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## ADHD and Comorbid Conditions

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### 1. Introduction

ADHD stands for Attention Deficit Hyperactivity Disorder. Comorbidities is the medical term for two or more disorders that occur at the same time with the primary disease or disorder. In this article we will talk about ADHD comorbidity.

ADHD (Attention Deficit Hyperactivity) is the most underdiagnosed condition in children. It is also a misdiagnosed disorder. The main reason for this is comorbidity since the comorbid conditions have many similar symptoms to ADHD. The million-dollar question though is: Where does ADHD stop and where do comorbid conditions take over?

ADHD affects 3-6% of school children (Mirsky, AF 2001). The risk of comorbidity with psychiatric disorders is high, and the presence of comorbid conditions warrants a special consideration in treatment of patient with these disorders. A child specifically with ADHD will likely have other difficulties.

Two-thirds of US children with ADHD will have a comorbid learning disorder, another mental health disorder, or a neuro-developmental disorder. Unraveling psychiatric comorbidity can often be a chicken or egg conundrum. Which came first: the ADHD or the supposed comorbidity? The presence of comorbidity conditions makes the diagnosis of ADHD more difficult.

The survey published by National Survey of Children Health, which involved over 60,000 children ages 6-17 years including over 5,000 with ADHD, showed that psychiatric and physical comorbidities were very common in children with ADHD. (Larson 2011)

Overall, 67% of ADHD children had at least one other mental health or neuro-developmental disorder compared to 11% of children without ADHD. 33% had one comorbidity disorder, 16% had two, and 18% had three or more. ADHD was associated with elevated prevalence of the following (Phend):

1. Learning disorders (46% vs 5%)
2. Conduct disorder (27% vs 2%)
3. Anxiety (18% vs 2%)
4. Depression (14% vs 1%)
5. Speech problems 12% vs 3%)
6. Autism spectrum Disorder (6% vs 0.6%)
7. Epilepsy/Seizures (2.6% vs 0.6%)

Psychiatric	Physical
1. Depression	1. Enuresis
2. Anxiety	2. Sleep Disorders
3. Bipolar Disorder (BD)	3. Eczema
4. Conduct Disorder (CD)	4. Allergies
5. Obsessive Compulsive Disorder (OCD)	5. Developmental Coordination Disorder (Clumsy)
6. Substance Abuse	6. Fibromyalgia
7. Tics and Tourette's Disorder (TD)	7. Perthes Disease
8. Pervasive Developmental Disorder (PDD)	8. Hypertension
9. Learning Disorder	9. Height and Weight Problems
10. Developmental Dyslexia	10. Epilepsy
11. Suicidality	

Table 1.

The core symptoms of ADHD are inattention, impulsivity and hyperactivity. Children with ADHD often have difficulty in concentration, are easily distractible, and are disorganized, hyper and impulsive. These symptoms of ADHD often are seen in comorbid conditions, as well. Various studies have looked into this overlapping of symptoms and provided evidence that ADHD is not artifact when shared with other psychiatric disorders and the comorbid conditions themselves are not artifact of overlapping symptoms and diagnostic criteria. (Farone2007)

There is a complex integrity between ADHD and commonly occurring comorbid conditions such as ODD, CD, etc. Comorbidity greatly influences presentation, diagnosis and prognosis, complicates treatment and significantly increases the morbidity and disease burden of ADHD. When ADHD is co-morbid with another psychiatric disorder, it is often the first disorder to develop. Children with severe ADHD symptoms have a higher chance of developing other psychiatric disorders.

When evaluating comorbidity, one should determine what the primary disorder and the symptoms present. If the primary condition fully explains the symptoms, a comorbid condition should not be diagnosed. If ADHD symptoms presents during episodes of bipolarity, ADHD would not be diagnosed. In practical life, which symptom causes the patient's impairment is difficult to determine when both disorders are chronic. If both conditions are contributing to patient's impairment, both ADHD and the comorbidity should be diagnosed and treated. This review will clarify how to diagnose and manage ADHD with comorbid psychiatric and other neuro-developmental disorders.

The term comorbidity first appeared in the psychological and psychiatry literature in the mid-1980s. Since that time, there has been a dramatic increase in the interest in this topic. In 1986, only 2 articles were published and by 1993, there were 243 articles. Since then, the number of articles has increased even further. It has been suggested that comorbidity has emerged as perhaps the single most important concept in psychiatry research.

## 2. Definition of comorbidity

A variety of definitions of comorbidity has been offered from the medical epidemiological perspective. Dr. Feinstein (1970) has defined co-morbidity as any distinct additional entity that has existed or may occur during the clinical course of the patient who has the index disease. Blashfield (2009,1994) has referred to the co-morbidity as a concordance of a different disease in the same individual. Likewise, Caron and Rutter have defined comorbidity as the simultaneous occurrence of 2 or more *unrelated* conditions.

As one can see from the definition, the term co-morbidity refers to the situation in which a person who has been diagnosed with one specific disorder is found to also meet the diagnostic criteria of one or more additional disorders. There has been a controversy regarding the use of this term, the primary reason highlighted by the definition of Carson and Rutter (1991). The word *unrelated* is the most relevant. One cannot be certain that an individual who meets diagnostic criteria for more than one psychiatric disorder actually has unrelated conditions. It has been suggested that what appears to be a separate disorder may actually be the result of overlapping diagnostic criteria or a different syndrome, like a variation of the underlying disorder, for example, anxiety disorders. What looks like a co-morbidity in younger children may reflect nonspecific expression of psychopathology associated with immature development of cognition and emotion, for example, anxiety and depression.

Both ADHD and co-morbidity disorders have a highly heterogeneous etiology, implying genetic and environmental risk factors. (Mick and Farone, 2008) Some authors have been advocated for distinct types of ADHD based on comorbid expressions (Barkley 2006) (Acosta, et al 2008).

Apart from the heterogeneity of ADHD, the overlap between comorbidity and differential diagnosis renders both clinical and etiology research and ADHD and comorbidity difficult. Conduct disorders, emotional disorders, tic disorders, autism spectrum disorders, bipolar disorders, or specific developmental disorders have been comorbid with ADHD but all these psychiatric conditions also have to be considered in the diagnostic process as a differential diagnosis. Comorbid disorders of ADHD may result in ADHD like symptoms; depressive symptoms, for example, may comprise inattention distractibility, aggression, and irritability: symptoms that could mimic the phenotype of ADHD. On the other hand, ADHD may be accompanied with the depressive disorders or result in depressive mood due to constant or repetitive psychological failure and discouragement. With this knowledge of these conditions, a clinician must be aware of the developmental course over time.

Concerning the temporal course of occurrence, comorbidities may be present before evidence of ADHD symptoms (pre-morbidity). The onset of the comorbid disorder coincides with the time the ADHD symptoms reach clinically significant level is called simultaneous comorbidity. However, the majority of co-morbidities seems to occur later in the course of disorder called post-morbidity (Taurine-2010).

## 3. Epidemiology

The mental disorders that children develop are commonly divided into two groups: disruptive or externalizing behavior disorders (Ex. ADHD and Conduct Disorders) and

emotional and internalizing behavior disorders (Ex. Anxiety and Depression). Concerning psychiatric comorbidity, externalizing disorders were found to be more frequently associated with ADHD; comorbidity rates range up to 90% (Spencer T 1999, Wilens TE 2002) for externalizing and 50% for internalizing disorders. (Jensen et al. 2001) A 5-year follow-up study in girls with ADHD ranged 6-18 years in comparison with girls without ADHD showed elevated rates of comorbidity associated with the ADHD females. (Biederman et al. 2008 ) In line with the formal reports (Stinhausen et al. 2006), a sample of 122 children and adolescents with ADHD between the ages of 6-18 years recruited by the Department of Child and Adolescent Psychiatry in the University of Wurzburg showed that 73% of affected individuals had one or more further psychiatric diagnosis according to a semi-structured interview. The most frequent comorbidity was oppositional defiant disorder (ODD) at 46.9%, followed by mood disorder at 27.9%, CD and elimination disorder (EID) at 18.5%, dyslexia at 17.6%, and anxiety at 16.7%, and TD (Tourette disorders) at 9.5% (Taurin 2010). In adult ADHD patients, lifetime comorbidity with mood disorder was 57.3% and anxiety disorder 27.2% (Spencer T. 1999), surpassing the already considerable rates following the pediatric population. Adults have a higher prevalence than children for substance abuse disorders, with a prevalence rate of 45.0% (Jacob et al. 2007). Personality disorders can develop throughout childhood and adolescent, but It is not until adulthood when personality disorders are able to be diagnosed in ADHD, for example antisocial PD (personality disorder). In childhood and adolescence, these potential personality disorders are known as conduct disorders. The presence of conduct disorders in children with ADHD has been found to be significant correlated with aggressive behavior or delinquency in adolescence and with the high road of antisocial personality in adult life. There has been awareness of a link between ADHD and emotional disorders (anxiety and depressive disorders), which has an important implication for a clinician assessing children with ADHD (that they don't miss the underlying internalizing symptoms because of the predominate presentation). Longitudinal research with children and ADHD and co-morbid major depression suggests that a concurrence of the two disorders may be associated with a particularly poor outcome. The high prevalence of developmental delay and neuropsychiatric disorders has long been established and may be indicative of an underlying developmental etiological pathway.

#### 4. Etiological consideration

Many people assume that if the child is hyperactive, the brain must also be overactive. This is not the case, as seen in brain scan research by Dr. Zametkin. In his study, the glucose metabolism was measured in the brain, which is an indication of energy or mental activity. When given a problem to think about, the normal control subject brain indicates energy being used to think about the problem posed, but ADHD subjects' brains show little activity. Does these data show that ADHD is strictly a biological problem? No. ADHD appears to be influenced by environmental factors such as home environment, classroom structures and peers. Saying that ADHD is influenced by environmental factors such as home or classroom environment doesn't mean that ADHD is caused by faulty parenting or education. Rather it means that we have an opportunity to make things better or worse. The etiology to ADHD is complex and includes neuroanatomic abnormalities, neurobiological dysregulation, CNS insults, genetics and environmental factors. The neurobiological abnormalities are in the prefrontal cortex and anterior cingulate gyrus involvement has been

demonstrated. The prefrontal cortex is involved in executive functioning, while the cingulate gyrus is involved in focusing attention and mediating response selection. Among individuals with ADHD, consistent findings have shown image regarding decreased dopaminergic transmission in these areas. A dopamine 4 (D4 receptor) is related to cognitive and emotional functioning is densely in prefrontal cortex of the brain. Genetics studies indicate the DRD4-7 repeat allele locus at higher rates among children with ADHD than among controls. (Leslie E. Parker 2010) Other numerous environmental factors predispose individuals to ADHD, including maternal smoking or alcohol abuse and low birth weight, which may have both genetic and environmental causes.

Other conditions must be ruled out before a diagnosis of ADHD is made because there are many other possibilities or explanations for hyperactive impulsive behavior. A few of the conditions are learning disability (that leads to poor school performance), frustrations, and a behavior pattern where the child stops paying attention or gives up. Attention lapses can be caused by partial complex seizure, obsessive thoughts, or silent impulsive rituals. A middle ear infection, causing an intermittent hearing problem, interferes with a child's ability to respond to an orally presented request. Disruptive unresponsive behavior can be due to anxiety, depression, or bipolar disorders. Environmental factors or stresses, such as divorce in the family, can lead to restlessness or inattention.

If executive dysfunction is a problem, the child often fails to give close attention to details or makes careless mistakes at school or during other activities, has difficulty sustaining attention in tasks or play, often does not follow thorough instructions, fails to finish school work or duties at the workplace, often has difficulty organizing tasks and activities, avoids/dislikes/is reluctant to engage in the task required to sustain mental effort like homework. In order to clarify the diagnostic issues, the neuropsychological assessment may be helpful. Although a variety of professionals including psychologists may be licensed to diagnose ADHD, in my opinion, the diagnosis should be confirmed by a developmental pediatrician, board certified neurologist or adolescence psychiatrist who can rule out other medical problems that mimic the symptoms of ADHD and offer treatment.

## 5. Clinical presentation

ADHD has historically been identified primarily in boys, but a substantial number of girls suffer from ADHD as well. The male to female ratio is approximately 10:1 (Biederman J 1999). In a comparative study of boys and girls with ADHD, both sexes were comparable in respect to rate of inattention, impulsivity, hyperactivity and comorbidity. However, rates of conduct disorders varied between boys and girls (20% in boys versus 8% in girls). Oppositional defiant disorders were manifested in approximately 62% of boys compared to 32% of the girls (Fredman 2001).

ADHD is highly comorbid with other psychiatric disorders. There has been controversy whether it exists as a primary disorder or only secondary to other psychiatric symptoms. The Nosological System advocates in the DSM that in the presence of two or more diagnoses, one should be considered primary and account for many of the symptoms observed in the secondary syndrome. Thus the mounting evidence of many conditions existing concurrently with ADHD each modifies the overall clinical presentation and treatment responses. The comorbid conditions should be considered as simultaneously present in order to broaden our understanding and maximizing the treatment.

A depressed patient demonstrates diminished concentration, whereas an individual with bipolar disorder often manifests psychomotor agitation and destructibility. It may be difficult to differentiate these from the cardinal symptoms of ADHD. There are several ways to deal with the symptom overlap through research and clinical settings. Subtraction method requires that the same absolute number of symptoms be present to diagnose either disorder except shared symptoms are subtracted or removed from the diagnostic consideration. Some people think that the patient with comorbid depression and ADHD still retains the diagnosis of ADHD whether subtraction or proportional method was used. The longterm follow-up study had demonstrated the individual with ADHD and comorbid disorder had poor prognosis and greater hospitalization rate than those with ADHD alone.

Pharmacological studies demonstrated a clinical contribution of each of the comorbid disorders and treatment strategies. For example, an individual with a comorbid ADHD bipolar may be first treated with a stimulant. Alternatively, if a mood stabilizer is used, significant improvement may be expected. If symptoms of ADHD continue to persist after a mood stabilizer, this supports a diagnosis of co-occurring diagnosis. When a stimulant addition is indicated, therefore, both comorbid conditions are equally treated, the ADHD symptoms may not be remit.

### 5.1 Identify comorbidity with handy tools

There are many efficient tools to gather data in a structured manner that quickly pinpoint ADHD, which further helps your clinical acumen. In a busy primary care setting, a child behavior check list can be used as a handout or behavior assessment scale for children. Both of these generally have very similar type of output. These are very easy to score, and one can look to the parent as well as teachers to help with the scoring.

## 6. Psychological problems associated with ADHD

### 6.1 Depression

*Does the person appear sad, blue or down and how can you tell? Is the person irritable, cranky, and moody? What does the person do in her spare time? Has the person been doing the activity once enjoyed? Does the person talk about suicide or about uselessness of life, has the person attempted suicide?*

A total of 10-40% (Spencer, T 1999) of children and adolescents with ADHD show depression with symptomology of low or irritated mood, loss of interest and pleasure of usually enjoyable activities, sleep disturbances, and reduced appetite. Depressive disorders in youth with ADHD typically occur as a post comorbidity several years after the onset of ADHD. ADHD rates in depressed children and adults range up to 57% (Angold, A 1993). Depression may be a reaction to unpredictable environmental stressors such as being rejected by peers, getting made fun of by others, or thinking that school is a negative and overwhelming place. In these cases, a separate diagnosis and treatment strategy is not necessary because depression is occurring in response to the ADHD and will likely decrease when ADHD symptoms are treated. In other instances, depression may run in the family or may be more directly linked to biological or genetic causes; therefore, a separate diagnosis and specific treatment for symptoms for depression would be more appropriate. Distinguishing between an emotional complication of ADHD and a separate depressive disorder may be very difficult. A therapist

would look for an indication whether these depression or ADHD symptoms came first and whether there is a history of depression or ADHD in the family. It is very important to take depressive symptoms seriously, regardless of their cause. Children with ADHD and depression can have suicidal thoughts and statements/behavior should be monitored and addressed by a mental health clinician. Since these symptoms may attribute to normal childhood behavior, the diagnosis of depression may be missed for a long time. Family studies suggest there is some genetic link between depression and ADHD. This suggests genetics can contribute to solely ADHD, solely depression, or both disorders.

With regard to the treatment, most treatments that are effective for ADHD, like stimulants, do not significantly improve depression. In addition, treatments for mood disorders are generally not helpful for ADHD. In the presence of comorbid mood disorder, stimulants themselves are less effective for ADHD. Non-stimulant treatments that are noradrenergic but not serotonergic are effective for ADHD. In contrast, serotonergic medicine is effective for juvenile depression but not for ADHD.

Bupropion, an agent that affects both noradrenergic and dopadrenergic neurotransmitters, has been shown to be efficacious for adolescents with ADHD and comorbid depression. It is important that both disorders be treated simultaneously. Studies show using the combination of stimulant and SSRI for comorbid ADHD and severe depression are consistent with this observation. However, one should be cautious in using an SSRI in children with mild to moderate depression, due to a black box warning by the FD because SSRIs may increase suicidal tendencies. If an SSRI is used, the child should be monitored closely, and the patient and guardian should be aware of this warning.

## 6.2 Suicidality

Children with ADHD and depression are at an increased risk for suicide. In boys, major depression and social phobia are risk factors for suicide, as opposed to post-traumatic disorder in girls.

Early stimulant treatment of ADHD reduces the prevalence of depression as a comorbidity, which reduces the risk for future suicidality.

## 6.3 Bipolar disorders

*Are there times where the person thinks he or she is able to do anything he or she want? Does the person appear unusually energetic at times or almost high without drugs? Does the person miss a lot of sleep at night but still acts energetic the next day? Does the person appear to have thoughts that appear so fast that it is impossible to keep up with them?*

Bipolar disorder may occur with ADHD or may mimic its symptoms. Half of the boys and one-fourth of the girls with bipolar disorder also meet the criteria for ADHD. Children and adolescents with bipolar disorder often show strong emotional feelings, hyperactive behavior, overbearing manner, and difficulty waking up in the morning. Children and adolescents with severe bipolar symptoms may have excessive and lengthy temper tantrums that are destructive and often based on gross distortion of objective events. For example, when a friend wants to a play different game, bipolar children may think the friend is trying to purposefully be mean. The child gets angry at such mistreatment. This

may result in a temper tantrum. Other symptoms include excessive talking, increased activity, inappropriate actions and verbal responses in social situations, lack of inhibition, chronic irritability, and distractibility. The prevalence is up to 20% (Singh, MK 2006) (Strober, M 1982). According to an Italian study, 24% of 7-18 year old clinic attendees with bipolar disease had existing ADHD (Masi, G 2003).

The child behavior check list score better discriminates between children with ADHD, comorbid bipolar disorders and control subjects.

For pharmacological treatment, mood stabilizers are the first line treatment for periodic bipolar disorders. However, when ADHD symptoms are present, subjects may benefit from short-term co-concomitant treatment with a stimulant or a co-medication of a non-stimulant.

The etiology of comorbid pediatric bipolar and ADHD have distinct characteristics. Neuro imaging studies suggest general changes in prefrontal areas in both disorders. However, there are a few primary differences between the two patient groups in the areas in indifference control, working memory, planning cognitive flexibility and fluency. Several authors reported that ADHD with comorbid pediatric bipolar disorder is its own distinct form of ADHD (Biederman 2008).

Fifty percent of the prepubescent depressed children in one sample manifest bipolar disorder within ten years of the onset of depression (Geller et al, 2002 a). Another study found 20% of depressed adolescents in another sample had revealed a bipolar disorder within 1-4 years (Kowatch RA 2005). When comparing to the children with ADHD without mania, the manic children have significantly higher rates of major depression, psychosis, multiple anxiety, conduct disorder, or oppositional defiant disorder, as well as significantly greater impairment of psychosocial functioning.

As with depression, bipolar must be treated effectively with symptoms of ADHD to resolve comorbidity affecting the individual. An atypical anti-psychotic agent appears to be effective in the elimination of juvenile mania. In an open study, Risperdal was found to be effective anti-manic but did not help ADHD symptoms. Among bipolar adults comorbid for ADHD, Bupropion is effective for ADHD and depression but may lower the threshold for inducing mania.

#### **6.4 Oppositional defiant disorder**

*Does the person defy you or the teacher by simply saying no or ignoring you? Does the person appear to be annoyed easily and bothered by trivial things? Does the person appear to annoy other people on purpose? When and where does this happen? Does the person appear angry, hot tempered, resentful, or full of spite?*

ODD is most commonly associated with ADHD. Oppositional defiant disorder symptoms occur in as many as 21% to 60% (Cunningham 2002; Wilens, TE 2002) of children with ADHD. It is when the individual defies rules and in some cases acts out in anger and violence. ODD symptoms tend to occur more often with people whom the child is close to or knows well such as family or care givers. Children with comorbid ADHD and ODD may form an intermediate group between those who have ADHD alone and those with ADHD and conduct disorder. However, studies suggest that children with comorbid ODD and ADHD will always develop conduct disorder. It is just a matter of time before that happens.

## 6.5 Conduct disorder

*Does the person lie a lot? Does the person get into physical fights? Does the person try to hurt people? Has the person ever stolen or damaged people's property?*

About 20-45% of children with ADHD also meet criteria for conduct disorders. It is very low in children without ADHD. This disorder involves aggression towards people or animals, property destruction, stealing, and violation of rules of society (i.e. missing school or running away from home).

Both stimulant and non-stimulant medicines will reduce aggressive behavior and antisocial acts, but a stimulant will work more rapidly. Mood stabilizers or atypical antipsychotics may be needed for highly aggressive cases. Besides pharmacotherapy, individual or family behavioral therapy may be required. Conduct disorder is a strong predictor for future substance abuse.

Medication just used for ADHD is also effective for treatment of comorbid ODD/CD as the first line of treatment. However, if ODD or CD persists, psychosocial treatment should be added. In clinical practice, it is not common to add atypical antipsychotics, but there is limited data to support this. (Kunwar, A 2007)

## 6.6 Anxiety

*Does the person appear to be nervous and anxious? Are there times when the person appears panicked, stricken, or frozen by anxiety? Does the person appear very shy compared to others his same age? Does the person repeat certain actions over and over like a ritual?*

Anxiety is a psychological and physiological state characterized by emotional, somatic, cognitive and behavioral issues. Anxiety is a well thought out, normal response to stress, but if the anxiety reaches its crest, it disturbs a person's normal routine. Anxiety with ADHD is a comorbidity with an estimated rate of 20-40%. Often general anxiety is thought to be the most prevalent disorder followed by social phobia, separation anxiety. Some children with ADHD may present with more than one anxiety disorder. Anxiety and ADHD may inhibit impulsivity so children with ADHD and comorbid anxiety may have less impulsivity but more inattention. For this reason, it is possible to overlook ADHD in children with anxiety (especially the inattentive types). Children with anxiety are often preoccupied with a fear that impairs their ability to focus on the task at hand. For anxious children who do not have ADHD, when their anxiety improves, their inattention improves, whereas children with comorbid ADHD/anxiety will continue to struggle with inattention even in the absence of an anxious episode.

It has been suggested that anxiety associated with ADHD is a product of the inability to function in daily life because of the social and cognitive limitations associated with ADHD rather than typical phobic/fearful behavior. In this case, early recognition and treatment of ADHD may itself improve anxiety. In a sub-group of an ADHD person with comorbid anxiety disorder, various therapeutic measures have been proven to be effective in reducing both ADHD and anxiety symptoms. Psycho stimulants plus behavior therapy, atomoxetine alone, or atomoxetine with a combination of stimulants and antidepressants can help treat these symptoms. However, comorbid anxiety symptoms in children and adults with ADHD were linked to poor treatment response with a psycho-stimulant. There is some evidence

that there is heritability between ADHD and comorbid anxiety disorders. There is also research suggesting ADHD and anxiety are independently transmitted in families (Freitag 2010).

It is very important to distinguish between the true anxiety disorders and those children who are experiencing anxiety in response to ADHD because treatment is very different. Stimulants, while helpful for ADHD symptoms, may actually worsen the symptoms of a true anxiety disorder.

### 6.7 Learning disorders of various kinds

*Even when the person is paying attention, is learning difficult? Are there certain subtypes that the person has extreme difficulty with? How does this person do in reading, writing, and mathematic? Has the person ever been tested for a learning disability?*

Over half of all children with ADHD also have learning disorders. ADHD, though it affects the ability to learn, is not a true learning disability. So treating the symptoms of ADHD will not correct the learning disorders that a child may have. A learning disability is a specific disorder that affects one of the four primary steps needed for learning. The steps are recording information (ex. input of a visual or auditory perception problem), understanding information (integration: ex. Sequencing and organization problem), storing information (placing information into memory), and retrieving information (memory: ex. Immediate recall of the recently learned information). Although ADHD may globally interfere with the success of these steps, it is the impulsivity, hyperactivity and distractibility that interfere with the learning process. ADHD does not specifically impact one of these four steps.

1. On IQ measurement, many studies have identified a fairly difficult profile of the neuropsychological test result in children with ADHD. This is seen commonly through certain attention loading subtests of commonly used IQ tests like the Coding Digit Span and the Wechsler scale. Two or more subtests on the Wechsler scale are often depressed relative to other subtests. Coding, digit response, arithmetic, and information subtests on the Wechsler scales are very often depressed related to the other subjects. Various tests of executive functions including Wisconsin card scoring test usually revealed moderate to major deficits. However, there are also those with ADHD who generally score low on all these tests without a particular learning disorder profile. 2. Overall decline in all IQ test values. 3. Higher than expected rate of subnormal intelligence in mental retardation/learning disability among children with ADHD 4. An increased rate of children with subnormal intelligence because the mistakenly diagnosed individual as suffering from ADHD.

Subnormal intelligence and ADHD: No formal study but clinical experience suggests that children with subnormal intelligence with no indices of specific subtest pattern of neuropsychological testing may show all typical symptoms of ADHD (particular symptoms of inattention is lack of persistence and forgetfulness).

Mental retardation/ learning disability and ADHD: Population studies show mental retardation may be 5-10 times as common in children with ADHD as compared children without ADHD. Though the rate of ADHD in mental retardation is rare, it is clear that relevance has increased beyond the level that is encountered in the population without

learning disabilities. In one study in the US, at least 15% of individuals with a profound level of mental retardation may meet criteria for ADHD even the mental age has been taken into account (Fox 1998).

Reading disorder, written expression and dysgraphia: Reading disorders are common in ADHD. About 25-40% with ADHD have major reading and writing difficulties (Shaywitz, RA 1992). Some studies suggest ADHD and reading disorders combined may be a visual motor problem, more severe than would be expected on the basis of simply adding a basic learning disorder to another. Disorders of written expression are characterized by significant impairment in writing, grammatically correct sentences and paragraph organization and occasionally with dysgraphia.

Mathematic disorders: The overlay between ADHD and mathematic disorder is considerably more. It appears it is more associated with an inattentive type of ADHD. Correlation of ADHD with learning disorders and cognitive delay is common.

Developmental Dyslexia: Some developmental disorders, such as developmental Dyslexia may manifest as a simultaneous comorbidity with ADHD. Although some ADHD symptoms are generally presented in infancy, it is not until the school age group that a full extent of symptoms becomes prevalent because of the highly structured school environment. The developmental dyslexia and dyscalculia become apparent when the child attends school and is required to read, write, and do calculations. Developmental dyslexia, especially reading and spelling disorders, is characterized by difficulty with reading comprehension, reading decoding and reading fluency and spelling. Impairment in multiple cognitive functions, such as executive functions, is common in ADHD and developmental dyslexia. The symptoms may negatively affect the developmental course of ADHD and will lead to stagnation of the process of learning to read. In some cases, ADHD and dyslexia may not share an etiological factor. A dyslexic child may be inattentive in some classes because he or she will be impaired due to generalized reading problems. Both dyslexia and ADHD are considered a complex polygenetic disorder and pose a shared genetic risk factor exerting a unique effect on either ADHD or dyslexia.

### **6.8 Pervasive developmental disorders/autism spectrum disorders**

It is commonly observed that children with ADHD frequently show symptoms of autism spectrum disorders and vice versa. Autism spectrum disorders are characterized by impairment in social interaction and communication and by restricted and repetitive behaviors (Frietag 2007). Intelligence is often impaired and the ability to learn and utilize new information is markedly restricted. Behavior symptoms may include hyperactivity, aggressiveness, impulsivity, short attention span and temper tantrums. Similarities between autism spectrum disorders and ADHD can lead to an early childhood diagnosis that suggest both are present. As this child grows up the difference becomes more distinct and one disorder often emerges as the true condition. Autism spectrum disorder children with additional ADHD symptoms showed exaggerated impairment in executive control and adaptive behavior. They show autistic traits as well as more severe oppositional defiance disorder type behavior than children with autism spectrum disorder only. For clarification of a possible etiological link between ADHD and autism spectrum disorders, well designed family based studies are required.

Children with Asperger's syndrome have a very high rate of concomitant ADHD symptoms. A community-based study indicated that up to 80% of all people meeting criteria for Asperger's, according to Gillberg, also meet the ADHD criteria (Ehlers 1993). Autistic features in ADHD will benefit from interventions that are appropriate for autistic children without ADHD.

### 6.9 Tics and Tourett's disorder

*Does the person have movement such as eye blinking, making an odd face, shrugging or moving an arm a lot that is not intentional? Does the person make noise without meaning to such as grunting, sniffing, or saying certain words? Do these symptoms get worse when person is under stress or anxiety and/or are these symptoms present while the person is sleeping?*

Tic disorders including Tourett's disorder (TD) are neuro-developmental disorders characterized by waxing and waning motor and /or phonic tics. There is data that suggests that tics and Tourett's are associated with 47% of ADHD (Sapiro AK 1988). There is evidence that the children displaying both disorders (Tourett's and ADHD) are more likely to be referred for assessment and treatment rather than be referred to learn which disorder alone is prevalent.

The core symptoms of tics disorders are motor and vocal tics which wax and wane over time. Tourett's shows concomitant symptoms of multiple motor tics and one or more vocal tics. About 85% of patients with Tourett's show associated neuropsychiatric problems. These are often responsible for psychosocial impairment. Tics can be found more frequently as a comorbidity to ADHD when there is a family history of tic disorders and or there is an early onset of a tic disorder of high severity of symptomology. Children with Tourett's and ADHD suffer from more externalizing and internalizing behavior problem and low social adaption than children without Tourett's disorder.

Usually ADHD starts 2-3 years before tics, while a similar proportion of cases of ADHD can be only after a tic's onset. It is not fully clear if ADHD with early onset may be related to a greater presence of another disorder that will only become symptomatically striking months to years later. Early ADHD can be seen as a risk factor for further associated psychiatric problems like tic disorders.

The pathophysiological mechanism of co occurrence of ADHD and Tourett's is not yet clarified. The stimulant medication in ADHD patient possibly triggers tic occurrence. Alpha<sub>2</sub> agonists and atomoxetine significantly improve tic symptoms. There is evidence that suprathreshold doses of dextroamphetamine worsen the tics but methylphenidate does not worsen tic severity in the short term. If tics or TD are socially disabling then consider behavior therapy.

Patients with co-existing tic disorders may occasionally need, beside treatment with a stimulant for ADHD, additional medication with a dopaminergic agonist, like Risperdal.

### 6.10 Obsessive compulsive disorders

Obsessive-compulsive disorders are characterized by recurrent intrusive thoughts and images or repetitive behaviors that aim to reduce anxiety. Up to 30% (Geller 1996) of children and adolescents with obsessive-compulsive disorders also present with ADHD

symptoms. The rate of OCD among children with ADHD is 8-11% (Arnold 2001), but that rate is higher among children with Tourette's disorder. Patients with comorbid ADHD and OCD were characterized by early onset of OCD symptoms. Patients with comorbid OCD and ADHD symptoms seem to require special care and treatment because the longer those symptoms persist, the more they increase in severity. OCD can be treated with an SSRI, like Prozac, and behavior modification.

### 6.11 Substance abuse and ADHD

*Do you suspect this person smokes, uses drugs or drinks alcohol? Why do you suspect this?*

Individuals with ADHD have several characteristics that make them more vulnerable to substance abuse. These include self-medication (i.e. teenagers taking Adderall), impulsive tendency to associate with other individuals who are not doing well in school, and social skill problems. Appropriately prescribed stimulant medication does not seem to increase the chance of later substance abuse. Several studies now show that stimulant treatment of ADHD does not increase the risk of later substance abuse and that if anything, such intervention considerably decreases the risk of substance use disorders.

Smoking is associated with ADHD. The presence of ADHD increases the risk he or she will be a cigarette smoker by at least 3 times the level of the general population. Smoking usually begins at an earlier age and persists throughout life. It is more difficult to give up in ADHD cohort. Alcohol another common type of substance abuse disorder in ADHD. In adolescence, alcohol abuse cases are seen in 1 in 3 individuals with ADHD in clinical based studies. In clinical practice, the suspicion of substance abuse warrants urine or blood screening to confirm the diagnosis. Adolescents with substance abuse disorders comorbid with ADHD are associated with a greater severity of substance abuse conduct problems and worse treatment outcomes (Sullivan 2001). Some have questions whether the long-term treatment of ADHD with a stimulant increases the risk for substance abuse in adolescents or adult. The most published study does not support this opinion. In fact, the study found that stimulant treatment in ADHD reduced the risk for substance abuse disorder by 50%, bringing it to the level of the general population (Farone, SV 2003). This suggests the treatment of ADHD may itself reduce the long-term risk for development of substance use disorder and thus highlights the importance of early recognition and treatment of ADHD.

In patients with comorbid ADHD substance use disorder, specific substance abuse treatment should be instituted first and once the patient is substance free, medication can be used to treat the impairment associated with ADHD. Atomoxetine, a non-stimulant may be more suitable for treatment of ADHD symptoms in this population, though a stimulant can also be used effectively. I often encourage group therapy in dealing with the drug and encourage abstinence. Family therapy is also a good idea. The individual may benefit from a 12 step group. Bupropion (Solhkhah, R 2005) and tricyclics (Weiss, RD 1989) are typically considered the first line of pharmacotherapy for comorbid ADHD and substance abuse disorders in children and adolescents. Second line agents of the stimulant are generally thought to be a safe and effective treatment of the ADHD. If untreated, ADHD is associated with high rates of alcohol use during adulthood. A 15 year follow up study showed ADHD and alcohol abuse are highly comorbid among adults. Treatment of ADHD in children and adolescents may actually reduce the long-term risk for development of substance abuse.

### **6.12 Personality disorders**

In the adult age group, individuals with ADHD are often diagnosed as suffering from one or more of the so-called personality disorders. Even in late adolescence, there is a very high rate of individuals with ADHD with and without concomitant developmental coordination disorders who meet full symptomatic diagnostic for one or more personality disorders. However, in children under 18-years-old, these disorders are classified as conduct disorder rather than a personality disorder. These personality disorders could be of any type, but it appears that those involved in major social dysfunctions may be particularly common. These include, for example, schizoid, schizo typical, paranoid, avoidant or obsessive compulsiveness and borderline personality disorders. It is unclear to what extent it is helpful or not to make an additional diagnosis of personality disorders in a person who is suffering a neuro developmental/neuropsychiatric disorder such as ADHD. It is doubtful whether the personality disorder diagnosis contributes any in the way for further explicating the underlying nature of problem faced by the individual. It is however important for the adult psychiatrist to be aware that many of their patients who are meeting the criteria for one or more personality disorders are really suffering from ADHD.

## **7. Non-psychological (physical) problems associated with ADHD**

There is substantial literature on the prevalence of psychiatric comorbidity in ADHD, but non-psychiatric disorders co-occurring with ADHD have recently gained wider attention. In addition to psychological issues, the person with ADHD may experience physical problems including recurrent headaches, muscle aches and pains, and abdominal pain, which may result from the bacterial infection, parasites, food allergies, neurotoxins, or environmental toxicity. Severe fatigue allergic disorders are asthma and eczema, respiratory infections, and ear infections. Many adults suffer from Fibromyalgia or chronic fatigue syndrome. A problem may arise with the medication. Those medications that are given for comorbid may have an undesirable affect on ADHD and vice versa.

### **7.1 Elimination disorders**

These include nocturnal enuresis, diurnal enuresis, and encopresis. According to one study, children with ADHD may have significant higher rates of incontinence, constipation, urgency, frequency voiding, nocturnal enuresis and dysuria than those without ADHD. For years, clinicians have anecdotally noted an increased incidence of enuresis in children with ADHD. Others have observed that their parents with enuresis have an increased incidence of ADHD. Because both conditions are fairly common, it is important to have more systemic studies that look at the relationship between enuresis and ADHD. An article in Southern Medical Journal published in 1997 compared a fairly large group of 6-year-old children with ADHD to a non-ADHD controlled group selected from a pediatric clinic population. That study found 6 year olds with ADHD had 2.7 times higher incidence of enuresis (Robson 1997). Sometimes enuresis may be more upsetting for children with ADHD. A non-ADHD child who successfully overcomes his fears may be able to accept his bedwetting more easily. However, a child with ADHD already feels different from his peers. His disorganization and impulsivity may lead to peer rejection and shame. Such children may cover his shame with appearance bravado. Some children with ADHD sleep deeply and have trouble waking up to go the bathroom when their bladder is full. A family study

suggested that ADHD and this type of elimination disorders are etiologically independent psychiatric conditions.

To treat the child with both ADHD and enuresis, it is important to first do a complete physical examination and ask the individual with ADHD about current and past bedwetting problems. Don't neglect to ask adolescents about this too. They will rarely volunteer this information on their own. Also, ask what treatment has been tried in the past. Some children in their teens with ADHD have tried with different therapies in the past. Because of this, they already might expect the treatment to fail. One may modify behavior intervention to accommodate for the child's short attention span. One must prioritize symptoms. If the child has a myriad of behavior difficulties, the family cannot address all of them at once. When the family decides this is the right time to treat the enuresis, they may have to back off with some of their other behavior goals to avoid being overwhelmed. The child and the family should be made aware that there are several ways to treat the enuresis. If one does not work, you are not a failure. That should lead to making a different plan for the future.

## 7.2 Sleep problems

Studies suggest that children with ADHD are more likely to have sleep problems than children without ADHD. As many as 56% of children with ADHD have problems falling asleep, compared to the 23% of normal children (Corkum 1998). Up to 39% of children with ADHD show a problem of waking up in the middle of the night. Resistance to go to bed and fewer total hours of sleep seems to be a major problem with many children with ADHD and likely adds to their difficulties in functioning at school. Studies on sleep pattern do not typically suggest specific difficulties with the nature of sleep itself in these children. Sleep related and involuntary movements appear to be more common in children, and these may be specifically linked to ADHD and coexisting disorders or treatment. One study suggested a link between ADHD and restless leg syndrome in children (Piccheietti 1998).

If sleep disorders are severe, polysomnography should be conducted. Treating sleep disorders may improve a child's attention at school. ADHD treatment with stimulant medication may cause insomnia. One should consider sleep hygiene before using medicine to reestablish new sleep-wake cycles.

## 7.3 Allergies

Minor allergic disorders have been implicated as a possible comorbid condition in ADHD. Most of the evidence runs to counter the notion that there is true association between allergies and ADHD. Despite various discussions in regards to the relationship between allergies and ADHD, studies on ADHD and allergic rhinitis and asthma have provided largely negative results, suggesting the relationship may be small, if it exists at all.

## 7.4 Eczema

A series evident immunological investigation reveals the strong association of ADHD and eczema (atopic eczema or atopic dermatitis). This eczema is a relevant cause of pediatric sleep disruption. Since disrupted sleep is a frequent feature of ADHD, this may constitute a putative causal link between both disorders. Even more interestingly, two independently

longitudinal based birth cohort studies found a persisting effect of early detection of atopic eczema on mental health. Children who suffered from eczema during the first years of life and showing remnants of symptoms thereafter will have an increased risk for behavior problems at age 10. Even though the causal relation is still unclear, this data demonstrates that eczema during early childhood predisposes kids to developmental behavior problems later on. In a population based study on adult eczema, an association was observed with a wide range of psychiatric issues including depression and personality disorders, indicating that eczema may predispose individuals to age-dependent mental health problems. (Schmitt et al, 2009)

### **7.5 Height and weight problems**

ADHD occurred in as many as 27% of children receiving treatment for obesity (Altfas, JR 2002). In addition, several studies suggest a negative effect on height and weight after years of treatment with central stimulant in ADHD. The evidence is equivalent and more recent studies say that a reduction of final height may be minimal or nonexistent. Although not related to the atopic mechanism, the assumption that nutritional components may cause or exacerbate ADHD symptoms further fuel various therapeutic diets and emphasizes the importance of dietary adjustments in ADHD children.

### **7.6 Hypertension**

Blood pressure is significantly increased in individuals with ADHD treated with central stimulant and/or atomoxetine. It is unclear at this stage whether such treatment may have a lasting effect on blood pressure or increased risk for later hypertension.

### **7.7 Fibromyalgia**

Fibromyalgia is a common condition in adults, particularly in women. Some adult psychiatrists with vast experience in this age group believe the rate of ADHD has increased the baseline population prevalence for this condition.

### **7.8 Perthe's disease**

This hip disorder is typically encountered in children of preschool age who more or less start limping. It is listed here not because of there has been published empirical studies of possible connection between ADHD and Perthe's disease but because some pediatric orthopedics have suggested that many young patients with a hip problem may have ADHD.

### **7.9 Clumsiness**

This occurs in 50% of children with clinical diagnosis of ADHD. Also, nearly half of children with clumsiness display ADHD. It is associated with attention, reading, and writing problems. Children with ADHD are more likely to experience injuries due to accidents than normal children.

Clumsiness improves over time, but 1/3 of children will carry it into adult life, causing problems with fine and/or gross motor movements (Kadesjo, B 1999).

### 7.10 Epilepsy

Three percent of children with ADHD have some kind of seizure disorder. Twenty five percent of children with epilepsy will have ADHD. Most children with ADHD and comorbidity will have staring episodes. It can be differentiated from any kind of seizure by asking the parents to make the child blink. If the child blinks, it is very unlikely that it is a seizure. If the staring is related to seizures, then there will be more autonomic nervous system related signs, such as increased heart rate and pupil dilation. Every child with the diagnosis of ADHD needs a routine EEG to rule out the most common disorder, childhood absence epilepsy. Though partial complex and generalized seizure disorders may exist, an EEG can confirm those findings.

Appropriate anti-epileptics should be used as treatment, in addition to treatment of ADHD. There is a 1-3% chance that stimulant medication may worsen the underlying seizure disorder.

## 8. Discussion

It can be challenging to identify and treat children with ADHD, especially in those with comorbidity. The high prevalence could be due to increased awareness by clinicians. Parents may refuse to accept their child's diagnosis of ADHD, and much less that of a comorbidity.

The high comorbidity rate between ADHD and other disorders have essentially created confusion regarding the definition of a true ADHD diagnosis. Since most children or adults with ADHD also have a second diagnosis where both sets of symptoms frequently overlap, critics suggest that the new scenes of ADHD have not been adequately described. Some even suggest that making an early ADHD diagnosis in a very young child is inappropriate. For instance, recently identified conditions in the DSM of early onset bipolar disorder mimics ADHD in the areas of impulsivity, mood inconsistencies and hyperactivity. It may not be clear whether a very young child suffers from ADHD, early onset bipolar disease or another condition that mimics ADHD symptoms. Obviously establishing an accurate ADHD diagnosis is very challenging for even the best clinician.

First point I would like to discuss is in regards to mental retardation. The diagnosis of ADHD should be given only when the symptoms of inattention or hyperactivity are present to the degree in excess of mental retardation of a child. However, there are no criteria for evaluating developmental inappropriateness in term of mental age. Some investigations consider it insufficient to establish deviation in terms of chronological age-appropriate behavior without special consideration to the mental age. Even with this difficult data determining developmental appropriateness, it is better to exclude the patient under mental age of 4 years and the patient of moderate to severe mental retardation with IQ under 50. The cases of mental retardation and borderline intelligence together show the significance of concomitant delay and mental development. There are no reports of an ADHD patient with mental retardation and borderline intelligence. This finding makes it necessary to incorporate intelligence testing in ADHD diagnosis for evaluating whether the patient has maladaptive behavior arising not only from ADHD but from mental delay, as well.

It is clear that the issues of comorbidity have important implications for understanding assessment and treatment of the children with ADHD. Children with ADHD significantly

display a learning disability, OCD, CD, anxiety disorder or depressive disorder while still others may show evidence of a co-occurring tic disorder or perhaps a bipolar disorder. Some show multiple comorbid disorders. The presence of comorbid conditions likely has a significant implication for long-term outcome. Children with comorbid features often show more serious levels of impairment, are more likely to have continuing problems and require a greater utilization of mental health services than do those without evidence of comorbidity. Assessing the presence of comorbid features complicate the clinical pictures essential in working with children with ADHD.

Giving the proper assessment should lead to optimal treatment. A treatment program for children with ADHD and comorbid conditions should address the full range of problems highlighted by assessment findings. For example, when a child not only shows the feature of ADHD but also meets the diagnostic criteria for oppositional defiance disorder and learning disorders, treatment should focus on all the problems associated with each of these areas. This might involve pharmacological treatment for dealing with the child's hyperactivity, impulsivity, and inattentive behavior. Parents must be oriented to behavior management approaches to modify oppositional defiance behavior. Specially designed educational approaches are available to assist the child academically. Likewise, in the case of a child with ADHD and comorbid depression, it will be necessary to treat the child's depression as well as ADHD symptoms. With children displaying other patterns of comorbidity, other combinations or approaches to treatment may be suitable.

Simply treating symptoms of ADHD is not enough. Appropriate case management involves addressing the full range of clinical problem displayed. Indeed, effective treatment for children with ADHD and comorbid condition is likely to be multi-disciplinary in nature and more extensive and complex than the treatment for children with uncomplicated ADHD. More research is needed to guide treatment of children with ADHD who display a specific pattern of comorbidity.

Thus, ADHD is a complex condition, affecting at least 5% of children population and therefore, needs to be better identified and treated (Farone, S 2003). Those who seek medical or psychological help have at least one or more majorly associated disorders or problems. These problems need to be appropriately identified and treated, as well.

Co-existing disorders affect the outcomes of individuals with ADHD. It is not well known about the long-term outcome of children with ADHD and comorbidity. Some of these conditions like ODD and conduct disorders have a long-term negative prognosis in terms of later substance abuse and anti-social personality disorder. The clumsiness may affect long term academic problems.

A long-term follow study is needed to address the outcomes of these comorbidities with ADHD.

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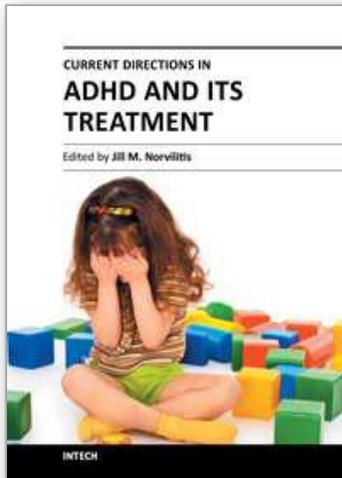
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## **Current Directions in ADHD and Its Treatment**

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The treatment of Attention Deficit Hyperactivity Disorder is a matter of ongoing research and debate, with considerable data supporting both psychopharmacological and behavioral approaches. Researchers continue to search for new interventions to be used in conjunction with or in place of the more traditional approaches. These interventions run the gamut from social skills training to cognitive behavioral interventions to meditation to neuropsychologically-based techniques. The goal of this volume is to explore the state-of-the-art in considerations in the treatment of ADHD around the world. This broad survey covers issues related to comorbidity that affect the treatment choices that are made, the effects of psychopharmacology, and non-medication treatments, with a special section devoted to the controversial new treatment, neurofeedback. There is something in this volume for everyone interested in the treatment of ADHD, from students examining the topic for the first time to researchers and practitioners looking for inspiration for new research questions or potential interventions.

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