Clinical Practice Guideline for Patients with Attention Deficit/Hyperactivity Disorder

Magellan Health Services
Clinical Practice Guideline Task Force

Robert Ciaverelli, M.D.
Kathleen K. Frampton, R.N., B.S.N., M.P.H.
Gary Henschen, M.D.
Richard Kamins, Ph.D.
Daniel P. McCarthy, Ph.D.
Charles Wadle, D.O.

Effective August 31, 2007, Magellan Health Services re-adopted the *Clinical Practice Guideline for the Treatment of Patients With Attention-Deficit Hyperactivity Disorder, Second Edition,* written by Magellan to serve as an evidence-based framework for practitioners' clinical decision-making with child, adolescent, and adult patients who have a diagnosis of attention-deficit hyperactivity disorder. *In June 2008, we revised the "Medications" section of this document to include the American Heart Association's (AHA) recommendations for screening children who may be vulnerable to sudden cardiac death. In September 2008, Magellan revised this section again to include a joint advisory statement of the American Academy of Pediatrics (AAP) and the AHA, issued as clarification to widespread misinterpretation of the earlier AHA recommendations. These new recommendations were endorsed by the American Academy of Child and Adolescent Psychiatry (AACAP), the American College of Cardiology, Children and Adults with Attention-Deficit/Hyperactivity Disorder, the National Initiative for Children's Healthcare Quality, and the Society for Developmental and Behavioral Pediatrics.* In preparation of the 2012 revision, we conducted another review of the published scientific literature through September 2011, along with available practitioner input. This guideline covers the main areas of psychiatric management of patients with this disorder, covering topics from clinical features and epidemiology to various aspects of treatment approach and planning. Nonetheless, it is not intended to be exhaustive. In addition, the behavioral health field is rapidly evolving and there are continuous changes in assessment and management techniques, so while this guideline provides a brief overview, the reader is encouraged to review other sources that may incorporate ongoing clinical developments, including the AACAP Practice Parameters for ADHD; the AAP Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents; and other sources (citations).

Obtaining Copies of the Guideline

This Magellan *Practice Guideline for the Treatment of Patients with Attention-Deficit Hyperactivity Disorder* is available on the Magellan provider website at www.MagellanHealth.com/provider.

As with all guidelines, the Magellan Guideline is intended to augment, not replace, sound clinical assessment and decision-making. As a matter of good practice, clinically sound exceptions to the treatment guidelines should be noted in the medical record. Additionally, this guideline does not supersede Food and Drug Administration (FDA) determinations or other actions regarding withdrawal or approval of specific medications or devices, and their uses. It is the responsibility of the treating clinician to remain current on medication/device alerts and warnings that are issued by the FDA and other regulatory and professional bodies, and to incorporate such information in his or her treatment decisions.

Providing Feedback on the Guidelines

Magellan welcomes feedback on adopted clinical practice guidelines. All suggestions and recommendations are taken into consideration in our review. Comments may be submitted to:

Clinical Operations Coordinator
Re: CPG
Magellan Health Services
6950 Columbia Gateway Drive
Columbia, Maryland 21046
CPG@MagellanHealth.com

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INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is a childhood-onset neurobehavioral syndrome characterized primarily by disorders in attention, concentration, and impulse control. These dysfunctions can lead to behavioral problems in home, school, work, and social settings. Children with ADHD may have difficulty with learning in school, developing appropriate social skills, and managing frustration and aggression (Wilens et al., 2002). ADHD is also a developmental disorder whose presentation may change with maturation. There is often a decrease in overt hyperactivity and impulsivity with age, while attention problems are more likely to persist (Mick et al., 2004). The diagnostic criteria for ADHD are outlined in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR®)* (American Psychiatric Association, 2000). These diagnostic criteria best apply to children and younger adolescents. There continues to be a need for criteria that are more appropriate for older adolescents and adults (Mick et al., 2004; McGough and Barkley, 2004; Spencer and Adler, 2004).

Epidemiology

As stated by Goldman in 1998, "Attention-Deficit/Hyperactivity Disorder is one of the best-researched disorders in medicine, and the overall data on its validity is far more compelling than for most mental disorders and even for many medical conditions" (Goldman et al., 1998). There is a great cost to society from ADHD because of the resulting academic and occupational underachievement, conduct problems throughout the lifespan, higher levels of associated substance abuse, motor vehicle accidents, and interpersonal relationship problems (Wilens et al., 2002; Mick et al., 2004; Wilens 2004).

ADHD appears to be a neurologically heterogeneous disorder, with varying patterns of impairment in different individuals and with significant subtypes. (American Academy of Pediatrics 2011; American Academy of Child and Adolescent Psychiatry, 2007; American Psychiatric Association, 2000; Nutt, 2007). A Canadian research team compared ADHD subtypes (n=371) on level of comorbidity, treatment response and etiology using data from subjects already enrolled in a randomized controlled trial of methylphenidate (Grizenko et al. 2010). Results showed significant differences in these parameters leading to speculation that ADHD subtypes may be separate and distinct disorders. Specifically, a higher frequency of ADHD children with combined/hyperactive subtype were good treatment responders, had a history of moderate stress during the mother's pregnancy and were of L/L genotype for the 5-HTT-linked polymorphic region along with other notable differences in age, gender distribution, severity of symptoms and comorbidity between the subtypes (Grizenko et al. 2010). Childhood ADHD is reported as much more prevalent in boys, though some experts argue that girls' ADHD more often is undetected. In contrast to earlier studies in which boys were reported as having poorer functioning, some reports suggest that non-referred boys and girls have similar impairment levels of cognitive, psychosocial, school and family functioning and that the previously described gender differences in functioning are due to referral biases rather than true gender differences (Biederman et al., 2005).

The childhood prevalence of ADHD is similar in every culture studied, and depending on the criteria used, has been reported as ranging from 3-15 percent, with at least 7 percent being a generally accepted average figure. These statistics indicate that it is the most common psychiatric disorder of childhood (American Academy of Child and Adolescent Psychiatry, 2007; Barbaresi et al., 2004). The majority of children with ADHD meet some or all of the criteria for this disorder as

adults. For example, at age 25 years, about 15 percent of people diagnosed with ADHD as children meet DSM-IV-TR criteria for the disorder, and about 65 percent meet DSM-IV-TR criteria for ADHD in partial remission (Nutt, 2007; Faraone, 2006). Adult ADHD is both significantly under diagnosed and under treated (Faraone, 2004). The prevalence appears to be about 4-5 percent (Nutt, 2007; American Academy of Child and Adolescent Psychiatry, 2007). A recent unpublished study suggests adult women with ADHD are less likely to be diagnosed despite having more severe symptoms and emotional impairment than male patients (Robison et al., 2005). This finding is of particular concern since women respond at least as well to treatment as men. One study was unable to demonstrate any differences in comorbidity, social functioning and cognitive functioning between adults meeting full diagnostic criteria for ADHD and those having only residual (not full criteria) ADHD symptoms (Mick et al., 2004). A large community sample examining the stability and structure of ADHD symptoms from childhood to adulthood showed a greater persistence of inattentive than of hyperactive/impulsive childhood ADHD symptoms and found executive function problems as the most specific and consistent predictor of diagnosis. These findings lend support to adding executive function problems to the future *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-V) criteria for Adult ADHD diagnosis (Kessler et al. 2010). Other research has shown that over 90 percent of adults with ADHD have inattentive symptoms requiring careful evaluation to determine or rule out comorbid conditions since inattention may be a component of several other disorders (Wilens et al. 2009).

The majority of adults with ADHD have at least one comorbid psychiatric disorder, which may be the clinician's first clue of the diagnosis of ADHD (Wiles et al., 2002; Montano, 2004). Common co-morbidities include anxiety disorders, depressions and substance abuse. A large clinical survey (n=447) conducted to determine the prevalence of current and lifetime Axis I and II disorders in adult men and women with ADHD revealed the following: (1) Men with ADHD were more likely to have antisocial personality disorder and higher rates of current drug use than women with ADHD; (2) women with ADHD had higher rates of past and current panic disorder and past anorexia and bulimia; and (3) women with ADHD were more likely to have bipolar disorder than men with ADHD (Cumyn et al. 2009).

Adults with ADHD are less likely to have graduated from high school or to have attended college. They have lower occupational achievement, change jobs more frequently, are more likely to be fired or quit and perform more poorly on the job. They have more psychological maladjustment, more occurrences of multiple marriages and much more substance abuse. A study of adult violent offenders found that after controlling for age, gender and substance use disorders, ADHD was associated with reactive but not proactive violence (Retz et al. 2010). In a study of older adolescents and young adults with ADHD, it was shown that the subjects exhibited "no driving knowledge deficits, but compared with controls, they had elevated rates of speeding citations, suspended licenses, crashes, and accidents causing bodily injury." It was also found that "They were more likely to be rated by themselves and others as having poorer driving habits" (Mick et al., 2004).

Despite the multiple issues arising from untreated or partially treated ADHD, it needs to be stressed that there is a broad range of social and occupational outcomes, with many individuals having success in the social and occupational realms despite ongoing symptoms.

The causes of ADHD have not been determined conclusively and continue to be studied. ADHD appears to be the result of a complex interaction of genetic, environmental and biological factors (American Academy of Child and Adolescent Psychiatry, 2007; Nutt DJ 2007; Pliszka 2006).

Evidence for the genetic factors includes a pool of 17 twin studies reporting heritability (genetic factors) influence of about 76 percent (Faraone, 2004). However, more recent review of these earlier studies has warned that heritability estimates were strongly influenced by rater effects and assessment instruments used in these studies (Freitag et al., 2010). In addition, parents of children with ADHD had been reported as being much more likely to have ADHD than are parents of children without ADHD (Faraone, 2004). Since then, a study of 323 trios (mother, father and identified ADHD patient) found that ADHD severity was higher for children whose parents had ADHD versus those whose parents did not; that both parents may confer risks for both subtypes with fathers conferring greater risk for severity of hyperactivity-impulsivity; and that biparental ADHD may not have an additive or synergistic effect on the probands ADHD severity (Takeda et al. 2010).

Suspected environmental factors include brain injury in utero, perinatal stress, fetal exposure to nicotine and alcohol, low birth weight/prematurity and traumatic brain injury (Nair 2006; Grizenko et al., 2008). More recent data from the 2001-2004 National Health and Nutritional Health Examination Survey (NHANES) have shown that both prenatal tobacco exposure (maternal cigarette use during pregnancy) and childhood lead exposure were associated with ADHD in children (Froehlich et al., 2009). Biological factors have been identified through studies that have employed brain-imaging techniques and neuropsychological testing. Such studies have revealed evidence of structural and functional brain abnormalities in ADHD. Of particular importance are functional abnormalities in the frontal, temporal, sub-cortical, left occipital and cerebellar neural circuits, decreases in white matter volume, and widespread brain pathophysiologic abnormalities. Such biological findings suggest that any causality theory must provide a model for understanding broad-based brain dysfunction (Faraone, 2004; Monastra 2005a; Valera et al., 2010).

EVALUATION

Children and Adolescents

The diagnosis of ADHD is determined using DSM-IV-TR criteria. The clinician should analyze data from a variety of sources, since no single test, rating scale, or observational finding determines the diagnosis (Cincinnati Children's Hospital Medical Center, 2004). However, the use of structured rating scales that have been found valid and reliable with large populations is recommended (Nutt, 2007). Any parental concern about inattention, impulsivity, over activity or ADHD in a child aged 4 through 18 years of age should be taken seriously by the clinician and lead to further investigation. A family history of ADHD lends support to suspecting the diagnosis (Faraone, 2004; AAP Subcommittee on ADHD, 2011).

At a minimum, data obtained for diagnosing ADHD in children and adolescents should include the following (American Academy of Child and Adolescent Psychiatry, 2007; Nutt 2007, AAP Subcommittee on ADHD, 2011):

- Psychiatric, developmental, social, educational, family and medical history from the patient and family. Family history should include questions about parental ADHD and cardiac history
- Review of medical evaluation, including physical exam and lab tests, to rule out medical causes of the signs and symptoms

- Rating scales from the patient and parents (e.g., Brown ADD Scales for Children, Adolescents, and Adults [Brown, 2001]; Conners Parent Rating Scale-Revised [Conners, 1997])
- Reports and rating scales from teachers (e.g., Brown ADD Scales for Children, Adolescents, and Adults [Brown, 2001]; Conners Teacher Rating Scale-Revised [Conners, 1997])
- Comprehensive assessment for comorbid psychiatric disorders
- Careful substance abuse evaluation for adolescents with newly diagnosed ADHD
- Clinical observation.

To make a diagnosis of ADHD in a child or adolescent, the symptoms must have been present prior to age seven, and/or prior to age 10 in girls, although there may be significant variation in the age of onset (Biederman and Faraone, 2004; Nutt 2007); and the other DSM-IV-TR criteria must be met . Some experts in the field have suggested that the DSM-IV-TR criteria were developed primarily from observations of boys and problems with attention, a salient feature in girls with ADHD, may not become apparent until they are closer to puberty. In the forthcoming *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-V), the proposed new criteria increases the age limit for when ADHD needs to have first presented from 7 to 12 years (APA DSM-5 Development, 2011). It is important to coordinate initial and subsequent evaluations with the patient's teacher(s).

Adults

Adults with ADHD often present for evaluation after one of their children is diagnosed. Reasons for the diagnosis being delayed until adulthood can include: 1) the diagnosis being obscured in childhood by associated problems such as Oppositional Defiant Disorder (ODD), Conduct Disorder and Mood Disorder, 2) being erroneously labeled as a "troublemaker" or a "daydreamer," and 3) no one considering the ADHD diagnosis. The DSM-IV-TR criteria form the basis for the diagnosis in adults but some interpretive flexibility may be needed on the part of the clinician, since some have suggested that a lower threshold, such as four or five out of the nine DSM-IV criteria, be considered sufficient in adults (Mick et al., 2004; McGough and Barkley, 2004; Biederman and Faraone, 2004; Wilens et al., 2004; Nutt 2007).

Adults commonly have more cognitive, e.g., inattentive, than hyperactive symptoms. When hyperactivity is present, it tends to become more of a subjective sensation rather than an observable sign. Inattentive symptoms affect executive functions and can manifest in problems with organized planning, multitasking and time management. A variety of self-report and clinician-administered rating scales is available to aid in the assessment for these symptoms in adulthood. Examples of such screening scales are the Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist developed by the World Health Organization (available at http://www.hcp.med.harvard.edu/ncs/asrs.php) (Kessler et al., in press; Nutt 2007) and the Wender Utah Rating Scale (Ward, 1993). The Brown ADD Scales (Brown, 2001), Wender-Reimherr Adult ADHD Scale (Ward et al., 1993) and others can be used to determine symptom severity. Clinicians make the diagnosis after considering the patient's reported ADHD symptoms from childhood, data from collateral sources, and current symptoms and functioning (Spencer and Adler, 2004; Wilens et al., 2004). As in children, "there must be clear evidence of clinically significant impairment in social, academic or occupational functioning" because of symptoms (DSM-IV-TR, 2000).

Differential Diagnosis

Determine that the symptoms are not better accounted for by another neuropsychiatric or substance abuse diagnosis, such as: adjustment disorder, anxiety disorder, conduct disorder, dissociative disorder, learning disorder, mental retardation, mood disorder, oppositional defiant disorder, personality disorder, pervasive developmental disorder, psychotic disorder, substance use disorder, chronic sleep deprivation such as caused by obstructive sleep apnea and borderline intellectual functioning. Neurobehavioral adverse effects of medication and sexual, physical and emotional abuse can also cause ADHD-like symptoms (DSM-IV-TR, 2000; Spencer et al. 2004; Cincinnati Children's Hospital Medical Center, 2004).

When evaluating a patient who presents with symptoms consistent with ADHD, it is recommended that clinicians also evaluate for behavioral health comorbidity. Significant overlap among symptoms of ADHD and other psychiatric disorders is common, complicating the diagnosis of comorbidities and the treatment process. Common comorbid disorders include anxiety disorders, learning disorders, mood disorders and oppositional defiant disorder (Pliszka 2003; Pliszka 2006; Wilens and Dodson, 2004).[19,20] Also, gender and age suggest differing likelihoods of the presence and type of behavioral health co-morbidities. While previous studies reported boys having a greater degree of comorbidity, more recent reports suggest that psychiatric comorbidities are similar for both boys and girls in non-referred cases of ADHD (Biederman et al., 2005). [8] One study suggested that ADHD is a stronger risk factor for comorbid substance use disorders in girls. Regarding age, comorbid depression in younger children may seem less frequent but could be easy to miss, given the difficulty of accurate diagnosis in this age group.

The presence of certain comorbidities may suggest the likelihood of different symptom types of the ADHD. Patients with co-morbid anxiety as a group tend to have a greater degree of inattention rather than impulsivity. Conversely, those with co-morbid oppositional defiant disorder or conduct disorder tend to be more impulsive rather than inattentive. Emotional lability (EL) in children and adolescents with the combined subtype may be associated with increased severity of ADHD core symptoms and more symptoms of comorbid psychopathology - i.e., ODD, affective symptoms and substance abuse (Sobanski et al. 2010; Barkley et al. 2010). Sleep disorders are highly comorbid with ADHD. Different sleep disorders seem to address different subtypes and correlate with severity of symptoms - i.e., sleep related movement disorders in hyperactive and combined ADHD subtypes (Silvestri et al. 2009).

In evaluating for comorbidity in children, a narrow-band scale, such as the Vanderbilt ADHD Diagnostic Parent and Teacher Scales (Wolraich et al., 2003), which is recommended by the American Academy of Child and Adolescent Psychiatry (American Academy of Child and Adolescent Psychiatry, 2007) and the American Academy of Pediatrics (American Academy of Pediatrics, 2000a; 2000b; Leslie et al., 2004), is sufficient for detecting comorbidity as well as core ADHD symptoms and impairment (Cincinnati Children's Hospital Medical Center, 2004; Pliszka, 2003; Frazier et al., 2004; Waxmonsky, 2003).

Adults with ADHD have higher rates of comorbid anxiety disorders, mood disorders, substance use disorders and cigarette smoking than adults without ADHD. Additionally, approximately 15-20 percent of adults with anxiety, bipolar, depressive and substance use disorders also have ADHD (Pliszka, 2003; Wilens, 2004). Studies from community samples continue to demonstrate significant association between the number of self-reported childhood ADHD symptoms and risk for overweight and obesity in adulthood (Fuemmeler et al. 2010).

Determine that a medical evaluation has occurred during the diagnostic process to rule out medical causes of the symptoms and any contraindications for stimulant medication treatment (Pliszka, 2006). Potential medical causes of inattention include seizures, sequelae of head trauma, acute or chronic medical illnesses, such as lead poisoning, other encephalopathies, poor nutrition, insufficient sleep, and hearing and vision problems. The following tests are <u>not</u> supported by the evidence for a routine use in the evaluation of ADHD, but may prove helpful in selected cases:

- Lead or thyroid testing
- Brain imaging
- Genetic or chromosomal testing
- Electroencephalogram (EEG)
- Computerized performance tests (CPT).

The latter two lack sufficient specificity and sensitivity for clinical use. In general, complete psychological or neuropsychological testing is not necessary in the absence of indications of low cognitive function or performance significantly below IQ that should be explored further (Cincinnati Children's Hospital Medical Center, 2004).

Psychological testing is indicated when needed to assist in the differential diagnosis, identify possible co-morbidity, help evaluate the extent of ADHD deficits, or to guide treatment modifications. Such testing is appropriate only after initial face-to-face diagnostic evaluation demonstrates one of these needs (Cincinnati Children's Hospital Medical Center, 2004; Frazier et al., 2004).

If psychological testing is suggested to evaluate a child or adolescent for educational purposes, e.g., to establish presence of learning disability, the school usually is the most appropriate agent to conduct the testing. Educational testing and accommodations for learning disabilities are federally mandated by the Individuals with Disabilities Education Act (IDEA) (Frazier et al., 2004; Waxmonsky, 2003).

TREATMENT

Treatment should address neurological dysfunction, and any concomitant behavioral manifestations, learning disabilities, comorbid disorders and psychosocial issues. Medications are supported by the preponderance of clinical literature as first-line treatments for core ADHD dysfunction and resulting symptoms, but are best administered in the context of a comprehensive treatment plan that considers evidence-based psychosocial interventions (American Academy of Child and Adolescent Psychiatry, 2007). Treatment progress can be assessed by clinical observations and interviews, as well as rating scales completed by parents and teachers. The hallmark of treatment planning in children is a firm alliance with the parents, patient and teachers to make sure that consistent, coordinated efforts are applied across settings (Pliszka, 2003; Wilens and Dodson, 2004; Waxmonsky, 2003).

Medications

Medication strategies should improve targeted ADHD symptoms with minimal adverse effects; address comorbidity, if any; be appropriate relative to the patient's abuse potential; provide smooth day-long coverage; target dopaminergic and/or noradrenergic systems; be administered in a form that maximizes compliance (e.g., extended release or transdermal patch) and preserve patient safety (Wilens and Dodson, 2004; Pliszka, 2006).[20] Combining medications may be required, but unnecessary polypharmacy should be avoided.

Long-term treatment with medications is necessary for many patients with ADHD. One meta-analysis of 13 studies found that improvements in symptoms from atomoxetine treatment persisted over 24 months with no dosage escalation and no evidence of tolerance or safety concerns (Wilens, 2006; Kratochvil et al., 2006a). Periodic medication-free trials may be useful to determine the need for continuing medication. However, the guideline group of the European Network for Hyperkinetic Disorders (EUNETHYDIS) argued that clinical evidence is not conclusive on the risk-benefits of drug holidays since there are inherent risks attached to the intermittent cessation of treatment - i.e., higher incidence of burn accidents and emergency room visits in children not receiving their normal medications (Graham et al. 2011).

Most children and adolescents with ADHD who do not have significant co-morbidity will respond satisfactorily to pharmacological agents (i.e., amphetamine and methylphenidate preparations and atomoxetine) after an adequate length of time at appropriate doses (American Academy of Child and Adolescent Psychiatry, 2007). If a patient does not respond, the physician should carefully review

the patient's diagnosis of ADHD and consider any undetected comorbid conditions or developmental disorders and determine whether these may be primary problems in impairing the patient's attention and/or impulse control. A referral to a child and adolescent psychiatrist may be considered at this point (American Academy of Child and Adolescent Psychiatry, 2007).

In general, when treating a patient with ADHD and suspected or confirmed comorbidities, it is appropriate to address the ADHD first if the co-morbidity is less severe (e.g., mild to moderate anxiety, mild to moderate depression); or to address the comorbidity first if it is severe and puts the patient at risk (e.g., severe depression, acute mania). Acute mania, if present, must be stabilized prior to initiation of a stimulant for ADHD symptoms (Pliszka, 2003; Waxmonsky, 2003).

Stimulants

The amphetamines and methylphenidate remain first line treatments and are available in short-acting and slow-release formulations, as well as a transdermal patch for methylphenidate (American Academy of Child and Adolescent Psychiatry, 2006; Nutt 2007; Pliszka et al, 2006; Brown, 2005; King 2006; Gibson, 2006; Banaschewski, 2006). A refined form of methylphenidate, dexmethylphenidate hydrochloride, is long acting and reported to be twice as potent (Weiss, 2004; Wigal et al., 2004; Arnold et al., 2004) with similar or less severe side effects than methylphenidate hydrochloride. Triple-bead mixed amphetamine salts (MAS) is an enhanced extended-release amphetamine formulation designed for duration of action up to 16 hours. It has been shown to be effective in the treatment of adults with ADHD resulting in significant improvements in executive function and quality of life (Spencer et al., 2008). Lisdexamfetamine dimesylate is the first pro-drug stimulant used in the treatment of ADHD. It is a therapeutically inactive molecule that is converted to the essential amino acid, l-lysine and active d-amphetamine after oral ingestion. This drug was developed for its long duration of effect and reduced potential for risk of abuse. At doses of 30, 50 and 70 mg. per day, it demonstrated significant improvements in ADHD symptoms in adults (Adler, Goodman et al., 2008). More recent research and development has focused on other modes of improved drug delivery in order to extend the duration of action, i.e., capsules, sprinkleable capsules, tablets, chewable tables, oral solution (Correll et al. 2011).

Higher stimulant doses are generally associated with better reduction in symptoms (Pliszka, 2006). At least 70 percent of school-aged children with ADHD respond favorably to stimulant medications. Preschool age children also benefit from these medications, although their response may be less robust than that seen in older children and a short-acting form may be needed to achieve appropriate dosing. Teens with comorbid conduct problems are usually insufficiently treated by stimulants alone, and need psychosocial treatments in combination (Chronis et al., 2006). Many adults, including those never treated in childhood, can benefit from the use of stimulant medications (Adler, Zimmerman et al., 2009).

An algorithm of the Texas Children's Medication Algorithm Project (TCMAP) recommends, for ADHD without comorbidity, an initial trial of either methylphenidate or amphetamine, and if response is not sufficient, switching to the stimulant not tried initially; if the second stimulant does not produce an acceptable outcome, an alternative medication, such as atomoxetine, can be tried (Pliszka et al., 2006; Newcorn et al., 2008; AAP Subcommittee on ADHD, 2011; Correll et al. 2011). In terms of treatment of adults with ADHD, meta-analytic findings support use of both stimulant and non-stimulant medications but with stimulants showing the greater treatment efficacy and no differences between short- and long-acting compounds (Faraone et al. 2010).

The stimulants primarily affect the core symptoms of hyperactivity, impulsivity, inattentiveness and associated aggressiveness. The onset is rapid, the dose easily adjusted and adverse effects are generally mild and easily managed. The optimal dose cannot be predetermined by age, weight, height, gender or severity of the ADHD, and weight-adjusted milligram-per-kilogram-per-day dosing is not supported by evidence and consensus (Pliszka et al., 2006). Rather, a careful milligram-based dose titration is thought to yield the most appropriate dose for a given patient (Pliszka et al., 2006). When medication is used, the prescribing physician, parents and teacher should clearly define the target symptoms. Rating scales may be useful in helping gauge the effectiveness of the medication on the target symptoms (Cincinnati Children's Hospital Medical Center, 2004; Pliszka, 2003; Steinhoff, 2004; Reeves and Schweitzer, 2004; Biederman and Spencer, 2004).

Selection of short vs. longer-acting preparations of methylphenidate and amphetamines should be based on the individual's symptom profile, history of response to an agent in the patient's family, ease of administration, likelihood of non-compliance if a school-day dose is required (Pliszka, 2006), abuse potential and adverse effects. Also, varying the wear time of the methylphenidate transdermal system or reducing an oral dose of one-daily methylphenidate in children can regulate the duration of the medication effect. This may be done in order to accommodate to the schedules of the patient. This reduction in exposure to methylphenidate results in shorter coverage of ADHD symptoms but fewer late afternoon or early evening drug side effects and insomnia (Wilens et al. 2008; Faraone et al. 2009). Stimulants should be used cautiously or withheld when there is suspicion of untreated mania, psychosis, substance abuse, tic disorder or concern about growth retardation (Pliszka et al., 2006; Steinhoff, 2004; Reeves and Schweitzer, 2004; Biederman and Spencer, 2004).

Stimulants are not effective in relieving core ADHD symptoms for 10 percent to 30 percent of patients, and negative side effects, including headache, insomnia, abdominal pain, blood pressure changes, appetite reduction, tics, weight loss and reductions in growth rate for children are common (Lindsay 2006; Kratochvil et al., 2005; Sadeh et al., 2006; Cortese et al., 2006). There is also some preliminary evidence that long-acting amphetamines or methylphenidate medications may produce rebound effects that may hinder late evening or early morning driving safety in adolescent male drivers (Cox et al., 2008). However, typical parental concerns, e.g., beliefs that there is haphazard diagnosing and over-prescribing, that school alternative programs are being neglected and that the causes of symptoms are only social and cultural, are not supported by research (Safer, 2000).

In a very small number of children (0.16 per million prescriptions and 0.53 per million prescriptions for methylphenidate and amphetamine, respectively) stimulant use has been associated with sudden death, usually from adverse cardiovascular events (Gephart, 2006). In May 2008, a joint advisory statement of the American Academy of Pediatrics (AAP) and the American Hospital Association (AHA), with endorsement by the American Academy of Child and Adolescent Psychiatry, the American College of Cardiology, Children and Adults with Attention-Deficit/Hyperactivity Disorder, the National Initiative for Children's Healthcare Quality and the Society for Developmental and Behavioral Pediatrics, was issued to address controversies in cardiac assessment prior to stimulant treatment for ADHD:

- An AHA Scientific Statement issued in April 2008 included a review of data that show children with heart conditions have a higher incidence of ADHD.

- Because certain heart conditions in children may be difficult (even, in some cases, impossible) to detect, the AAP and AHA feel that it is prudent to carefully assess children for heart conditions, if they need to receive treatment with drugs for ADHD.
- Obtaining a patient and family health history* and doing a physical exam focused on cardiovascular disease risk factors (Class I recommendations in the statement) are recommended by the AAP and AHA for assessing the patient before treating with drugs for ADHD.
- Acquiring an ECG is a Class IIa recommendation. This means it is *reasonable* for a physician to *consider* obtaining an ECG as part of the evaluation of children being considered for stimulant drug therapy, but this should be at the physician's judgment, and it is *not mandatory* to obtain one.
- Treatment of a patient with ADHD should not be withheld because an ECG is not done. The child's physician is the best person to make the assessment about whether there is a need for an ECG.
- Medications that treat ADHD have not been shown to cause heart conditions nor have they been demonstrated to cause sudden cardiac death. However, some of these medications can increase or decrease heart rate and blood pressure. While these side effects are not usually considered dangerous, they should be monitored in children with heart conditions as the physician feels necessary. (AHA Newsroom, 2008)

* Specifically, the AAP ADHD guideline notes "It is important to expand the history to include the specific cardiac symptoms, Wolf-Parkinson-White syndrome, sudden death in the family, hypertrophic cardiomyopathy, and long QT syndrome" (AAP Subcommittee, 2011, p.10).

Another previously reported safety concern for treatment with methylphenidate and mixed amphetamine salts was whether these drugs induce chromosomal damage in peripheral blood lymphocytes of children with ADHD posing an increased risk for cancer. A more recent study found that treatment with these drugs for three months did not induce cryogenetic damage (i.e., structural aberration, micronuclei and sister chromatid exchanges) in children, but that longer-term effects of these drugs on chromosomal changes still need to be investigated (Witt et al., 2008).

Concern about the potential for abuse of stimulant medications is legitimate, and there have been reports of children/adolescents giving or selling their medication to others. Abuse potential can be decreased by using long-acting stimulant preparations or drugs from other classes with established efficacy in treating ADHD with no abuse potential (i.e., atomoxetine or extended-release preparations of guanfacine or clonidine discussed in the following sections). Stimulants appear to have a protective effect against the development of a substance use disorder in children and adolescents, with a significant reduction of risk (Wilens et al., 2003). The AAP ADHD guideline specifies the following stimulant medications having less abuse potential: (1) lisdexamfetamine; (2) dermal methylphenidate; or (3) OROS (sustained release) methylphenidate due either to their chemical composition or preparation, making extraction of the stimulant more difficult (AAP Subcommittee on ADHD, 2011).

Atomoxetine

Atomoxetine, a non-stimulant, selective norepinephrine reuptake inhibitor, was introduced in 2002 as an effective first line medication for both childhood and adult ADHD. It is not a controlled substance, making prescribing more convenient for patients and physicians, as well as eliminating abuse potential. Another advantage is that it is relatively long-acting, with once daily dosing in most patients. Clinical research continues to demonstrate the efficacy and tolerability of atomoxetine in treating children and adults with ADHD (Adler, Spencer et al., 2008). Meta-analytic findings from six controlled trials show that atomoxetine is an effective and generally well-tolerated treatment of ADHD in both younger (6-7 years) and older children (8-12 years) (Kratochvil et al., 2008).

Atomoxetine shares some adverse effects with stimulants, but appears to have much less potential for aggravation of tics and insomnia. It is purported to be a good choice when anxiety, depression, tics, substance abuse and Oppositional Defiant Disorder (ODD) symptoms complicate ADHD in children or adults (Cheung et al., 2007; Bangs, Hazel et al., 2008; Wilens et al., 2008). There have been reports of sexual adverse effects. Clinicians have reported using atomoxetine in combination with stimulants when a patient has not responded adequately to a trial of either alone (Pliszka et al., 2006). For example, if atomoxetine did not remit symptoms during the day and stimulants did not remit symptoms in the evening, the two types of medications might productively be combined. The TCMAP panel included a stimulant-atomoxetine combination as a third line treatment in the absence of controlled data but warned that it should be used only after full monotherapy trials of two stimulants sequentially, and atomoxetine alone, have not provided full remission (Pliszka et al., 2006).

Atomoxetine has been associated with six reported cases of hepatotoxicity but none of these cases resulted in a liver transplant. A Postmarket Review of the FDA cautions both patients and caregivers to be alert to the signs and symptoms of liver injury throughout atomoxetine treatment and directs prescribers to discontinue the drug if a patients presents with jaundice or laboratory evidence of hepatotoxicity (FDA, 2009; Pliszka et al., 2006; Steinhoff, 2004; Reeves and Schweitzer, 2004; Biederman and Spencer, 2004). In addition, atomoxetine has a black box warning from the FDA regarding possible increased suicidality (Lindsay, 2006). More recent meta-analytic findings also showed that although uncommon, suicidal ideation was significantly more frequent in pediatric ADHD patients treated with atomoxetine compared to those treated with placebo. However, no patients in atomoxetine ADHD clinical trials committed suicide (Bangs, Tauscher-Wisniewski et al. 2008).

Atomoxetine has not been found as effective at treating primary ADHD symptoms as the stimulants and has more recently come to be considered a second-line treatment (American Academy of Child and Adolescent Psychiatry, 2006; Pliszka et al., 2006; King, 2006; Gibson, 2006; Soreff, 2009; Newcorn et al., 2008; Newcorn et al., 2009). New clinical trial data have shown that while both treatment with atomoxetine or osmotically-released methylphenidate produced robust improvements in ADHD symptoms, response to osmotically-released methylphenidate was superior to that for atomoxetine. Also, approximately one-third of the patients in this large (n=516), placebo-controlled, double-blind, cross-over study responded better to one or the other suggesting that there may be preferential responders. Researchers argued that this supports the practice of changing to a different class of medication if there is a poor response to or tolerance of the first agent (Newcorn et al. 2008). Similarly, The Integrated Data Exploratory Analysis Study showed that the clinical response to atomoxetine was bimodal in that most subjects were either responders (47 percent) or

non-responders (40 percent) or showing a minimal response (13 percent). No demographic or clinical factors were associated with these divergent profiles of response, but patients who ultimately achieve a good response show at least a partial response by the fourth week of treatment (Newcorn, 2009).

Antidepressants

Third-line medications used to treat ADHD include bupropion and tricyclic antidepressants (TCAs). Bupropion is a weakly dopaminergic and adrenergic agent and is available in slow-release forms. Meta-analytic findings of bupropion clinical trials indicated a beneficial effect compared with placebo for improvement of ADHD symptoms in adult patients (Verbeeck et al., 2009). Additionally, in at least one study, it has shown efficacy comparable to methylphenidate. It may be a useful agent in patients with comorbid unipolar and bipolar depression, anxiety disorders and/or substance abuse including the diversion of psychostimulant prescriptions (Verbeek, et al., 2009). Bupropion carries a higher risk of seizures than most other antidepressant medications, especially at higher doses, and should not be used in patients with a history of seizures. It should be used with caution in children with a history of eating disorder (Kratochvil et al., 2006b; Pliszka et al., 2006).

Before the advent of atomoxetine, tricyclic antidepressants (e.g., imipramine and nortriptyline) were the primary alternative to stimulant treatment of ADHD having shown efficacy in symptom reduction in ADHD. Desipramine use in children and adolescents should be avoided due to reports of sudden death (Amitai and Frischer, 2006; Pliszka et al., 2006). TCAs can be lethal in overdose. Children being treated with TCAs should be monitored with electrocardiogram at baseline and on stable dosing. For these reasons, there has been a decline in the use of TCAs for the treatment of ADHD (Schatzberg et al., 2010).

Antidepressants have been the subject of concerns regarding possible increased suicidal behavior in children, adolescents and young adults (Hammad et al., 2006), especially at initiation and around changes in dosing. The FDA identified specific antidepressants in a 2004 analysis and eventually directed manufacturers of all antidepressants to include a boxed warning and expanded warning statements alerting clinicians to an increased risk of suicidal thinking and behavior in children and adolescents being treated with these agents (U.S. Food and Drug Administration, 2004a, 2004b, 2004c; 2005a). Clinical evidence, however, has not been conclusive in guiding clinicians toward or away from use of these agents in children and young adults (Bridge et al., 2007; Hughes et al., 2007).

In the absence of definitive evidence from clinical literature, FDA advisories or other credible sources determining that the risk of increased suicidality for patients treated with antidepressants makes their use inadvisable, Magellan's position remains that clinical evidence strongly supports the use and effectiveness of antidepressant medications in all age groups, and that careful, frequent and proactive monitoring for changes in status that could indicate suicidality is crucial to preserving the safety of these patients (U.S. Food and Drug Administration, 2004a, 2004b; 2004c; 2005a; Hughes et al., 2007; American Academy of Child and Adolescent Psychiatry 2007; Cheung et al., 2007; Williams et al., 2009; Marshall et al. 2010). When a current or past history of suicidality is present, such monitoring should occur at every session. In addition, Magellan recommends that the clinician contact patients who miss appointments, especially when there are reasonable grounds for concern about safety. Further, prescribing physicians and other clinicians involved in the care of patients taking antidepressants, as well as patients and their families, should stay alert and watchful for

warning signs of possible increased suicidality and take prompt action if any adverse effects are observed (Hughes et al., 2007).

Other Medications

Modafinil does not have FDA approval for the treatment of ADHD, but there are reports of its usefulness in children, adolescents, and adults (Pliszka, 2003; Waxmonsky, 2003; Steinhoff, 2004; Biederman and Spencer, 2004; Spencer et al., 2002; Lindsay, 2006; Ballon, 2006; Kahbazi et al., 2009). However, more research is needed to establish the safety and efficacy of this agent for ADHD treatment (Pliszka et al., 2006).

Alpha-adrenergic agonists (e.g., clonidine and guanfacine) effect ADHD symptoms by affecting the noradrenergic system and generally have greater benefit for hyperactivity/ impulsivity symptoms than for inattention. In 2009, the FDA approved guanfacine extended release tablets for the once-daily treatment of ADHD in children and adolescents ages six to 17 years. The approval was based on data from two similarly designed phase three double-blind parallel group trials of 669 children and adolescents. Significant clinical improvement was demonstrated for patients who were randomized to receive guanfacine once daily and uptitrated by 1 mg/week to a maintenance dose of 1 to 4 mg/day (Waknine, 2009; Biederman et al. 2008). Sedative side effects may limit their usefulness in daytime, but may make them useful at bedtime for assistance with sleep. Abrupt discontinuation of these agents can be associated with rebound hypertension. In 2010, the FDA also approved clonidine extended release tablets for the treatment of ADHD based on two double-blind parallel group trials of 433 children and adolescents (FDA.gov, 2011). There are reports of serious cardiac adverse effects with clonidine, especially when used in combination with stimulants. However, a more recent examination of the safety and tolerability of clonidine when used alone or with methylphenidate in children with ADHD reported that it appeared safe and well-tolerated in children with ADHD who do not have a baseline or family history of cardiovascular problems. Nonetheless, these researchers reported that 17 percent of their sample who were treated with clonidine experienced asymptomatic bradycardia (HR < 60 bpm) and underscored the need to regularly monitor changes in blood pressure and heart rate when prescribing clonidine. The AAP ADHD guideline also indicated that both guanfacine and clonidine have evidence to support their usage as adjunctive therapy with stimulants (Waxmonsky, 2003; Steinhoff, 2004; Biederman and Spencer, 2004; Spencer et al., 2002; Pliszka et al., 2006; Daviss et al., 2008, AAP Subcommittee on ADHD, 2011). Additionally, a randomized control trial (n=198) demonstrated the safety and clinical efficacy of using extended-release clonidine in combination with stimulant medication for children and adolescents with ADHD experiencing a partial response to stimulants (Kollins et al. 2011).

Off-label use of the second generation antipsychotic (SGA) drug, risperidone, has shown promise in reported study results of children with aggressive behavior associated with conduct disorder, disruptive behavior disorders, ADHD, and/or mental retardation/subaverage IQ (Correll et al. 2011; Agency for Healthcare Research and Quality 2011). These findings need to be corroborated with supporting evidence from future clinical studies comparing antipsychotics with behavioral intervention, combination treatments and placebo (Correll et al. 2011).

The central nervous system stimulant, pemoline, has fallen from use due to a risk of liver failure that is 10-25 times greater than the risk in the general population (Marotta and Roberts, 1998). In 2005, the FDA concluded that the risks associated with this drug outweigh any potential benefits and the manufacturer stopped sales and marketing of the drug in the United States (FDA, 2005).

Psychosocial Treatments

Psychosocial treatments for ADHD include both psycho educational interventions and psychotherapeutic interventions, such as behavior modification, parent behavior training and family therapy.

Psychoeducation, which should be delivered to all patients with ADHD and in the case of minors, to the parents or other caregivers as well, should include information about:

- ADHD, its presentation in the patient, the plan of treatment and rationale, available treatments, including medications and their benefits, risks, side effects and psychotherapeutic interventions
- Co-morbid disorders, if any, and how treatment of these is integrated with ADHD treatment
- Social and peer support available locally for children and adults with ADHD and their families, such as CHADD (Children and Adults with Attention-Deficit/Hyperactivity Disorder) activities and resources
- Rights to educational needs assessments through the school system, if appropriate, under the Individuals with Disabilities in Education Act (IDEA) and Section 504 of the Civil Rights Act
- Increased risk for suicidal behavior and early warning signs of possible increases in such behavior, if antidepressants or atomoxetine are prescribed.

Although carefully titrated pharmacotherapy with stimulants has been found superior to psychosocial treatments and combination treatments in reducing ADHD core symptoms, most patients experience social, familial, occupational and/or educational effects of the disorder that are responsive to psychotherapeutic intervention (MTA Cooperative Group, 1999a, 1999b; Correll et al. 2011). Psychotherapeutic interventions can be administered in combination with medications, or, in rare cases, as the sole intervention, such as after the failure of adequate trials of first, second, third and fourth line medications and/or in response to parental refusal to allow medication or inordinate health and safety risks associated with medication treatment (American Academy of Child and Adolescent Psychiatry, 2007; Pliszka et al., 2006). In child/adolescent patients treated with medication and who have co-morbid mental health disorders and/or unsupportive, chaotic or conflict-ridden family environments, the use of family interventions (American Academy of Child and Adolescent Psychiatry, 2007; Chronis 2006) is recommended. In addition, the revised AAP ADHD guideline (2011) recommends the initiation of ADHD treatment in preschool-aged children (ages 4-5 years) with behavioral therapy *alone* and in using medication only for those pre-school aged children who have moderate to severe dysfunction (AAP Subcommittee on ADHD, 2011).

Family interventions that coach parents on contingency management methods have been shown to be useful in decreasing punitive and ineffective parenting styles that may perpetuate behavioral problems in children and adolescents with ADHD. Behavioral models that focused on parent training specifically for fathers also have resulted in symptom improvement in children along with increased satisfaction and engagement in the treatment process by the fathers (Chronis, 2006; Fabiano et al., 2009). Manual-based parent training has been evaluated in two dozen studies noting that it is associated with less severe parental ratings of problem behavior in their children, and fewer rater-observed, negative child-parent interactions, with an average effect size of .87 (Chronis, 2006).

Classroom behavior-management techniques have been found to be effective, particularly the daily report card intervention that addresses child-specific targeted improvements with measurable goals (Chronis 2006; Evans and Youngstrom, 2006). Teachers are taught to use points and token reward systems, time outs, planned ignoring and response costs, as well as to provide a highly structured environment by setting schedules for the child's use throughout the day. Limiting distraction during class and study, both in school and at home, may be helpful. Academic interventions and special education placement may be necessary.

Particularly in children or adolescents for whom aggressive behavior is a problem or who have a co-morbid conduct disorder, behavioral modification techniques that address social skills should be a component of treatment (Chronis, 2006). The short-term effectiveness of behavioral therapy has been demonstrated, but there is little evidence to show that the gains made during therapy are maintained after treatment is stopped and behavioral modification may be best delivered in combination with medication treatment (Pliszka et al., 2006; MTA Cooperative Group, 1999a, 1999b; 2004a, 2004b).

After-school programs are in early stages of development using manual-based treatment focused on targeted educational, social, and recreational skills, home-work completion, and school and home behavior. In one clinical trial, individual counselors provided support to students in achieving goals and implemented a behavioral-point system to reward both individual and group behaviors. Parents also participated to review program content and to learn skills for managing home behaviors. Preliminary findings for these public middle school students showed modest beneficial effects on behavioral and academic outcomes. Continued research on these types of after-school interventions is necessary (Molina et al., 2008).

Adults

Psychotherapeutic treatment of ADHD has been studied far less in adults than in children, and consensus guidelines are not available. Cognitive behavioral therapy, life-skills coaching and training in organizational skills appear useful, but evidence to support their long-term benefit in reducing core symptoms of ADHD is lacking. Accepted psychotherapies can be used to treat co-morbid disorders in adults, as well as children, with ADHD (Wilens et al., 2004).

Alternative Therapies

Numerous case and controlled-group studies have been published regarding use of EEG biofeedback (aka neurofeedback) in the treatment of ADHD (Gevensleben, 2010/2009 et al., 2009; Strehl et al., 2006; Monastra 2005a, 2005b; Carmody 2001; Fuchs 2003; Linden 1996; Monastra 2002; Rossiter 1995). EEG biofeedback uses analysis of brain wave patterns (i.e., beta and theta activity, sensorimotor rhythms) and/or slow cortical potentials (negative or positive EEG polarizations) along with a reward system to help patients with ADHD change patterns of wave activity in their brains. Several published case studies have suggested that EEG biofeedback is an effective treatment for the primary symptoms of ADHD, especially attention, hyperactivity and impulsivity, with no adverse effects and persistence of treatment effects over time (Gevensleben, et al., 2010/2009; Strehl et al., 2006; Monastra 2005a, 2005b; Carmody 2001; Fuchs 2003; Linden 1996; Monastra 2002; Rossiter 1995). However, the limitations of both study size and design create

significant questions about the efficacy of this treatment modality (Monastra, 2005a, 2005b) and further research is needed if benefits from this and other alternative treatments are to be established.

Additional alternative treatments including the use of St. John's Wort (Weber et al., 2008), homeopathy (Heirs et al., 2007), dietary sugar reduction and dietary supplementation with herbs and vitamins, have been unsupported by research (American Academy of Child and Adolescent Psychiatry, 2006). Also, there are very limited data supporting the premise that food dyes, preservatives or other additives adversely influence behavior in children (Cruz et al., 2006). Conversely, there have been other more recent studies of alternative treatments that have shown positive results. Findings from a randomized clinical trial conducted in Italy showed that compared to placebo, the nutritional supplement L-acetylcarnitine (LAC) was effective for ADHD symptoms in Fragile X Syndrome Boys. LAC is the acetyl ester of L-carnitine, a fundamental compound that plays an essential role in the metabolism of fatty acids in mitochondria. These results were promising because it is estimated that over 70 percent of FXS boys meet diagnostic criteria for ADHD. Researchers reported previous observations that have shown while FXS boys respond to stimulants, their mood becomes unstable at higher doses necessitating a need for alternative pharmacological treatment (Torrioli et al., 2008).

Another scientific study reported promising results for iron supplementation (80 mg/day) in iron-deficient (30ng/mL) non-anemic children with ADHD where clinical improvements in symptoms were significant. Here authors suggested that careful dietary history and necessary lab work be done and then re-evaluated prior to instituting treatment. (Konofal et al., 2008) Another clinical trial revealed that supplementation with omega-3/omega-6 fatty acids did not result in symptom improvement for the majority of ADHD subjects. There was, however, a distinct subgroup of patients in this study characterized by inattention and associated neurodevelopmental disorders (i.e., Developmental Coordination Disorder, Reading Disorder and Disorder of Written Expression) who responded with meaningful reduction of ADHD symptoms after six months of treatment (Johnson et al., 2009). Other studies have reported promising findings on the impact of polyunsaturated fatty acids (PUFA) in the treatment of ADHD symptoms and attendant emotional and sleep problems. One systematic review supported daily supplementation of both combination long-chain *n*-3 and *n*-6 fatty acids and another large observational study (n=810) reported beneficial effects of combination omega-3 and omega-6 fatty acids along with supplemental zinc and magnesium in treating children with the disorder (Transler et al. 2010; Huss et al. 2010).

Level of Care

It is rare that a patient with a sole diagnosis of ADHD would require a hospital level of care. Usually, the need for an intensive level of care is based on the presence of symptoms associated with a comorbid condition. Such symptoms would likely be of the hostile or violent type associated with bipolar disorder, conduct disorder, oppositional defiant disorder, psychotic disorder, or adjustment disorder with disturbance of conduct. Alternatively, symptoms requiring a more intensive level of care could be associated with risk of self-harm[4]* or hospitalization for actual injury from being the victim of interpersonal violence, since children and adolescents with ADHD are at higher risk for suicidal behavior and interpersonal violence (Lam 2005). Of these, conduct disorder would present

* Magellan has adopted a clinical practice guideline that addresses suicidal behavior: the *Magellan Clinical Practice Guideline for Assessing and Managing the Suicidal Patient* (Magellan Health Services, 2012). Clinicians are referred to that document for additional information on managing suicidal behavior in patients with ADHD.

most often with a pattern of violent behavior toward people and/or animals that potentially at times could require the safety of a hospital level of care, although for this population there have been effective multi-focused treatment approaches that include both medication and psychosocial treatments (Connor et al., 2006).

Most often, treatment for ADHD and co-morbidities occurs in an outpatient setting. When aggressive behavior is not responding to outpatient care, in-home treatment may be an adjunctive or alternative course. In-home treatment can be an effective way to deliver family interventions, including modeling ways for parents to deal with their child's aggressive and hostile behaviors and providing problem-solving and social skills training.

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