

Attention Deficit Hyperactivity Disorder and Primary Care

BACKGROUND

Attention Deficit Hyperactivity Disorder (ADHD) is a common impairing psychiatric condition affecting large numbers of children and adolescents. Core features of ADHD are a persistent pattern of inattention and/or hyperactivity/impulsivity that is frequently displayed and more severe than that observed in individuals with a similar developmental level. Patients with ADHD experience significant functional problems that include school difficulties, academic underachievement, troublesome interpersonal relationships, low self-esteem and diminished quality of life. Symptoms of the disorder are typically present before the age of 7 and frequently persist into adulthood. Early recognition assessment and appropriate treatment of this condition can often improve the educational and psychosocial development of these children and adolescents.

CLINICAL FEATURES OF INATTENTION AND HYPERACTIVITY/IMPULSIVITY

Symptoms of inattention:

- Failing to give close attention to details, may make careless mistakes in school work or other duties. Work is often messy and performed carelessly.
- Difficulty sustaining attention in task or play activities.
- Frequently unable to complete tasks; unable to persist even in play activities.
- Frequently daydreaming or appearing that their mind is elsewhere, or as if they are not listening.
- Frequent shifts from one uncompleted activity to another. Often begins a task and moves to another, and then turns to something else.
- Difficulty following through on a requests or instructions.
- Failure to complete school work, chores, or other duties.
- Difficulty organizing activities or tasks.
- Aversive reaction to tasks that require sustained mental effort or attention, resulting in frequent avoidance or dislike for activities that demand sustained effort, such as homework or paperwork.
- Work habits are frequently disorganized and materials for doing the task are often scattered, damaged, or lost.
- Easily distracted by irrelevant stimuli and these stimuli frequently interrupt ongoing tasks. Attending to trivial noises or events.
- Frequently forgetful in daily activities, forgetful of objects or appointments.
- In social situations, often frequent shifts in conversations, not listening to others, and not keeping one mind on conversations.

Symptoms of Hyperactivity:

- Fidgetiness or squirming in one's seat.
- Excessive running or climbing in situations where it is inappropriate.
- Behaving as if driven by a motor, or often on the go.
- Talking excessively with difficulty quietly engaging in activities or play.
- Hyperactivity varies with individual age and developmental level. In early childhood, may be excessive activity, such as running about the room, jumping on furniture. During school age symptoms of being unable to remain seated, squirming, standing up, fidgeting with objects, tapping their hands, shaking their legs, excessive talking and making noises are frequent. In adolescence, hyperactivity takes the form of a sense of restlessness and difficulty engaging in sedentary activities.

Symptoms of Impulsivity:

- Impatience.
- Difficulty in delaying responses.
- Blurting out answers before questions have been completed.
- Frequent trouble in waiting for ones turn.

- Frequently interrupting and intruding on others to the point of causing difficulties in academic, occupational or social settings.
- Often may make comments out of turn, fail to listen to and interrupt directions, initiate conversations at inappropriate times, and butts into others conversations or activities excessively.
- May physically intrude on others, grab objects from others, touch things they are not supposed to touch, excessive clowning.
- Impulsivity may lead to accidents and engagement in potentially dangerous activities without consideration of possible consequences.

ASSOCIATED MANIFESTATIONS AND FEATURES

The presence of attentional, hyperactivity and impulsivity problems frequently appear in multiple areas including home, school, work, and social situations, often resulting in initiating negative responses from peers, families and teachers resulting in a path of academic and social difficulties. These children and adolescents often have:

- Difficulty getting along with others.
- Conflicts with peers as these children frequently have symptoms of aggression, impulsivity, and non-compliance with rules. Peers indicate that ADHD children cause trouble, get others into trouble, and bother others.
- Often seen as bossy and stubborn. They may have few friends or enduring friendships, leading to social isolation. They also demonstrate mood lability that frequently makes them unpopular with their peers, siblings, and teachers.
- Parents of ADHD children frequently interact with the child in a more harsh, intrusive and negative manner.
- In studies controlled for intelligence, ADHD children are frequently behind normal children, in grade level, for reading, spelling, and arithmetic.
- ADHD children frequently have associated deficits in fine and gross motor skills, impacting hand writing. They are noted to have an inefficient cognitive style, poor sequential memory and poor organization.
- ADHD children have higher rates of school failure and lower level of academic achievement, and poor vocational outcomes.
- Due to frequent academic difficulties or problems in social development, children with ADHD frequently have poor self-worth, frequently feel criticized and embarrassed.

PREVALENCE AND COURSE

- Estimates of the prevalence of ADHD range from 3-7% in school age children. The nature of the population sampled and methods of evaluation influence reported rates. There are marked differences in prevalence rates when evaluation is done utilizing combined reports from parents, teachers and physicians, with rates appearing less than when diagnosed by one source. ADHD rates tend to increase with lower socio-economic status. In clinic referred samples, rates for boys are typically much higher than that found in girls. This may be due to girls having lower rates of oppositional behavior in community and clinical samples. Male to female ratio ranges from 4:1 to 2:1.
- Patients with ADHD tend to have persistence of symptoms as they age, with 60-85% of children diagnosed with ADHD continuing to meet criteria during their teenage years. For those adolescents not meeting full criteria for ADHD, they often feature multiple symptoms of the ADHD complex. Adults with a childhood history of ADHD demonstrate higher than expected rates of criminal and anti-social behavior, injuries, accidents, employment and marital difficulties, higher rates of teen pregnancy and overall health problems. It is important to realize that many children with ADHD will have ongoing problems and impairments into adolescence and adulthood that require treatment.

CO-MORBID CONDITIONS

The prevalence of co-morbid conditions in ADHD is commonplace – with over 60% having one or more psychiatric diagnoses. There are high rates of Oppositional Defiant Disorder, Conduct Disorder, Anxiety Disorders, Mood Disorders, learning disabilities, speech and language disorders.

- **Oppositional Defiant Disorder:**
Diagnosed individuals demonstrate a pattern of negative, hostile, and defiant behaviors for greater than 6 months. These individuals are characterized as often losing their temper, arguing with adults, actively defying or refusing to comply with adult requests or rules. These individuals often deliberately annoy others, blame others for their mistakes or misbehavior, are often seen as touchy or easily annoyed by others, angry, resentful and seen as spiteful and vindictive. Between 35-65% of children with ADHD meet criteria for Oppositional Disorder and/or Conduct Disorder.

- **Conduct Disorder:**
May be viewed on a continuum with Oppositional Defiant Disorder, but in more extreme form. Characterized by repetitive and persistent pattern where basic rights of others, social norms or rules are violated. Examples include aggression to people, as evidenced by bullying, threats, intimidation or physical fights. Other features include being physically cruel to people or animals, stealing, forcing someone into sexual activity, destruction of property, deceitfulness, frequently lying, runaway and truancy.
- **Mood Disorders:**
The prevalence of mood disorders in patients with ADHD remains an area of controversy. Studies have revealed a variety of rates from 0 to 33% of patients with ADHD meeting the criteria for depressive disorder with most studies finding a higher association of ADHD with depression.
The presence of Bipolar Disorder in association with ADHD remains unclear is a very contentious issue. In the recent National Institute of Mental Health (NIMH) Multimodal Treatment of ADHD (MTA) study, no child was excluded for enrollment because of a diagnosis of Bipolar Disorder. Other studies have found rates as high as 16% of sample ADHD patients meeting criteria for mania.
- **Anxiety Disorders in ADHD** have been found in 25-40% of clinic-referred children. The MTA study found 1/3 of children referred with ADHD meeting criteria for an anxiety disorder.
- **Tic Disorders: Tourette's Syndrome.** Higher rates of ADHD have been found in patients with Tourette's Syndrome, with some investigations documenting 50-75%. The exact relationship between ADHD and TD is not clear. There is some indication of higher evidence of tics in children with ADHD, but no clear evidence of higher rates of Tourette's Disorder in children with ADHD.
- **Learning and language problems:** Higher rates of learning and language problems are found in patients with ADHD, with estimates ranging from 25-35%. Children with ADHD often score below control groups on standardized achievement tests.

BRIEF REVIEW OF ETIOLOGY

- The principal cause appears genetic. Heritability is estimated to be 76%.
- Other causes of ADHD include perinatal stress, low birth weight, neonatal hypoxia, traumatic brain injury, maternal smoking and/or drinking during pregnancy, lead exposure, and child maltreatment with deprivation in early life.
- Patients with ADHD have deficits in executive functions in domains of response inhibition, vigilance, working memory, and measures of planning. Not all patients demonstrate these executive functional deficits.
- Neuroimaging reveals reduced cortical white and gray matter volume relative to controls and decreased frontal and temporal lobe volume in children with ADHD.
- Functional studies demonstrate differences in brain activation relative to controls in the caudate, frontal lobes and anterior cingulate.

ASSESSMENT AND DIAGNOSIS OF ADHD

The American Academy of Pediatrics and the American Academy of Child and Adolescent Psychiatry have provided guidelines for the assessment and management of ADHD children. These practice parameters have based many of the recommendations from findings of The National Institute of Mental Health Multimodal Treatment Study of ADHD (MTA).

The primary care clinician should initiate an evaluation for ADHD in children who present with inattention, hyperactivity, impulsivity, academic underachievement or behavioral problems.

Screening questions include:

- How is your child doing in school?
- Is your child having any problems with learning?
- Are you concerned with any behavioral problems at home, school, or with friends?
- Is your child struggling with assigned work or homework, or struggling academically?

Children must meet DSM-IV TR criteria for the diagnosis of ADHD.

- For diagnostic purposes a child must demonstrate 6 of the potential 9 symptoms of inattention or 6 symptoms of hyperactivity/impulsivity, and demonstrate functional impairment. Please refer to the [ADHD Diagnostic Criteria – Table 1 \(PDF\)](#)

- A child might be diagnosed along 3 different subtypes: (1) Attention Deficit Hyperactivity Disorder, combined type, with both significant symptoms of inattention and hyperactivity/impulsivity are evident; (2) Attention Deficit Hyperactivity Disorder, predominantly inattentive type, where inattention is predominant with limited hyperactivity/impulsivity; or (3) Attention Deficit Hyperactivity Disorder, predominantly hyperactive/impulsive type, where inattention is limited with clear evidence of hyperactivity/impulsivity.
- Evidence of symptoms must be evident before the age of 7 and occur in more than 2 or more settings

In the assessment of ADHD, direct reporting from parents or caregivers is required in the evaluation of core symptoms of ADHD, the degree of functional impairment, age of onset of symptoms, and duration.

- This information may be obtained by open-ended interview, semi-structured interviews, or frequently helpful is the use of structured questionnaires and rating scales.
- Standardized rating scales assist in systematically collecting data from parents and teachers that assist in the diagnostic process and symptom monitoring after initiation of treatment.
- These scales provide effective, well-validated methods of assessing presence, frequency, and severity of ADHD symptoms. Please refer to the [ADHD Rating Scales – Table 2 \(PDF\)](#)
- Some of these scales are available at no charge such as the NICHQ Vanderbilt Assessment Scale. Please refer to the following: [Parent Assessment Follow-up \(PDF\)](#), [Teacher Assessment Follow-up \(PDF\)](#), [Parent Assessment Scale \(PDF\)](#) and [Teacher Assessment Scale \(PDF\)](#), [Initial Scoring Instructions \(PDF\)](#), and [Follow-up Scoring Instructions \(PDF\)](#).

Assessment of ADHD requires direct evidence from classroom teachers and school professionals. Assessment includes core symptoms of ADHD, duration of symptoms, degree of functional impairment, and co-existing conditions.

- This allows establishment that the core symptoms exist in more than one setting.
- The majority of ADHD questionnaires and rating scales have teacher-specific versions, and these rating scales accurately distinguish between children with, and without, the diagnosis of ADHD.
- Evaluation of the child with ADHD includes assessment for co-existing conditions.
- Clinicians should review any school based multidisciplinary evaluations.

Evaluation of the child with ADHD requires assessment for coexisting conditions.

- Evidence for co-occurring conditions is typically evident to the primary care clinician; symptoms such as dysphoria or sadness may alert the physician to the possibility of a depressive syndrome. History of frequent fears or avoidance may indicate an underlying anxiety disorder. Screening tests are available and are incorporated into many ADHD evaluation tools. Referral to a mental health specialist may be required for further diagnostic assessment.

Diagnostic tests are not routinely indicated in the evaluation of ADHD.

- If the medical history and physical exam are unremarkable, laboratory and neurological testing is not indicated. Examples include: neurological studies, such as electroencephalography, magnetic resonance imaging, single photon emission computerized tomography, or positron emission tomography. These are not indicated for the routine evaluation of ADHD.
- Continuous performance tests do not adequately discriminate between controls and children with ADHD. Data does not support their use.

DIFFERENTIAL DIAGNOSIS:

There are many mental health conditions that mimic or co-exist with ADHD.

- Learning disorders frequently share common difficulties of underachievement in school and disruptive behavior, but are differentiated by difficulties with academic work, rather than disruption in multiple settings.
- Oppositional Defiant Disorder also shares common symptoms of disruptive behavior, however ODD alone does not demonstrate the full symptom complex of inattention and hyperactivity.
- Conduct Disorder does share symptoms of disruptive behavior with ADHD, but defiance is typically more extreme, with frequent lack of remorse and history of aggression and hostility.
- Depressive Disorders may overlap with ADHD in regards to irritability and poor attention, however they are differentiated by persistent feelings of sadness, irritability or diminished interest in usual or pleasurable activities.
- Bipolar Disorder shares multiple symptoms with ADHD such as irritability, impulsivity, hyperactivity and poor attention. Oftentimes it is very difficult to differentiate from ADHD. Symptoms of Bipolar Disorder not found in ADHD are expansive mood, grandiosity and overt episodic manic episodes. Longitudinal evaluation is often required.

- Anxiety/Obsessive Compulsive Disorder/Post Traumatic Stress Disorder: These disorders frequently share symptoms of poor attention, fidgetiness, and over-reactive nature to stimuli. They often differentiate themselves from ADHD by having excessive worries, presence of obsessions or compulsions and fearfulness.
- Adjustment Disorders often will demonstrate poor attention, hyperactivity, poor academic performance and have an identified stressor and lack the chronic nature of problem. Developmental history often helps to differentiate.
- Substance Use Disorders are often part of conduct symptoms and frequently impair attention impulse control, academic achievement, family and social functioning. Developmental history assists with differentiation with later onset of substance use induced effects.
- Intellectual Disability, Cognitive Delay often demonstrate academic and social difficulties with poor attention and impulsivity. Academic and intellectual ability testing may be required. More global deficits with delays in adaptive skills often separate from ADHD.

TREATMENT OF ADHD

The American Academy of Pediatrics and The American Academy of Child and Adolescent Psychiatry provide recommendations for the treatment of ADHD.

Primary care clinicians must provide a program of treatment that recognizes ADHD as a chronic condition.

- Families must be provided adequate resources and education to fully understand and advocate for their children.
- Education of parents regarding impact of ADHD on learning, self-esteem, social skills and family function must be provided by primary care physicians.
- Better outcomes are obtained with development of comprehensive treatment plan with specific goals.
- Involvement of education system is important in the chronic management of ADHD.

The management of ADHD is developed in collaboration between the primary care clinician, parents, care-givers, patients and educators and target outcomes guide the course of care.

- Examples of sample goals and outcomes include improved academic performance as measured by grades, improved organization, less errors in school work; behavioral outcomes such as improved compliance with rules, improved behavior in public places or self esteem; social and family goals such as improved family relationships, improved compliance, improved interactions in family and peer relations.
- Goals should be designed in accordance to the major areas of concern for the patient and need to be realistic and attainable.

Stimulant medications or behavioral therapy should be utilized to improve these target outcomes.

- Stimulants are highly effective in the treatment of ADHD – 65-70% of subjects have positive clinical response to stimulants.
- Stimulants are considered safe medications with very few contraindications with side effects typically being short lived and minor.
- If one class of stimulant is not effective, then another stimulant should be tried.
- The Multimodal Treatment Study of Children with ADHD with ADHD (MTA) provided a comprehensive assessment of the effectiveness of different treatment strategies. The MTA found that a combination of medication and behavior therapy is more effective than medication therapy alone, behavior therapy alone, or usual community care.
- Behavior management treatments typically focus on providing skills and training to caregivers to improve management of their ADHD child's behavior. These are often provided in group or individual formats.

When target outcomes are not met with current management plans, the clinician must reevaluate diagnosis, use of appropriate treatments, adherence to the treatment plan and the presence of complicating/coexisting conditions.

- Lack of adherence to the treatment plan and/or the presence of complicating conditions are frequent causes of poor response. Ongoing family difficulties may also play a role.
- Clinicians, if unable to determine the reason behind the child's poor response, may consider referral to appropriate subspecialist for further evaluation.

Periodic monitoring of patients with ADHD is required to determine if they continue to meet targeted outcomes and for the detection of adverse effects of treatment. Information must be obtained from the child, parent, caregiver and school.

- Repeat rating scale data, interim progress reports, report cards, teacher, parent, and patient report should be reviewed.
- Monitoring of potential adverse side effects of therapy is required, along with verbal reports, rating scales may include assessments of medication side effects.

PSYCHOSOCIAL TREATMENTS

- Most treatments focus on providing skills to care givers to improve management of children’s maladaptive behaviors. Typical areas to be addressed are the use of structured systems of rewards and consequences that include contingency programs, token economies, point systems, effective use of time outs, effective organization of school work and home duties.
- Behavioral interventions are typically more effective with improving targeted behaviors such as completing homework and disruptive episodes rather than reducing core symptoms of ADHD such as hyperactivity and inattention.
- Behavioral therapy is different than psychological interventions that assist the child with emotional difficulties or disruptive thought patterns such as addressed by play therapy or cognitive behavioral therapy.
- Parents and caregivers are given training to provide a structured system of rewards and consequences. Training often includes how to give clear and effective instructions, setting up structured routines, distraction free environments, use of rewards, increasing praise, positive attention to improve relationships, and teaching the child to monitor his or her own behavior.
- Behavioral Management Training is particularly helpful for children with ADHD with co-occurring behavior, anxiety, or mood disorders.
- The MTA study indicated that ADHD comorbid with anxiety had better outcomes from combined medication and behavioral management than medication alone.
- Other psychosocial interventions include Collaborate Problem Solving, this treatment focuses on parent-child conflict and emotional distress in children and trains parents and children in effective problem solving. Social skills training is aimed to assist the patient’s management of social deficits and other social difficulties and is often taught in groups.

MEDICATIONS FOR ADHD

Over the past decade, there have been many new developments in the number and type of medications available to treat ADHD allowing new options for treatment resistant patients and improvement of tolerability. Most advances have been on the drug delivery system of psychostimulants producing longer acting agents. FDA approval of non-stimulant medications, atomoxetine and a long-acting form of guanfacine have allowed alternatives to patients with a poor response to stimulants.

- Psychostimulants are first-line therapy for treatment of ADHD. As in most cases, stimulants provide the greatest improvement in the core symptoms of ADHD of inattention, impulsivity, and hyperactivity. They have been extensively studied and found to be highly effective, in the vast majority of ADHD patients.
- Stimulant Varieties
 - Many formulations of psychostimulants are available and have been approved by the US Food and Drug Administration (FDA). These are all derivatives of methylphenidate or amphetamine. They have one of the highest response rates in all of psychopharmacology and both methylphenidate and amphetamine are extensively supported by data in regards to their safety and efficacy.
 - Improved delivery systems have allowed the availability of multiple formulations of stimulants including short, intermediate and long acting varieties. With a variety of options in regards to administration including liquids, chewable tablets, and transdermal patches. Please refer to the [ADHD Approved Medications – Table 3 \(PDF\)](#)
- Choosing a Stimulant
 - Elements of past treatment history, families preference, family history of response, duration of effect are all considerations.
 - Long acting formulations are equally efficacious as immediate release forms and have shown to be effective in adolescents as well as children.
 - These offer greater convenience for the patient and family and allow confidentiality in regards to administration at school.
 - Single daily dosing is associated with greater compliance and long acting forms may be used as initial treatment.
 - Short acting forms are often used as initial treatment in small children.
 - Some patients may have a preferential response to the amphetamine or methylphenidate preparations.
 - Approximately 40% of subjects with ADHD responded similarly to both methylphenidate and amphetamine whereas 44% responded preferentially to one class of stimulant. The response rate to stimulants may be as high as 85% if both stimulants are tried.
 - There are no means currently available to predict which stimulant class is more effective in a given patient.

- Improvements with Stimulants
 - Typically behavioral and cognitive measures improve with increasing dosages within therapeutic range.
 - Children with oppositional or conduct symptom complexes and aggressive behaviors tend to respond positively with psychostimulant medication.
 - Emotional over reactivity is reduced and diminished speed of emotional state changes.
 - Interactions between child, his/her peers, families, teachers, and other adults improve.
 - Additional evidence demonstrates that psychostimulants improve sustained attention, impulse control, reaction time and following rules.
 - Improvement in academic, social and family structures leads to improved social interactions and self-esteem. Social interactions are less disruptive in individuals with ADHD, especially in group settings.

NON-STIMULANT MEDICATIONS

Atomoxetine is a noradrenergic reuptake inhibitor that in trials and treatment of ADHD is found to be superior to placebo in children, adolescents and adults. This medication can be given once or twice daily and may have less pronounced effects on appetite and sleep than stimulants. To obtain the drugs full effect, individuals must be maintained on medication for several weeks.

- Direct comparisons of the efficacy of atomoxetine with methylphenidate and amphetamine showed greater treatment effect of the stimulants.
- Atomoxetine is often considered first line for patients with active substance abuse problems, comorbid anxiety or tics.
- Atomoxetine is also frequently used for patients that have significant mood lability or other severe side effects to stimulants.

Guanfacine: The extended version of the Alpha 2 adrenergic agonist, guanfacine, recently received FDA approval for treatment ADHD in children over the age of 6. Efficacy was established in two placebo controlled trials in children ages 6 to 17. There was a statistically significant greater reduction in ADHD symptoms compared to placebo in both studies. Response was dose dependent with most clinically relevant improvements observed at doses beginning in the range of 0.05 to 0.08 mg/kg/day range. Doses up to 0.12mg/kg/day showed additional benefits. Individuals taking guanfacine extended release appeared to demonstrate similar growth compared to norms, with height, weight, and BMI percentile remaining stable over 12 months in long-term studies.

USE OF SECOND LINE AGENTS

The vast majority of patients with ADHD who do not have significant comorbidity have a satisfactory response with FDA approved psychostimulants or atomoxetine. If significant adverse side effects or treatment failures are encountered with these agents, the clinician should undertake a review of the patient's diagnosis of ADHD. The evaluation should determine whether comorbid conditions are present and if these disorders are the primary problem impairing the individual's attention and impulse control.

- Second line medications, that are not FDA approved, have been utilized for ADHD. Please refer to the [ADHD Medications Not Approved By FDA – Table 4 \(PDF\)](#). These include bupropion, tricycling anti-depressants and the adrenergic agonists.
- Clinical evidence for these medications is far weaker than the FDA approved agents. Strong consideration should be given to recommendation for behavioral therapy, before moving to second line agents. Bupropion, alpha-2 agonists and TCA's have shown effectiveness in open trials. Although TCA's need to be used with caution as there has been association with sudden death, specifically for desipramine. For TCA's, electrocardiography (ECG's) must be performed at baseline and after each dose increase; plasma levels will also need to be managed to avoid toxicity. Most primary care providers refer to psychiatry for management of these second line agents with the exception of the alpha-2 agonists.
- The alpha-2 agonists, clonidine and guanfacine, have been utilized widely for patient's with ADHD. Studies have varied in results; the effect size has been small. Alpha-agonists may be more effective in treating hyperactivity and impulsive symptoms rather than inattention. Titration of dose needs to be gradual along with discontinuation to avoid significant changes in blood pressure.

STIMULANTS: MANAGEMENT OF SIDE EFFECTS

Stimulant medications are usually well tolerated both short and long term. Dose adjustment, switching to a different stimulant or use of adjunctive medications are frequent management techniques to address adverse effects.

- The most common side effects are decrease in appetite, weight loss, insomnia or headache. These side effects to stimulants are often transient. Their severity and functional impact must be judged. Mindful monitoring of the side effects may be the best course as they often resolve without active interventions. Insomnia may be addressed by low doses of clonidine, melatonin, or an anti-histamine if alteration in dose or administration schedule is ineffective.
- Rebound irritability and moodiness describes an increase in hyperactivity/impulsivity in the evening when the stimulant is no longer effective. Laboratory classroom studies have demonstrated that behavior of ADHD children is worse in the afternoon or evening even when on placebo. How much of a drug effect contributes to rebound is unclear. The situation may be managed by giving a short acting preparation in the afternoon.
- Some children may experience diminished energy, social withdrawal when taking stimulants. They may refer to themselves as zombie-like with diminished spontaneity and social interaction. This side effect is frequently managed by dose adjustment as this may be a sign of excessive dosing or poor toleration of the medication.
- Rare side effects include extreme mood lability, increased aggressiveness, emotional distress, suicidality, or psychosis. Immediate discontinuation of the medication is required for these side effects.
- Tics have been reported as a side effect to stimulants; however, this relationship is unclear. In some clinical trials, stimulants did not increase the rate of tics relative to placebo. Emergent tics during stimulant treatment may be addressed by using an alternative stimulant, or a non-stimulant medication or combined therapy of stimulant with an alpha agonist.
- Cardiac issues – in 2006 the FDA raised concerns of possible sudden death occurring with agents used in the treatment of ADHD. This resulted in an advisory committee recommending a boxed warning be issued for cardiovascular events including stroke and myocardial infarction. The Pediatric Advisory Committee did not support this. Currently there is no evidence for the need for routine cardiac evaluation such as electrocardiography or echocardiography; however, children with a history of pre-existing heart disease or symptoms suggestive of syncope and cardiovascular disease should be managed carefully. The American Academy of Pediatrics recommends assessment of all children before initiating ADHD medications with a targeted cardiac history, including cardiac disease, palpitations, syncope, seizures, family history of sudden death, hypotrophic cardiomyopathy and long QT syndrome. Positive findings would require additional evaluation and potential consultation with a pediatric cardiologist prior to stimulant medications or prior to use of atomoxetine.
- Concerns regarding growth. Suppression of growth is a common concern of caregivers. Most recent evidence suggests ADHD patients treated with stimulants have demonstrated small but statistically significant height deficits suggesting slower growth than expected. Over time, height velocity seems to normalize. Weight deficits also tend to normalize with time and these deficits are more significant than that seen in height. There appears to be no significant differences in growth between methylphenidate and amphetamine. Cessation of treatments seems to normalize growth. Height deficits may be dose dependent. Atomoxetine has also been linked with changes in height and weight trajectories.
- Atomoxetine Side Effects: Many of the side effects of atomoxetine overlap with stimulants, such as loss of appetite nausea, vomiting, irritability, and headaches. In clinical trials, suicidal thoughts were found in small but higher numbers compared to placebo. There were no completed suicides, but a boxed warning was applied. Patients and families need to be educated of this potential risk.

TREATMENT MONITORING

- Initiation of medication treatment involves selecting a starting dose with titration upward every 1 to 3 weeks until remission of ADHD symptoms, or reaching maximum dose, or emergence of prohibitive side effects.
- Ongoing frequent contact with either the clinician or trained staff is required during this time.
- Use of teacher and parent rating scales after reaching target doses of medication assist in determination of treatment response and need for continued adjustment.
- In patients with ADHD who show normative functioning in academic family and social domains, then psychopharmacologic intervention is satisfactory. However, if there is sub-optimal response, psychosocial treatment with medication is often beneficial.
- Monitoring includes ongoing assessment of the need for treatment. If ADHD symptoms are present and cause impairment, treatment should continue.
- Visits should include review of academic, social, and behavioral progress. Height, weight, and monitoring of growth chart is required, along with blood pressure, pulse, and assessment of any evolving adverse effects or medical conditions.

- Most patients experience long-term effectiveness with stimulant treatment. Side effects in long-term treatment is usually without serious medical complication and are mild to moderate and typically respond to dose adjustment or change in medication.
- The MTA study indicated that some children improve and may not need ongoing treatment. Clinicians need to review progress and if indications such as sustained functioning without medication are present, they may consider a withdrawal from medication.
- Also identified in the MTA study where children with a course of deterioration over time. This group is characterized by high levels of aggression and lower IQ's. This group requires more comprehensive psychosocial intervention.

SUBPOPULATIONS

Preschool Children:

Many developmental disorders are associated with attentional problems and hyperactivity, and therefore, initial evaluation requires a detailed history and complete examination and assessment of developmental milestones. Temperament difficulties, parent/child relationship problems, and anxiety all mimic ADHD symptoms. Utilization of psychostimulant medication in preschoolers is complicated by higher rates of social withdrawal, irritability, crying, and overall increased emotional responsiveness. The NIMH funded Preschool ADHD Treatment Study (PATS) examined methylphenidate use in children age 3 to 5 years. It showed that methylphenidate was effective in preschoolers with ADHD; however, with lower mean optimal dose of methylphenidate as compared to the MTA study. This group showed higher rates of adverse events of being crabby, irritable, and frequently crying. Recommendations included cautious titrations and that lower doses may be effective.

Adolescent Population:

In adolescence, adherence to treatment plans frequently diminishes. Consequences of untreated ADHD may be of greater severity in adolescence; such as automobile accidents, sexually transmitted disease, unplanned pregnancy, legal difficulties, school dropout and substance use. Stimulant medications continue to be effective for the majority of adolescents. Response appears dose dependent and demonstrates improvements in behavioral and cognitive symptoms. Beneficial effects mimic those of school-age children. Atomoxetine has been shown to be of benefit in the adolescent population.

Helpful websites:

- National Resource Center on ADHD – A Program of CHADD: www.help4adhd.org
- Centers for Disease Control and Prevention – ADHD: www.cdc.gov/ncbddd/adhd/
- Children and Adults with Attention Deficit/Hyperactivity Disorder: www.chadd.org
- National Institute of Mental Health: www.nimh.nih.gov
- American Academy of Child and Adolescent Psychiatry Section for Families: www.aacap.org/cs/forfamilies
- ParentsMedGuide.org: www.parentmedguide.org
- Practice Parameters AACAP for ADHD: www.help4adhd.org
- NICHQ-Tool Kits: www.nichq.org/adhd_tools

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