440 accessed 02-18-2011

Etiology

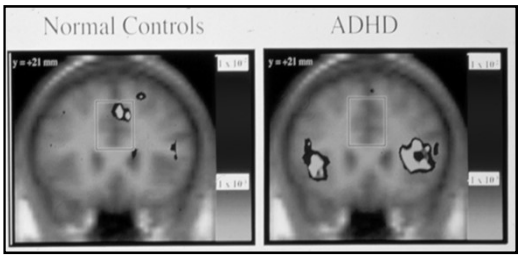
ADHD is a behavioral disorder with multiple possible etiologies



Pathophysiology

- MRI images of the brain of individuals with ADHD show smaller frontal areas (right side); basal ganglia and cerebellar vermis

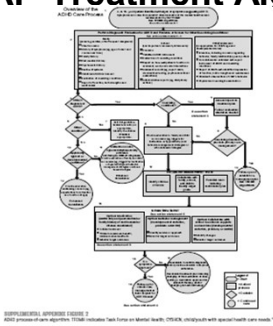
fMRI in Adults with ADHD



MGH-NMR Center & Harvard- MIT CITP

Bush G, et al. *Biol Psychiatry*. 1999;45(12):1542-1552

AAP Treatment Algorithm



http://pediatrics.aappublications.org/content/suppl/2011/10/11/peds.2011-2654.DC1/zpe611117822p.pdf accessed 01-20-2014

Remember….

- 67% of children diagnosed with ADHD have other psychiatric diagnoses

Moser, SE, Bober JF: Behavioral problems in children and Adolescents. In: Rakel RD, ed. Textbook of Family Practice. 6th ed. Philadelphia, PA: WB Saunders Company, 2002;641-44.

Coexistent Conditions

- Conduct disorders
- Learning disabilities
- Anxiety disorder
- Speech/language disorder
- Mood disorder
- Oppositional defiant disorder

Standardized Rating Scales

- Barkley ADHD Behavior Checklist
- Brown Attention Deficit Disorder Scale
- Preschool:
  - The Early Childhood Attention Deficit Disorder Evaluation Scale

Rating Scales Based on Age

- Elementary School
  - Conners Parent and Teacher Rating Scales (CPRS and CTRS)
- Adolescent
  - Conners/Wells Adolescent Self Report of Symptoms (CAAS)
- Adults
  - Conners Adult Attention-Deficit Rating Scale (CAARS)
- Children/Adolescents
  - Vanderbilt Rating Scale
  - http://www.ncfahp.org/Data/Sites/1/media/images/pdf/CHIP-Vanderbilt-parent.pdf
  - Also hints at other mental health issues i.e. Anxiety, conduct

One Such Scale

Figure 2-1: SNAP-IV (DSM-IV ADHD Symptom Checklist)

Child's name_____Date___/___/___

Filled out by:_____Relationship:_____

Please check for each behavior whether it describes this child not at all, just a little, quite a bit, or very much in comparison to normal children of the same age and intelligence.

Behaviors	Not at All	Just a Little	Quite a Bit	Very Much
1. Often neglects details or makes careless mistakes in schoolwork or tasks				
2. Often has difficulty sustaining attention in tasks or play				
3. Often does not seem to listen when spoken to				
4. Often does not follow through on instructions; fails to finish schoolwork, chores, or duties				
5. Often has difficulty organizing tasks and activities				
6. Often avoids, dislikes, or engages reluctantly in tasks that require sustained mental effort				
7. Often loses things necessary for tasks/activities				
8. Often easily distracted by outside stimuli				
9. Often forgetful in daily activities				
10. Often fidgets with hands or feet, or squirms				
11. Often leaves seat in situations in which remaining seated is expected				
12. Often runs or climbs excessively in situations where not appropriate (or for adolescents/adults, feels restless)				

SNAP –IV

Figure 2-1: SNAP-IV (DSM-IV ADHD Symptom Checklist) *(continued)*

Behaviors	Not at All	Just a Little	Quite a Bit	Very Much
13. Often has difficulty playing or engaging in leisure activities quietly				
14. Often 'on the go' or acts as if 'driven by a motor'				
15. Often talks excessively				
16. Often blurts out answers before questions are completed				
17. Often has difficulty waiting for a turn				
18. Often interrupts or intrudes on others (conversations, games)				

When did these behaviors first start?

Adapted with permission from James M. Swanson, PhD, previously appeared in: Swanson JM: *School-Based Assessments and Interventions for ADD Students*. Irvine, CA, KC Publishing, 1992.

Laboratory Evaluation

- CBC and Ferritin
  - Rule out anemia
- Lead
  - Screening
- TSH
  - as indicated
- Other labs
  - as indicated by history and physical examination (Lyme)
- Consider sleep apnea and pediatric hypoventilation syndrome

Neuropsych Testing

- Can be very beneficial to diagnosing ADHD
- Also helps with diagnosis of comorbidities
- Referral to neuropsychologist may be warranted
- Schools are often overwhelmed and testing can be delayed

American Academy of Pediatrics

- Guidelines
  - Evaluate children (6 – 12 years of age) who exhibit the following:
    - Inattention
    - Hyperactivity
    - Impulsivity
    - Behavioral problems
    - Academic underachievement

American Academy of Pediatrics

- Guidelines
  - Utilize the DSM-V criteria
  - Obtain evidence from parents, teachers, caregivers
    - School setting, home, social situation
  - Rule-out coexisting conditions
  - Additional diagnostic tests should only be conducted if the history and physical examination warrants

http://pediatrics.aappublications.org/content/suppl/2011/10/11/peds.2011-2654.DC1/zpe611117822p.pdf accessed 01-20-2014

Three Classifications

- Inattentive
- Hyperactive-impulsive
- Combined

http://pediatrics.aappublications.org/content/suppl/2011/10/11/peds.2011-2654.DC1/zpe611117822p.pdf accessed 01-20-2014

Diagnostic Criteria

- Symptoms of inattention OR impulsivity/hyperactivity OR BOTH
  - Which have persisted for 6 months
  - Are more frequent and severe than that which is typical for the individuals level of development
  - Onset must be prior to 12 years of age
  - Cause impairment in 2 or more settings
    - social, academic, or occupational functioning
  - Are not caused by another mental disorder

http://www.dsm5.org/Documents/ADHD%20Fact%20Sheet.pdf accessed 01-20-2014

Inattentive Disorder

- 5 or more of the following:
  - Often fails to give close attention to details or makes careless mistakes
  - Often has difficulty sustaining attention
  - Often does not seem to listen when spoken to
  - Often does not follow instructions or fails to finish work/chores
- 5 or more of the following (continued)
  - Often has difficulty organizing tasks
  - Often avoids or is reluctant to do things which require sustained mental effort
  - Often loses things necessary for tasks
  - Often easily distracted by extraneous stimuli
  - Often forgetful in daily activities

Hyperactivity
(5 OR MORE OF THE FOLLOWING)

- Often fidgets with hands or feet or squirms
- Often leaves seat or gets up in situations where seating is expected
- Often runs around or climbs excessively in situations in which this is inappropriate
  - (adults and adolescents – feelings of restlessness)
- Blurts out answers before questions are complete
- Often talks excessively
- Often "on the go" or often acts as if "driven by a motor"
- Often has difficulty playing or engaging in leisure activities quietly
- Difficulty waiting turn
- Interrupts or intrudes on others

DSM-V

- DSM-V:
  - Important difference from DSM-IV:
  - Symptoms must be present prior to age 12 years, compared to 7 years as the age of onset in DSM-IV

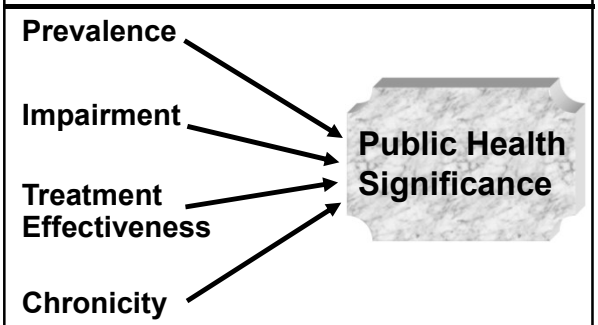
Differential Diagnosis

- Age appropriate high activity level
- Thyroid disorders
- Absence seizures
- Sensory deficits
- Tourette's syndrome
- Sleep disorders
- Asperger's or autism
- Psychosis
- Substance abuse
- Lead exposure
- Visual or hearing defects
- Anxiety or Depressive disorders
- Lyme disease

Treatment Options

Why Treat ADHD??

ADHD IS A Serious Public Health Concern?



ADHD Affects The Future

- Despite similar educational levels and IQ scores, individuals with ADHD (not taking medication) display
  - significantly more academic problems in school (25% repeat a grade)
  - trends toward lower occupational attainment

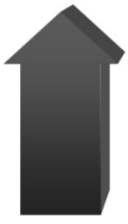
Seidman et al. *Biol Psychiatry* 1998;44:260
Biederman et al. *Am J Psychiatry* 1993;150:1792.

Social Impact of ADHD

- Social issues
  - Difficulty establishing and maintaining peer relationships
  - Significant amount of peer rejection
  - Peer rejection creates a vicious circle
    - Feelings of despair
    - Delinquency
    - Maladjustment
    - Low self-esteem
    - High school and college drop-outs increase
    - Increase in substance abuse
    - Increase in MVA's

Important Considerations: Impact on Family

Parents of children with ADHD experience higher levels of



- Stress
- Self-blame
- Social isolation
- Depression
- Marital discord

Mash and Johnston. *J Clin Child Psychol* 1990;19:313.
Murphy and Barkley. *Am J Orthopsychiatry* 1996;66:93.

Multiple Therapies Work Best

- Considered to be the mainstay of treatment for individuals with ADHD
- Should be combined with behavioral/cognitive therapies

One Proposed Treatment Algorithm

- Inattentive ADHD
  - Low dose stimulants
  - Antidepressants
  - Organizational training
- Hyperactive ADHD
  - Higher dose stimulants
  - Behavioral therapies
  - Other medications used as an adjunct
- Combined-Type ADHD
  - Combination treatments

Adapted from: Arnold, L.E. 2nd edition. 2002. *Contemporary Diagnosis and Management of Attention-Deficit/Hyperactivity Disorder*. Handbooks in Healthcare; Newtown, PA.

First Line Medications

- Numerous guidelines have listed the psychostimulants as first line pharmacotherapy for the individual with ADHD
- Psychostimulants
  - Methylphenidate
  - Amphetamine preparations

Prior to Initiating Treatment

- Needs comprehensive history and PE, aimed at identifying cardiac anomalies, abnormalities, dysrhythmias
- Ask about any family history of cardiac surgeries or family history of sudden cardiac death
- No need for ECG or echo

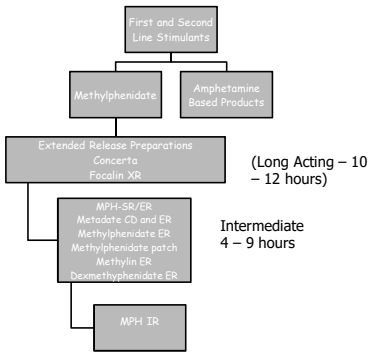
http://pediatrics.aappublications.org/content/suppl/2011/10/11/peds.2011-2654.DC1/zpe611117822p.pdf accessed 01-20-2014

2017 AAP Guidelines on Management of ADHD

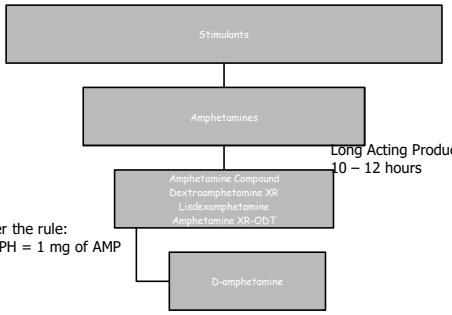
- For preschool-aged children (4–5 years of age), the primary care clinician should prescribe evidence-based parent- and/or teacher-administered behavior therapy as the first line of treatment and….
- May prescribe methylphenidate (a medication to treat ADHD) if the behavior therapy does not provide significant improvement and the child continues to have moderate to severe symptoms

https://www.cdc.gov/ncbddd/adhd/guidelines.html accessed 01-04-2018

Medication Options



Additional Stimulants



Long Acting Products:
10 – 12 hours

Remember the rule:
2mg of MPH = 1 mg of AMP

46

Short Acting Immediate Release Stimulants

- Methylphenidate (Ritalin, Methylin)
- Dexmethylphenidate (Focalin)
- Dextroamphetamine (Adderall)
- Dextroamphetamine (Dexedrine, ProCentra, Zenzedi)
- Amphetamine (Evekeo)

In the past, these were often first line medications
Now….given the newer, long-acting agents, these are used less frequently

Wright, 2018 47

Mechanism of Action

- Increase synaptic levels of dopamine and norepinephrine
- Numerous studies cite efficacy
  - Improvement in disruptive behaviors
  - Improved academic functioning

Wright, 2018 48

Disadvantages

- Frequent administration
  - Bid – tid dosing is the norm
  - Requires school time administration
  - Patient often feels levels fall and rise
  - Potential for abuse

Long-Acting Stimulant Agents

- Methylphenidate
  - Concerta
  - Metadate CD
  - Ritalin LA
  - Focalin XR
  - Daytrana
  - Methylin ER
  - Aptensio XR
  - Quillichew ER
  - Cotempla XR-ODT
- Amphetamine
  - Dextroamphetamine (Adderall XR, Mydayis)
  - Lisdexamfetamine (Vyvanse)
  - Amphetamine (Dyanavel XR)

Newer ADHD Treatment

- Single entity amphetamine product (Mydayis)
  - Three different types of coated beads
  - Released at separate intervals
  - Duration of symptom control (16 hours)
  - 13 years of age and older
  - 12.5 or 25 mg once daily dosage
- Once daily extended release ODT formulation of methylphenidate (Contempla XR-ODT)
  - Ages 6 – 17 years
  - 12 hour of symptom control
  - 8.6 mg, 17.3 mg, and 25.9 mg strengths

New ADHD Agents/Approvals

- Lisdexamfetamine (Vyvanse)
  - Ages 6 years and older
  - Available in a chewable tablet
  - 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, and 60 mg

Stimulant Dosing: Pediatric

Medication	Starting Dose	Maximum Dose Range	Duration/ Dosing
Short acting:			
MPH (IR) (Ritalin, Methylin®)	5 mg qd or 5 mg bid	0.8 -2.0 mg/kg/day	3 to 5 h BID-TID
Intermediate acting: (Ritalin SR, Metadate ER,)	10-20 mg	60 mg/day	QD-BID
Long-acting:			
Metadate CD	20 mg QD	60 mg/day	QD - BID
OROS® MPH (Concerta™)	18 mg qd	18 mg - 54 mg/day	10 to 14 h QD

Stimulant Dosing: Pediatric

Medication	Starting Dose Range	Dosage Range	Duration/ Dosing
Short acting:			
D-AMPH (Dexedrine®, DextroStat®)	2.5 to 5 mg qd (5-15 mg BID-TID)	0.1 - 1.5 mg/kg/day BID - TID	4 to 6+ hr
Intermediate acting:			
Amph Comp (Adderall®),	2.5 to 5 mg qd	0.1 -1.5 mg/kg/day	6 to 8 h
Dexedrine spansules	5-15 mg BID		QD or BID
Long acting:			
Adderall-XR	10 mg	10-30 mg QD	10 hour

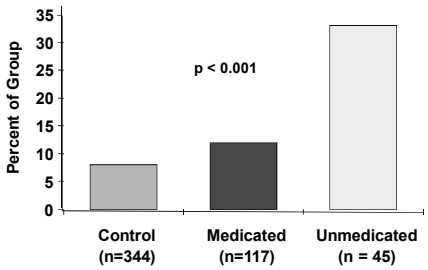
Side Effects of Psychostimulants

- Decreased appetite
- Headaches
- Abdominal discomfort
- Insomnia
- Irritability
- Flat affect
- Increase in BP and heart rate
- Motor tics
  - This occurs in approximately 15 – 30% of individuals started on these medications

Motor Tics or Tourette's

- Coexist in approximately 7% of individuals with ADHD
- Stimulants are known to exacerbate these conditions by increasing neurotransmitter release in not only the prefrontal cortex but also centers responsible for fine motor movements

Do Medications Lead to Substance Abuse: Overall Rate of Substance Use Disorder



Biederman, Wilens, Mick et al., NIH Consensus Conf, 1998

Concerns Regarding Abuse Potential

- Stimulants are C-II substances thus limiting prescriptions by a nurse practitioner who practices in states where DEA numbers are limited to class or restricted in general
- Difficulty with refills – 30 day rule
- In addition, many states do not allow filling across state lines

Success Rates

- 80% of children will respond to one of these stimulants
- May need to try different formulations

http://pediatrics.aappublications.org/content/suppl/2011/10/11/peds.2011-2654.DC1/zpe611117822p.pdf accessed 01-20-2014

Atomoxetine

- Strattera
- Selective presynaptic norepinephrine reuptake inhibitor
- Differs from stimulant medications
  - Increases norepinephrine and dopamine in the prefrontal cortex only

According to American Academy of Child and Adolescent Psychiatry

- Atomoxetine (Strattera) can be considered first line
- Yet…many clinicians position this medication as 2nd line
  - individuals who can't tolerate or will not take a stimulant medication

Head-Head Trials

- 1 study has been conducted comparing atomoxetine vs. methylphenidate
  - 228 patients (7 – 15 year old boy and 7 – 9 year old girls) with ADHD were randomized to atomoxetine vs. methylphenidate
  - Equal efficacy in both groups
  - Both drugs reduced symptoms from baseline
  - Higher vomiting, somnolence and weight loss occurred in the atomoxetine group

Kratochivil CJ, et al. Atomoxetine and methylphenidate Treatment in children with ADHD: a prospective, randomized, Open-label trail. J Am Acad Child Adolesc. Psychiatry. 2002; 41(7):776-784

Monitoring

- Should monitor height and weight in this group
  - Slowing of weight gain and growth in the first 9 – 12 months of therapy
  - This rebounds and normalizes by year 3

Advantages

- Non-stimulant therapy
- Non-controlled substance
  - No issues regarding abuse
  - Easier refills
  - More nurse practitioners can prescribe

Newer Agent

- Guanfacine (Intuniv)
- Indicated for ADHD; ages 6 – 17 years of age
  - Dosed once daily
  - Dose is weight-based
- Monotherapy or in combination with stimulants
- Side effects:
  - Low blood pressure
  - Bradycardia: 8 – 12 bpm decrease in heart rate
  - Somnolence: 38% vs. 12% placebo
  - Headache: 24% vs. 19% placebo
  - Nausea

Guanfacine

- Dosage: 1- 4 mg daily
  - 0.05 mg – 0.08 mg/kg/day – benefits seen
  - Max: 0.12mg/kg/day – or 4 mg daily
- Class: selective $alpha_{2A}$ adrenergic receptor agonist
- Should not be taken with high fat meal – increases medication exposure
- Should taper off medication

Other Treatment Options

- TCA's
  - Imipramine: 10 mg once or twice daily
  - Nortriptyline 10 mg once or twice daily
- Miscellaneous Treatments
  - Bupropion 37.5 mg qam – 300 mg qd
  - Clonidine 0.03 – 0.010 mg/kg/day
    - ECG should be conducted before initiating
    - Helpful with sleep issues associated with ADHD
    - Caution with combination – Methylphenidate/clonidine – 3 deaths
  - Venlafaxine XR 37.5 mg – 225mg daily
  - Fluoxetine 5 – 40 mg daily

There Are Many Other Therapies Which Are Tried

- Eliminating food additives
- Enzyme potentiated desensitization
- Elimination of sugar alone
- Amino acid supplementation
- L-carnitine
- Vitamin therapy
- Zinc therapy
- Magnesium supplementation
- Antifungal therapies
- Chelation therapy

Behavioral Therapy

- Should definitely be employed
  - Aimed at modifying behavior
  - Increasing consistency and structure into the child's day
  - Positive reinforcement of behavior is crucial
  - Punishment is a must
- Children with ADHD are not "codable" at school
- As such, may need to initiate a 504 plan – to allow accommodations to be made for the child

Behavioral Tools

- Reward system
- Time out
- Social reinforcement
- Sports skills
- Modeling
- Daily report card
- Support for parents

Clinical Pearl

- Morning awakening and bedtime are very difficult times for children with ADHD (hyperactivity) particularly
- Encourage parents to:
  - Consistent bedtime routine
  - Give MPH early in am
    - 1 hour before child is due to get up – have parent awaken child to take medication

Another Pearl

- If already on methylphenidate and it is ineffective, add on Strattera to current regimen.
- Then…start to decrease methylphenidate

All of These….

Make Pharmacologic Therapy More Effective!

Follow-up Visits

- 2 – 4 weeks is usually needed before significant benefit is seen
- Book follow-up in approximately 1 month to assess progress
- At visits:
  - Repeat scales (including teacher scales)
  - Weigh child

HEDIS Measurements

- Follow-up care for children prescribed ADHD medication
  - Ages 6-12 years
- Children who received an initial prescription for ADHD medication and:
  - Received at least one follow-up visit with a prescriber within 30 days of initiation of medication
  - Remained on the medication for at least 210 days and who, in addition to the visit in the initiation phase, had at least two more follow-up visits between four weeks and 9 months

http://pediatrics.aappublications.org/content/suppl/2011/10/11/peds.2011-2654.DC1/zpe611117822p.pdf accessed 01-20-2014

Thank You!

I Would Be Happy To Entertain Any Questions

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