CHAPTER 2: DIFFERENTIAL DIAGNOSIS AND COMORBID DISORDERS

Introduction

Making an ADHD diagnosis is as much about inclusion as it is about excluding the other disorders that might overlap with ADHD or look like ADHD; the differential diagnosis. Consider a second opinion or referral to a speciality ADHD centre if the patient has a clinical history that is complex or if you are contemplating medication treatment beyond those recommended in these Guidelines.

Disorder-based Differentiation

Differential diagnoses are disorders that mimic ADHD while comorbid disorders are disorders that occur together with ADHD (either causally-related or independent and concurrent with ADHD). A careful assessment of other possible diagnoses should be undertaken at the time of evaluation.

Common Differential Diagnosis for ADHD

This table is modified from Clinician’s Guide to ADHD with permission of the author, Dr. Joseph Sadek.

<table>
<thead>
<tr>
<th>Conditions that Can Mimic ADHD</th>
<th>Symptoms or Signs not Characteristic of ADHD</th>
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</thead>
<tbody>
<tr>
<td><strong>Axis I: Psychiatric Disorders</strong></td>
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<tr>
<td>Generalized Anxiety Disorder</td>
<td>Worry for six months or more that the person cannot control; lack of energy; anxious mood and somatic anxiety symptoms.</td>
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<tr>
<td>Obsessive Compulsive Disorder</td>
<td>Presence of obsessions or compulsions that interfere with level of function.</td>
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<tr>
<td>Major Depression</td>
<td>Episodic decline in mood or depressed mood and/or dysphoria; suicide-related issues; low energy; psychomotor retardation</td>
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<tr>
<td>Bipolar Disorder I or II (manic or hypomanic episode)</td>
<td>Episodic change from baseline; psychotic symptoms; grandiosity; pressured speech; recent decreased need for sleep.</td>
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<tr>
<td>Psychotic Disorder (schizophrenia or schizoaffective disorder)</td>
<td>Psychotic symptoms</td>
</tr>
<tr>
<td>Autism Spectrum Disorder</td>
<td>Qualitative impairment in social interactions, communication or odd eccentric behaviours</td>
</tr>
<tr>
<td>Oppositional Defiant Disorder</td>
<td>Defiant; loses temper; annoys others and is easily annoyed; spiteful or vindictive</td>
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<tr>
<td>Conduct Disorder</td>
<td>Presence of conduct disorder criteria e.g. aggression to people and animals; destruction of property; deceitfulness or theft; serious violations of rules</td>
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<tr>
<td>Substance Abuse</td>
<td>Urine toxicology screen confirms presence of substance</td>
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<tr>
<td>Learning Disorder</td>
<td>Consultation with psychologist or neuropsychologist confirms presence of the disorder</td>
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<tr>
<td>Language Disorder</td>
<td>Consultation with speech-language pathologist confirms presence of the disorder</td>
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<tr>
<td>Tic Disorder/Tourette syndrome (TS)</td>
<td>Presence of vocal or motor tics (or both for TS)</td>
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<tr>
<td><strong>Axis 2 Disorders</strong></td>
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<tr>
<td>Borderline Personality Disorder</td>
<td>Abandonment anxiety; hourly mood fluctuations; suicidal threats; identity disturbance; dissociative symptoms or micro psychotic episodes; feelings of emptiness.</td>
</tr>
<tr>
<td>Antisocial Personality Disorder</td>
<td>Lack of remorse; lack of responsibility; lack of empathy</td>
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<tr>
<td>IQ-related problems:</td>
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<tr>
<td>Mental Retardation</td>
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<tr>
<td>Gifted child</td>
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<tr>
<td><strong>Axis III Medication-related</strong></td>
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<tr>
<td>Medication with cognitive dulling side effect (e.g. mood stabilizers)</td>
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<tr>
<td>Medication with psychomotor activation (e.g. decongestants, beta agonist)</td>
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A thorough history and full functional review accompanied by a physical examination will often confirm underlying physical conditions. In certain instances, laboratory work up will be needed in order to eliminate a suspected pathology. However, most individuals with ADHD do not need laboratory investigations. Some special investigations may be relevant: polysomnography, electroencephalogram or brain imaging. Psychological testing, like WISC-IV (in children) or the WAIS (in adults), is imperative as it addresses any learning issues and helps to ascertain specific components of cognitive functioning that have overlaps with executive functioning (e.g. working memory and processing speed). Other tests, like personality assessment or projective testing, are useful indicators to establish personality traits and assessing contact with reality.

**Comorbidities**

**Comorbid Problems that can complicate ADHD evaluation and treatment**

<table>
<thead>
<tr>
<th>Psychiatric Problems</th>
<th>Clinical aspects to take into account in the treatment process when comorbid with ADHD</th>
</tr>
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<tbody>
<tr>
<td><strong>Mood Disorders</strong></td>
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<tr>
<td>Major Depression</td>
<td>Treat the most impairing disorder first. Moderate to severe depression should be treated first and suicide must be assessed in all cases. Stimulants can be combined with antidepressants when monitored. Also consider CBT. In adults, Bupropion and Desipramine may reduce ADHD symptoms, but with an effect size significantly lower than psychostimulants.</td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td>Treat Bipolar Disorder first. Treatment of ADHD can be offered when Bipolar Disorder is stabilized. Refer to specialist.</td>
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</table>
### Psychiatric Problems

#### Anxiety Disorders
- Generalized Anxiety Disorder
- Panic Disorder
- Social Phobia
- OCD
- Post-Traumatic Stress Disorder

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<th>Clinical aspects to take into account in the treatment process when comorbid with ADHD</th>
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<tbody>
<tr>
<td>Treat the most impairing disorder first. Take into account possible pharmacological interactions with meds metabolized through CYP2D6. ADHD treatments can be less tolerated in some individuals in this population. Start low, go slow, but titrate up to therapeutic dose. If not tolerated, switch to another medication, like atomoxetine. Also consider CBT.</td>
</tr>
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</table>

#### Autism Spectrum Disorder (ASD)
- ADHD treatments can be less tolerated in some individuals in this population. Start low, go slow, but titrate up to therapeutic dose. If not tolerated, switch to another medication. Refer to specialist for specific interventions for ASD.

#### Psychotic Disorders
- Treat both conditions. Oppositional Disorder needs psychosocial interventions. Moderate and severe cases might require combinations of psychostimulants and an Alpha 2 agonist such as Clonidine. Conduct Disorder needs psychosocial interventions and may involve legal issues. Pharmacological treatment of ADHD may help better modulate reactive-impulsive behaviours. Adding an antipsychotic might improve the symptoms of conduct disorder in some cases that were cited in the literature.

#### Borderline Personality Disorder
- Reducing impulsivity and increasing attention when treating comorbid ADHD may help the patient with a personality disorder to better participate in their psychological treatments.

#### Antisocial Personality Disorder
- Treating patients with APD+ADHD requires more complex and comprehensive interventions.

### Medical Problems

#### Epilepsy
- Treat epilepsy first, then ADHD. New onset seizure should be managed with antiepileptic medications. Level of antiepileptic medications may increase with methylphenidate due to enzyme inhibition 245.

#### Tics
- ADHD medications do not cause tics but some may increase or reduce tics. However, the presence of tics is not a contraindication for ADHD medication. Atomoxetine, Clonidine and Guanfacine have shown promise in this population. Addition of antipsychotic may be required in severe cases.

#### Sleep-related Disorders
- Treat primary disorder first.

- Sleep Apnea
- Psychostimulants can reduce residual sleepiness and improve daily function in sleep apnea and narcolepsy with or without ADHD.

#### Cardiovascular problems
- Physical exam before treatment (BP, pulse and cardiac auscultation). EKG and cardiac consult if positive cardiac history. Measure BP and pulse and monitor vital signs and cardiac side effects during treatment.

#### Obesity
- Discuss healthy eating and sleep habits and increase exercise. ADHD treatment may improve patient’s capacity to implement lifestyle changes.

### Other Problems

#### Learning disorders
- Treat specific learning disorders. ADHD treatments can improve attention, allowing improvement in learning skills. School adaptations should be considered and offered when needed.

#### Speech Disorders
- Treat specific speech disorders. Refer to special education teacher, psychologist and/or speech and language therapist for specific interventions.

#### Developmental Coordination Disorder
- Treat coordination disorders. Refer to occupational therapist and/or physiotherapist for specific interventions.

#### Low IQ
- Treat ADHD and adapt non pharmacological approaches to the patient’s IQ level.

#### High IQ
- Treat ADHD and adapt non pharmacological approaches to the patient’s IQ level.

### Note:
Drug combinations and antipsychotics use described in this table is off-label use and reserved for complex cases.

Most individuals with ADHD have co-occurring conditions which often complicate the clinical pictures of ADHD and have to be dealt with concomitantly. Eighty-seven per cent of ADHD children have at least one comorbid condition. Sixty-seven per cent of ADHD children have at least two comorbidities. Seventy-seven per cent of ADHD adults meet criteria for a comorbid condition. Comorbidity contributes to the failure to diagnose ADHD in adults. The most common comorbidities identified in the Multimodal Treatment Study of ADHD18 and in other comorbidity studies have been remarkably consistent.

Follow-up studies of children with ADHD and comorbidity show they have a poorer outcome than children with just ADHD as evidenced by significantly greater social, emotional and psychological difficulties59.
ADHD subtypes and associated comorbid disorders change over time and by developmental stage. The most common comorbid disorders in early childhood are oppositional defiant disorder (ODD), language disorders and enuresis. In up to 70% of children with ADHD, there are either general learning disabilities or specific learning disabilities \(^20\). ADHD is two to three times more common in children with developmental disabilities or borderline IQ and mental retardation. In the mid-school-age years, symptoms of anxiety or tic spectrum disorders may also be observed. Mood disorders tend to be more observable by early adolescence\(^{21-23}\).

We will briefly describe the key comorbidities and the auxiliary treatments they require. The DSM-IV-TR criteria for each diagnosis are listed in the Weiss Symptom Record and will not be reiterated here. An important clinical note is that outcome is generally determined by the most serious comorbid condition. Very little systematic research exists on sequencing of treatment for comorbidities, and this is generally handled on a case-by-case basis.

**ADHD and Learning Disorders**

ADHD and learning disabilities (LDs) often coexist and can mimic each other. Teachers and parents often express concerns about a child’s level of productivity and may label this child ‘lazy’ or ‘unmotivated’. Children with ADHD frequently fall below control groups on standardized achievement tests\(^24, 25\). The comorbidity rates of LD with ADHD vary greatly depending on how the term LD is understood. If it is defined as a specific learning disability in reading, arithmetic or spelling relative to intelligence and achievement at or below a 7% level, then the comorbidity rate ranges from 19% to 26%. If the term LD is defined as a significant difference between intelligence and achievement, the comorbidity rate increases to 53%\(^26\). As many as 80% of children with ADHD may have a LD if defined as the student functioning two grades below grade level\(^26\). Children with ADHD may also have speech and language difficulties.

Children with ADHD often have weaknesses in the cognitive areas of executive functioning like organization, planning, self-directed activity, working memory and processing speed\(^27\). While there is considerable overlap between ADHD and problems with executive function, children with ADHD may have a range of skills in these areas\(^19\). Although children with ADHD have a high rate of specific learning disabilities, such as coordination disorders, disorder of written expression, dysgraphia, dyslexia or dyscalculia\(^18\), it is just as important to understand that a child who cannot follow instructions, listen, or stay on task is going to be learning-disabled in the global sense of underachieving as compared to his/her potential. Many children with ADHD have difficulty with written output, and compensate for this in later years by keyboarding. Children who had difficulty with developmental coordination disorder may find forms of exercise such as walking beneficial in adulthood because they do not require extensive coordination or balance. They may, however, still continue to have difficulty with various tasks and be referred to as “clumsy”.

When psychoeducational assessments are done, emphasis should be placed on identifying such weaknesses as well as assessing the child’s abilities in written output and auditory processing. If LDs are documented, it will assist the teacher and school to know what type of educational adaptations are most likely to be effective. It will also help the child, adult or parent differentiate their overall level of intelligence from specific deficits that can be remediated, thus improving self esteem. The physician diagnosing the child or adolescent with ADHD has a responsibility to aid the individual in accessing appropriate classroom accommodations to help them cope with their weaknesses. Templates that can be used as a guide for writing letters requesting school accommodations are found in Chapter 6, supporting document 6A. In recent years, schools have been much more willing and skilled in providing appropriate adaptations for children with ADHD, executive dysfunction, written output problems and learning disabilities. These adaptations should be understood as “levelling the playing field for these children” and not perceived as an indication of academic incompetence. This is true from kindergarten through university.
**Practice Point:** The templates for requesting psychoeducational testing and accommodations can be downloaded from the CADDRA ADHD Assessment Toolkit and printed on your letterhead. You can personalize and adapt them to suit your needs.

A latent learning disability may become more overt during adulthood when executive functions become more important for independent learning. In adults, as in younger children, ADHD can occur along with specific problems in reading, math or with written expression. These can usually be identified by assessing whether these difficulties have caused problems in school and continue to cause more or less residual difficulty. What is more complex is the differential between a primary attention problem (ADHD-inattentive subtype) and various processing disorders, executive function problems secondary to organic conditions (e.g., head injury, exposure to toxins, drug abuse), or language deficits. The childhood history should be positive in ADHD. It is important to determine if the patient is inattentive only in the area in which learning deficits present a challenge, if the problems followed an accident involving a concussion or brain injury, or follow a period of heavy drug use.

*Educational accommodations are a right* (recognized in the Ontario Human Rights document, “Guidelines in Accessible Education”28). Although some school boards across Canada do not currently recognize ADHD as qualifying a student as a ‘special needs student’, this perspective is changing. Both CADDRA, the national physician’s ADHD alliance, and CADDAC, the national parent and patient support and advocacy network, will be advocating to the Ministries of Education for standardized educational accommodations across Canada. CADDRA and CADDAC believe that all neurobiological and mental health disorders need to be recognized by educational institutions in order for individuals to receive the necessary multimodal care.

**ADHD and Oppositional-Defiant Disorder (ODD)**

Behavioural problems (including ODD, aggression and delinquency) account for most of the comorbidity in children with ADHD. The presence of comorbid ODD with ADHD is likely to generate substantial impairment and would be expected to result in increased referrals for treatment29. Between 25-75% of adolescents with ADD may have concurrent ODD30. Distinguishing between normal adolescent self-assertion and ODD may not always be easy. Among adults with ADHD, 12% meet diagnostic criteria for continued ODD, though likely now referred to as passive-aggressive personality traits.

The most common reason for ODD is parental vulnerability resulting in insecurity of the child who responds with a need to control. This manifests by active confrontation of authority they perceive as being weak. The treatment for psychosocial-based ODD is to reestablish the generational boundaries using positive parenting techniques. However, in patients with comorbid ODD with ADHD, it is advisable that the first step is optimization of pharmacotherapy of ADHD followed by augmentation with psychosocial treatment, including parent and other behavioural treatments. It is important to distinguish ODD from CD. Children with ODD have recurring negativistic, defiant, hostile and disobedient behaviour, especially toward authority figures, whereas those with CD repeatedly violate the basic rights of others or age-appropriate societal norms, as defined by a pattern of repeated aggression, lying, stealing, and truancy31. The onset of both disorders is usually prepubertal, thus making early identification, diagnosis, and treatment crucial. ODD is a prodromal to conduct disorder in some cases but an unlikely outcome in more than 50% of the cases. Many children with ADHD and ODD do not evolve into CD32.

**ADHD and Conduct Disorder (CD)/Aggression**

CD comorbid with ADHD is a severe, persistent condition that has an earlier age at onset and is frequently preceded by ODD, therefore it is important to distinguish between the two disorders32, 33. CD is not always pre-pubertal onset; another group of children have adolescent-limited CD. Co-occurrence of ADHD and CD in
adolescents is often a precursor of antisocial behaviours; nicotine use; substance use or abuse; anxiety or depression; and development of antisocial personality disorder as adults.\textsuperscript{34, 35}

Pharmacotherapy for patients with ADHD, CD and aggression may be useful (stimulant and non stimulant medication). Although medications are usually effective in reducing the symptoms of ADHD and impulsive aggression\textsuperscript{18, 36}, these patients typically benefit from multimodal treatment. Medications initially should treat the most severe underlying disorder, after which targeting specific symptoms is appropriate. Some of these patients show aggression before and during the course of treatment, making it imperative to document their aggressive behaviours before the introduction of medications and to make these behaviours an explicit target of treatment. Clinicians should assess treatment tolerability and efficiency if patients show aggression after starting medication for ADHD.

Conduct problems are generally reduced by all effective ADHD treatments (stimulant and non stimulant medication and psychosocial treatment). However, treatment of the ADHD may not be sufficient to resolve all symptoms. Higher doses of medication with a multimodal treatment approach should be attempted. Psychosocial treatment, individual, family interventions and medication optimization and, sometimes, a trial of a mood stabilizer or an atypical anti-psychotic may be beneficial\textsuperscript{10, 39}.

Research shows that ADHD and CD represent two complex and distinct entities that are often associated. Children with these conditions without comorbidity present with different core symptoms and perform differently on objective measures of ADHD symptoms. Children with these comorbidities show the poorest outcome within each individual group.\textsuperscript{30, 39}.

Researchers have attempted to understand the reasons for the high comorbidity between ADHD and CD. They have suggested several reasons for this:

- that one disorder is a precursor to another
- one disorder is a risk factor for developmental of the other
- the disorders share the same related risk factors, or
- there is a common underlying symptomatic basis for one or more of these behaviours.\textsuperscript{41, 42}

**ADHD and Borderline Personality Disorder (BPD)\textsuperscript{43}**

BPD may occur in either gender. It is advised that the individual should be over 16 before a formal diagnosis of BPD is applied due to prevailing biases associated with this disorder. While patients with BPD are often impulsive, labile and have difficulties with executive function, the presence of rage, emptiness, planned manipulative behaviours, primitive defence mechanisms, deliberate self-destructive actions, abandonment anxiety and suicide attempts differentiate the two disorders. While patients with BPD may have ADHD, the BPD is the more severe disorder and more likely to impact outcome. Treatment of ADHD in the context of BPD, especially with short-duration stimulants, should be undertaken with caution. However, effective treatment of underlying ADHD can improve active participation in psychosocial treatments. Patients with BPD who have clear evidence of ADHD in childhood often expect that treatment of the ADHD in adulthood will resolve the personality issues. In these cases, it is important to explain the treatment limitations of ADHD medications. This will reduce the risk that patients will react with feelings of abandonment, rage, disappointment, devaluation or feel that they have been rejected.

**ADHD and Antisocial Personality Disorder (ASPD)\textsuperscript{43}**

Some children with ADHD and conduct disorder go on to have ASPD after the age of 18 (the age criterion is required), and show an absence of remorse, compassion and conscience. Since some patients with ASPD may be psychopathic and also drug-seeking, it is important to screen for cruelty, aggression, problems with
the law and stealing. Treatment of ADHD in the context of ASPD may not lead to significant functional improvement in the patient’s actual well-being but may improve the extent of their impulsivity. Whether or not they are less impulsive, less hyperactive and more focused may or may not improve their functioning if symptomatic improvement is directed to antisocial activities rather than improved interpersonal relationships and life skills.

ADHD and Anxiety

The natural course of ADHD moves towards an internalization of the symptoms. As a result, the emergence of anxiety may be a natural extension of ADHD. Individuals with the Inattentive Subtype have a stronger propensity for anxiety as they typically have internalizing temperaments. This is particularly true in females who may be highly sensitive and have more Inattentive Subtype symptoms. However, having ADHD also exposes the individual to considerable negative situations and anxiety may be a compensation for environmental insults (i.e. in order to avoid conflict situations due to their impulsiveness, they use anxiety to create excessive internal control). Once anxiety develops, attention can be severely compromised. As a result, there are patients with comorbid anxiety and inattention which results in significant damage to their self esteem, lack of academic success and other types of impairment. There are many forms of anxiety within the DSM-IV-TR but they all have some components in common:

a) the cognitive message always begins with the words “what if...” which is a need to anticipate a negative outcome before it has happened

b) a tendency to hold on to beliefs, thoughts, belongings and emotions (i.e. not being able to easily “let go”)

c) is likely related to heightened noradrenaline activity, and

d) the behaviour leads to impairment in functioning.

As many as 33% of children with ADHD have comorbid anxiety and that number increases to as many as 50% of adults. Once the specific type of anxiety is identified the treatments are generally as follows:

- Behavioural intervention: Relaxation therapy, yoga, meditation, exercise, simplifying their environment by throwing things out, delegating anxious activities, improved organization skills etc. are all useful interventions

- Psychological therapy: Cognitive behavioural therapy (CBT) and individual therapy focusing on the specific anxiety disorder

- Medical treatment: If ADHD exists with anxiety, treat the ADHD first. There may be a risk of increasing anxiety in the short term so it is important to start very slowly and increase the doses gradually. If the anxiety becomes too intense, then the ADHD medication should be reduced or withdrawn and the anxiety should be treated until the symptoms are tolerable. Then the ADHD medication should be restarted. The most common medication used for anxiety is a serotonin-based medication. Any of the ADHD medications can be successfully used when anxiety is comorbid although atomoxetine has been found to be specifically helpful in management of anxiety with attention disorder. Due to 2D6 inhibition, atomoxetine should be used with caution if combined with fluoxetine or paroxetine for example.

There are anxious patients in whom problems concentrating, restlessness and other aspects of dysregulation are caused by a primary anxiety disorder and not ADHD.

- Check for other signs of anxiety and family history of anxiety

- Check to see if the patient has symptoms of ADHD not typical for anxiety, such as stimulus-seeking behaviour, disinhibition or difficulty with organization and time management
• Determine if symptoms have developed de novo as a result of new onset anxiety or a particular stressor.

**ADHD and Major Depression**

There is considerable overlap between MD and ADHD. MD patients (without ADHD) may still have transitional inattention, short-term memory problems, irritability, impulsivity, trouble sleeping, trouble concentrating, restlessness and being fidgety. However, the differential with ADHD is based on two factors. Primary MD typically has consistent negative mood and anhedonia. A drop in mood is qualitatively different from the lifelong deficits in maintaining focus or motivation that are typical in ADHD. There is a difference between poor concentration in the presence of depression and deficits in organization, impulsivity and lifelong difficulty with forced effort and listening even when happy.

Patients with primary ADHD often have to deal with failure and may become demoralized, depressed or dysthymic as a result. In that case, they will present with both disorders. Patients with ADHD may look like they have a mood disorder when they do not. Lack of motivation may mimic anhedonia, chronic difficulty going to sleep and restless sleep may mimic insomnia secondary to MD. ADHD patients typically have dysregulated mood, are reactive and sometimes irritable, but it is not typical for ADHD in the absence of a mood disorder to be associated with entrenched, depressed affect. On the contrary, many ADHD individuals maintain reasonable mood despite chronic rejection and difficulties with relationships and life skills. Some patients with ADHD are negative or chronically irritable (“life is a bore” or “I've never felt well”) in the absence of major neurovegetative features. The most appropriate designation for this particular attribute would be a dysthymic disorder since these symptoms are not included in the diagnostic criteria for ADHD itself. Antidepressants can be helpful in some cases.

It is not uncommon for ADHD and depression to coexist. It may be helpful to try to determine if the patient is depressed secondary to ADHD or vice-versa. Depression or more commonly dysphoric symptoms are also possible due to the withdrawal effects of the medications used to treat ADHD. Different guidelines differ on sequence of treatment, but clinically the “primary” disorder - meaning the more severe, early onset and pervasive disorder - is usually treated first. When initiating treatment with stimulants in a patient with untreated melancholic depression, worsening of already impaired sleep and appetite issues may be a problem.

When the depression is associated with problems in the psychosocial environment, treatment strategies including individual (e.g. CBT) and family therapy are primarily indicated. However, pharmacological treatment is a useful intervention in the adolescent and adult age group. The evidence for successful treatment of childhood depression with medications is mixed. Fluoxetine and fluvoxamine have been indicated for depression in children. Stimulant medications have a mild antidepressant effect but may produce a dysphoric look in 30% of patients, even though the patient is not clinically depressed or reports depression. Adjustment of dose may improve the dysphoric symptoms; failing that, switching to a different ADHD medication may be successful. Treatment of the most disabling condition should be undertaken first. This is particularly true in the presence of suicide risk. If the MD continues to be impairing or worsens, referral is recommended. All of the drugs used to treat ADHD have potential antidepressant effect or can cause mood symptoms particularly in the rebound of their use ... If suicide risk is imminent, an immediate referral or intervention must be carried out. Suicide risk should be assessed in the follow-up visits as well.

**ADHD and Bipolar Spectrum Disorder**

In most cases of bipolar disorder (BD) in children or adolescents, ADHD is comorbid. Most children with ADHD, however, do not go on to have BD. A patient with ADHD who is currently depressed may be misperceived as having BD based on the contrast to his/her reported usual state of high energy.
However, any patient who experiences a new and acute onset of increased energy, irritability, grandiosity and decreased need to sleep is, by definition, suffering a hypomanic/manic episode since ADHD is developmental and chronic.

Some patients have an early onset form of BD characterized by severe mood swings, anger outbursts, irritability, distractibility, hyperactivity and impulsive self-destructive behaviour. A differentiating feature includes the symptoms of grandiosity, euphoria and periodicity. Family history of BD is important. Children of bipolar parents are more likely to have ADHD (8-10%), rather than BD (5%)\(^4^5\). Other differentiating features include: discrete cyclical symptoms of emotional lability in BD as opposed to continuous symptoms in ADHD; greater likelihood of psychosis or grandiose perceptions in BD; and possible depression and sleepiness after rage episodes in BD as opposed to baseline recovery in ADHD-based rages. There is a group of patients in which ADHD is complicated by severe mood dysregulation which may not be episodic, may have existed developmentally, and is severely impairing. The debate as to what to call this disorder requires further empirical research. Early follow-up studies of this population suggest that emergence of BD in patients previously diagnosed as ADHD is a significant concern.

In adolescence and adulthood, BD should be considered as the primary diagnosis if there are prominent, episodic, distinct, cycling mood symptoms. Lithium carbonate or anticonvulsants with mood regulating effects can be considered for patients with bipolar affective disorders (BAD), as well as atypical neuroleptics\(^4^6\). Treatment of BD or BD + ADHD should be referred to experts.

**ADHD and Pervasive Developmental Disorder (PDD)**\(^1^5, 4^7 - 5^0\)

When symptoms of PDD are present, this is the primary diagnosis and takes precedence over ADHD in terms of treatment intervention strategies.\(^4^8\) While the DSM-IV Criterion E suggests that PDD is an exclusionary diagnosis, the CAP-Guidelines Committee note that ADHD and PDD do coexist in some patients. Evidence of possible PDD includes late onset of language, prominent social disabilities and excessive and unusual preoccupations in particular areas of interest. Severe ADHD symptoms in the presence of PDD require referral.\(^6^\)

According to the literature:

- until recently, ADHD was not recognized in persons with autism spectrum disorder but researchers and clinicians have now recognized the importance of attending to both syndromes when both are present and clinically impairing
- up to 58% of the individuals diagnosed with autism and 85% of those diagnosed with Asperger's syndrome tend to meet full criteria for ADHD as well\(^2^4^\)
- attentional impairments in autism tend to be more of the "not listening" and "difficulty shifting focus" type than of "the short attention span" and "excessive distractibility" type
- medications used to treat ADHD can help alleviate ADHD impairments in the majority of patients with comorbid ADHD and autism spectrum disorder, though the effect is somewhat less than in those presenting with ADHD alone
- in people presenting with ADHD and ASD, side effects such as dysphoria are more common\(^5^1\)
- **dosage titration in this population should be done at a slower rate to minimize adverse effects.**

**ADHD and Addictions**

*Substance Use/Abuse (SUD)*\(^2^4, 5^2 - 5^6\)

ADHD patients are at significant risk of using illicit substances, particularly nicotine, cocaine and cannabis, and of starting at an earlier age than the general population.\(^5^6\) Concurrent disorders with ADHD, like CD
and BD, increase the likelihood of SUD\textsuperscript{55}. While ADHD patients do self-medicate with substances, it is important to dispel their belief that the use of illicit substances has a positive therapeutic benefit. SUD is a diagnosis in its own right, and data to date does not demonstrate that treatment of ADHD in this population will eliminate the substance abuse\textsuperscript{56}. A history of substance abuse should be explored with the individual in private.

**Practice point:** With adolescents, ask whether their friends use drugs or alcohol first. A positive response suggests they are likely a high risk candidate. Where substance abuse exists, there continues to be controversy about the timing of ADHD pharmacological treatment. Though the CAP-G Committee feels it is important to treat the SUD first, it is recognized that ADHD treatment might be required concurrently.

Patients with ADHD have a two-fold risk for substance abuse and dependence, including daily marijuana use, alcoholism, smoking and other drugs\textsuperscript{57}. On the other hand, it is also true that patients with these substance abuse/dependence problems present with attention, behaviour and self-control symptoms that mimic ADHD. For this reason, we do not recommend making a diagnosis of ADHD in the face of current substance abuse or dependence, even when childhood history is positive. The primary diagnosis in this circumstance is the substance problem and diagnosis of ADHD should be deferred until the patient is in recovery. Treatment of ADHD in patients who use marijuana without dependence or abuse is controversial and the risks and benefits of doing this have not been studied. Marijuana smoking (to calm themselves or facilitate sleep) is extremely common in this population. No treatment carries risk in itself and that treatment may minimize self-medication. Marijuana may be laced with substances that are more dangerous and it makes little sense to use a medication to help a patient focus when they are self-medicating with a substance that impairs attention skills in the long term.

According to current literature:

- methylphenidate does not have the same abuse liability as cocaine does due to slower dissociation from the site of action, slower uptake into the striatum, and slower binding and dissociation with the dopamine transporter protein relative to cocaine
- in some studies, 11% of subjects with ADHD reported selling their medication and 22% reported misusing their medication compared with 5% of controls. The ADHD group at highest risk for diversion and misuse were those with SUD and CD. Immediate-release, but not extended-release, stimulants were diverted or misused
- patients with ADHD and SUD require multimodal intervention incorporating both addiction and mental health treatment.

**ADHD and Other Addictions**

The need for immediate feedback, the desire for reward and the enjoyment of risk all lead ADHD patients to be vulnerable to addictions. These may include not just substance abuse but also sports, shopping, sex, internet and gambling addictions. Therefore it is essential that an ADHD assessment screen for any addiction is begun with a broad question, followed by a more detailed evaluation, and that both disorders be treated \( \text{CB} \). There is no evidence that treatment of ADHD will treat the addiction, or that resolution of the addiction will lead to improvement in ADHD core symptoms.

**ADHD and Enuresis**

Enuresis treatment may be improved with medication initiation, particularly for daytime events. Nocturnal enuresis often requires separate management. The most effective intervention for the motivated child and family is the alarm-based training system. Medical treatment options may include the use of Desmopressin, DDAVP, imipramine and (recently determined) atomoxetine\textsuperscript{58-60}.
ADHD and Tic Disorders\textsuperscript{61-64}

The most common tic is blinking. Tics present as either phonic or physical movements. Research on tic disorders and ADHD is complex and this may be a disorder where the population statistics do not always reflect the risk to the individual. While stimulants do not cause tics, they may be implicated in uncovering a patient's propensity for them. There is some evidence that while atomoxetine may be associated with improvement in tics, it may also cause tic emergence. Some recent research studies suggest:

- patients with Tourette Syndrome (TS) co-occurring with ADHD may suffer from more impairment related to ADHD than tics
- treatment interventions for TS include education about tics and related disorders, clinical monitoring, pharmacological or psychological treatments and school interventions for kids as needed
- some studies indicate that methylphenidate is a safe and effective treatment for ADHD in most children with comorbid tic disorder
- the alpha-2-adrenergic agonists, Clonidine and Guanfacine, have shown promise in the treatment of tics, particularly in combination with ADHD.

ADHD and Epilepsy

Some studies have suggested a higher incidence of symptoms of ADHD in children with epilepsy. The five common epilepsy comorbid conditions are reduced bone health and fractures, stroke, depression, migraine and ADHD\textsuperscript{65}. Other research noted a strong trend toward a higher incidence of epilepsy among children with ADHD than among children without ADHD\textsuperscript{66}. Epilepsy in children with ADHD appears to be more severe than in those without. Finally, there appears to be a reluctance to diagnose and initiate treatment for ADHD in children with epilepsy\textsuperscript{67}.

Stimulant medications may lower seizure threshold, though current data suggests that this may not always be the case. Adult epilepsy patients received relief from sedation with MPH and showed an improved quality of life without significant alteration of seizure control\textsuperscript{68}. There are some studies that suggest drug interactions between methylphenidate and antiepileptic drugs\textsuperscript{69}. Until further replicated studies can be done, a conservative approach is still indicated.

ADHD and Brain Injury (any etiology)\textsuperscript{70-74}

Individuals with ADHD of all ages are at risk for physical injuries because they are impulsive, hyperactive and inattentive\textsuperscript{70}. Any injury to the brain, particularly to the frontal lobes, can produce a syndrome known as Secondary-ADHD (S-ADHD). Trauma to the brain can also worsen the symptoms of pre-existing ADHD. Children and teens with ADHD are three times as likely to experience a moderate or severe brain injury than their peers without ADHD. Children and adolescents with a moderate or severe brain injury have a 20% chance of developing S-ADHD. The literature on adults is less clear. S-ADHD can be treated using the same principles and medications as ADHD, but the research literature supporting this is not as extensive or compelling as it is for ADHD.

Given that concussion and brain injury are relatively common experiences, it is recommended that all patients being assessed for ADHD be questioned as to whether they have ever had a concussion or brain injury in the past. It is generally accepted that the more severe the brain injury, the greater the likelihood of developing or worsening ADHD. This is the one instance in which a patient may present with de novo ADHD symptoms, having no past history of these types of symptoms before the injury. Motor vehicle accidents are a major cause of traumatic brain injury and patients with ADHD need to receive specific advice on driving only when medication is in effect (please see the section on ADHD and driving). The literature on non-traumatic acquired brain injury, such as fetal alcohol syndrome or stroke, is less clear,
but many patients with ADHD symptoms may respond to standard treatments. Patients with brain injury may be more sensitive to medication and starting out with lower doses may be recommended. As with all patients, however, the best advice is to start low, go slow, but to persist with upper dosage adjustments until symptoms remit or side effects are evident or suggested maximum dosage is reached.

**ADHD and Sleep Disorder**

Twenty-five to fifty per cent of children and more than half of adults with ADHD reportedly suffer from sleep problems. Sleep plays a pivotal role in cognitive function, learning and memory consolidation. Sleep deprivation and disturbances of sleep architecture can result in symptoms varying in severity, from unrecognized deficits in cognitive performance to disabling sleepiness and/or fatigue that noticeably affect cognitive, emotional, and physical function, giving rise to, or exacerabting, ADHD symptoms. However it is not clear whether sleep disturbances are intrinsic to ADHD or whether they occur as a result of an underlying primary sleep disorder. On the one hand, if sleep disturbances in ADHD are caused by an underlying primary sleep disorder, the extent to which ADHD-like symptomatology is attributable to the sleep disorder is not sufficiently studied. The manifestation of ADHD-like symptoms in primary sleep disorders such as sleep disordered breathing (SDB), periodic limb movements in sleep (PLMS) in restless legs syndrome (RLS), and disorders of excessive daytime sleepiness (EDS) such as narcolepsy and idiopathic hypersomnia (IH) have been documented. In light of the similarity of symptom presentations between ADHD and primary sleep disorders, it has been suggested that misdiagnosis may be an issue between these two disorders.

On the other hand, the association between sleep disturbances and ADHD-like symptomatology appears to extend to brain structure. Neuroimaging studies have shown similar metabolic changes in the prefrontal cortex (PFC) of patients with ADHD and sleep deprived subjects. Some areas of the brain that are affected in ADHD are the very same structures that are involved in the regulation of sleep. Activation of areas of the cortex by the midbrain and locus coeruleus is required for sustained attention and alertness. Attention and alertness, in turn, are properties that define the awake state. Cycling through the awake state and sleep state is an autonomically governed process that reflects changes in brain arousal. In ADHD, subjects appear to have problems with arousal, and deficits in cortical functioning have been reported. Thus, it has been proposed that sleep problems such as insomnia or hypersomnia result from abnormal cortical arousal and, therefore, sleep problems are intrinsic to ADHD.

**ADHD and Obsessive Compulsive Disorder (OCD)**

Some studies suggest that one third of children and adolescents with OCD may have ADHD. Clinicians assessing patients for ADHD should routinely enquire about symptoms of OCD to establish the diagnosis of OCD. Treatment of both disorders should be carried simultaneously. Medications used to treat ADHD are not useful for treatment of OCD and medications used to treat OCD are not effective for treatment of ADHD. CBT is often effective in treatment of certain types of OCD.

**ADHD and Developmental Coordination Disorder (DCD)**

While there is no clear prevalence rate for the co-occurrence of these two disorders, evidence suggests that when ADHD and DCD occurred, there was a 58% rate of a poor outcome. Balance problems, dyslexia, and poor handwriting may be related to cerebellar dysfunction and may be associated with DCD. Occupational therapy assessment is warranted to provide recommendations. Having the child learn key boarding can often be beneficial. Relevant software programs can also help to overcome problems (e.g. voice recognition, etc).