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ADHD: an overview

by Dean Elbe, BScPharm, PharmD, BCPP, ACPR



Learning objectives

Upon successful completion of this lesson, the Pharmacy Technician will be able to do the following:

- 1. Recognize the symptoms of ADHD (including different course specifiers (formerly called "subtypes"), common comorbid (concurrent) illnesses, and some of the myths surrounding ADHD and its treatment
- 2. Understand the mechanism of action and time course of onset/offset of pharmacological effects for the various ADHD treatments
- 3. Review strategies for management of stimulant-induced appetite impairment
- 4. Describe ways that registered pharmacy technicians can assist in the management of patients with ADHD, including promotion of adherence to treatment.

.....

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder that begins during childhood. A genetic link has been suggested, as ADHD appears to run in families. However, inheritable factors (e.g., density of dopamine receptors in the prefrontal cortex) and non-inheritable risk factors (e.g., chaotic family environment) are both involved, and influence each other. ADHD is the most common childhood psychiatric disorder in Canada. Studies estimate approximately 5-9% of children meet ADHD diagnostic criteria.¹⁻³ As pharmacy technicians become more involved in direct care, a working knowledge

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TABLE 1 - ADHD Symptoms & Diagnostic Criteria⁽²⁾

Inattentive Symptoms	Hyperactive/Impulsive Symptoms
 Fails to give close attention to details or makes careless mistakes in work/ schoolwork, or during other activities Difficulty sustaining attention in tasks or play activities Does not seem to listen when spoken to directly Does not follow through on instructions and fails to finish schoolwork, chores, or duties Difficulties organizing tasks and activities Avoids, dislikes or is reluctant to engage in tasks that require sustained mental effort Loses things necessary for tasks or activities Easily distracted by extraneous stimuli Forgetful in daily activities 	 Fidgets with or taps hands or feet, or squirms in seat Leaves seat in situations when remaining seated is expected Runs about or climbs in situations where it is inappropriate Unable to play or engage in leisure activities quietly "On the go" or acting as if "driven by a motor" Talks excessively Blurts out an answer before a question has been completed Difficulty waiting his or her turn Interrupts or intrudes on others

of this common disorder, such as symptoms, comorbidities, common myths and treatment options is important.

Symptoms

ADHD is defined by symptoms of inattention (e.g., frequently appears to not be listening), disorganization (e.g., frequently losing items), hyperactivity (e.g., appears as if "driven by a motor") or impulsivity (e.g., excessive risk-taking behaviour) (see Table 1).2 Symptom presentation may be predominantly inattentive, predominantly hyperactive/impulsive, or a combination of both symptom clusters.

ADHD symptom presentation can change over time. Hyperactivity symptoms frequently lessen as a person ages, though symptoms of inattention often persist into adulthood. More than 50% of persons diagnosed with ADHD as a child remain impaired by ADHD in adulthood.³

ADHD is a disorder of executive functioning (EF), which is the mental process that allows individuals to start and finish a task on time by planning ahead while applying learning from past experience. EF skills help individuals to identify a problem, find solutions, regulate behaviour and emotions, control attention levels and resist distractions.⁴ EF is regulated by an area of the brain known as the prefrontal cortex, which is among the last areas of the brain to fully develop.5

ADHD causes functional impairment, at a level exceeding that expected for the individual's developmental age. Note that devel-

TABLE 2 - Common ADHD

learning disabilities

Comorbidities⁽³⁾

- oppositional defiant disorder
- conduct disorder
- anxiety disorders (e.g., generalized anxiety disorder)
- tic disorders/Tourette syndrome
- obsessive compulsive disorder
- mood disorders
- disruptive mood dysregulation disorder
- developmental coordination disorder
- autism spectrum disorder
- sleep disorders
- substance use disorders
- epilepsy

opmental age may be lower than chronological age, if intellectual disability or another neurodevelopmental disorder (e.g., autism spectrum disorder) is present.²

Diagnosis/Comorbid Conditions

Pediatricians and primary care providers are often involved in the diagnosis and management of ADHD due to the high prevalence of ADHD and relative scarcity of access to child psychiatrists. While it might seem obvious at first glance that a patient with prominent hyperactive/impulsive symptoms has ADHD, the diagnosis of ADHD can actually be guite challenging. There is currently no reliable diagnostic test or scan available that can confirm or rule out an ADHD diagnosis. Patients with a primarily inattentive presentation of ADHD may "fly under the radar" and not be clinically recognized until adolescence or adulthood, when the complexity of school/occupational demands exceeds their functional capacity.

Accurate diagnosis of ADHD is based on a clinical evaluation that requires a thorough history taking, physical examination and full functional assessment, combined with information gathered from parents/caregivers and teachers. Obtaining a correct diagnosis that includes relevant comorbidities is essential for treatment success.

The majority of patients with ADHD have concurrent (comorbid) conditions that contribute to the psychological distress and functional impairment that patients with ADHD may experience at school or work and in social settings (see common comorbidities in Table 2). The presence of certain comorbidities may alter response or tolerance to certain ADHD treatments. For example, while patients with ADHD and comorbid epilepsy may benefit from methylphenidate-based treatments, stimulant use can lower the seizure threshold, and should usually only be added after the patient is stabilized on an appropriate anticonvulsant regimen. Specialist referral and management is recommended for patients with complex presentations and multiple comorbidities.³ Certain comorbid conditions such as substance use disorders and mood or anxiety disorders can mimic, overlap with or worsen ADHD, and if more impairing than ADHD, may require treatment first prior to implementing effective treatment for ADHD.3,5

ADHD Myths

A significant level of stigma surrounds ADHD and its treatment, and a number of myths surrounding the illness are commonly (and often strongly) held (see Table 3 summary). These myths can be barriers that discourage patients/parents from seeking evaluation/diagnosis. They can also reduce patients' willingness to adhere to effective, evidence-based behavioural and pharmacological treatments.⁶ The lack of routinely available objective diagnostic testing or biomarkers for ADHD may contribute in part to some of these erroneous beliefs.

Treatments for ADHD

The pathophysiology of ADHD is related to inefficient tuning of the prefrontal cortex by

TABLE 3 - Common Myths About ADHD and its Treatment^(3, 19)

Myth	Facts
Excessive use of television/video games/smartphones causes ADHD	Neurological abnormalities related to ADHD are present from birth. ADHD has been recognized clinically for more than 200 years, long before such technology was available.
Excessive intake of sugar, food additives, dyes or environmental toxins causes ADHD	There is no evidence to show that excessive intake of junk food or a diet with high sugar content causes ADHD. Neurological abnormalities related to ADHD are present from birth. Exposure to certain food dyes appears to worsen ADHD symptoms in some individuals.
Eliminating certain foods from the diet can effectively manage ADHD	Studies of elimination diets claiming benefit for ADHD symptoms are methodologically flawed. Typically, the person implementing the dietary changes for the patient is also the symptom rater/assessor and is therefore biased due to not being "blind" to the treatment condition.
Poor parenting causes ADHD	There is no evidence to support this statement. Neurological abnormalities related to ADHD are present from birth. Certain behavioural management techniques employed by parents can help improve some ADHD symptoms.
ADHD is overdiagnosed	Diagnostic criteria for ADHD have evolved over time. Current criteria/age requirements have increased the frequency of diagnosis somewhat, especially in adolescents and adults. The increased awareness of ADHD and availability of newer, more convenient treatment options (e.g., long-acting stimulants, non-stimulants) may increase the likelihood of patients seeking evaluation and treatment. There is evidence that ADHD remains underdiagnosed and undertreated. ²⁰
People "grow out of" ADHD as they get older	Neurological abnormalities related to ADHD are present from birth and remain throughout life. Hyperactive symptoms often lessen as patients age, and some patients learn to adapt or find occupations where ADHD symptoms may be of benefit. The majority of patients diagnosed with ADHD as children remain impaired by ADHD symptoms into adulthood.
Stimulant use in childhood will lead to "addiction"	Patients with ADHD (especially when untreated/undertreated) are at elevated risk for substance use disorders compared to the general population because of an increased risk for impulsive behaviour or attempts to self-medicate their condition. Evidence shows that stimulant treatment does not appear to change or increase the risk for development of a substance use disorder.

circuits involving the neurotransmitters dopamine and norepinephrine.^{3,5} All ADHD drug treatments act on one or both of these neurotransmitters. The most commonly used ADHD treatments are the stimulants, primarily amphetamine derivatives and methylphenidate, which work by inhibiting reuptake and in some cases promoting release of these neurotransmitters into the synapse.⁵

It may seem counter-intuitive to prescribe a stimulant to someone with ADHD who appears quite overstimulated to begin with. However, in an individual with ADHD, the activity of dopamine and norepinephrine in these circuits is actually too low and administration of a stimulant corrects the deficiency and restores optimal function and tuning of the prefrontal cortex.⁵ The role of norepinephrine is to strengthen the ability to pay attention to desired information (the "signal," such as a math lesson) and the role of dopamine is to reduce the ability to pay attention to undesired information (the "noise," such as a squirrel outside the classroom window).⁵ However, moderation is key. Overloading these circuits with excessive constant stimulation or bursts of dopamine and norepinephrine leads to recruitment of additional neurons and misdirection of attention, which is not beneficial.⁵

Knowing the pharmacological class,

mechanism of action and basic pharmacokinetics (such as time of onset and offset of action, and duration of action) of the various ADHD treatments is key to advising caregivers and patients how to take their medication to achieve optimal results. The Canadian ADHD Resource Alliance (CADDRA) publishes a free downloadable colour chart that summarizes this information in both English and French (https:// www.caddra.ca/resources/medication-chart/).⁷

Stimulants

Stimulants have been used to treat ADHD for over 50 years and are among the best studied psychotropic medications in children.⁸ Unlike some other psychiatric medications, there is no delay in onset of action of stimulants and many patients notice an improvement in ADHD symptoms even following the first dose. Whether a patient takes an immediate release (IR) stimulant, or a long-acting/extended-release stimulant, the onset of action against ADHD symptoms typically occurs within 0.75-2 hours following a dose. The duration of symptom relief is short-lived with IR formulations: approximately 3-4 hours with methylphenidate IR and 4-6 hours with dextroamphetamine IR, though this is somewhat variable based on dosage.

Prior to the availability of long-acting stimulant formulations, patients with ADHD usually took two divided doses of dextroamphetamine IR or three divided doses of methylphenidate IR throughout the day to maintain control of ADHD symptoms. In recent years, various drug delivery systems have become available which make stimulant dosing more consistent and convenient. Most long-acting/extended-release formulations work by releasing a portion of the drug contents immediately, while also delaying or controlling release of the remaining portion of drug contents by several hours. This extends the duration of action and allows once-daily dosing, which is important to many children, and helps avoid embarrassment or stigma of having their peers witness them taking a medication during school hours. In some school settings, staff will not participate in medication administration, making once-daily dosing critical.

Long-acting stimulants are recom-

mended as first-line ADHD treatments according to CADDRA guidelines, while short- or intermediate-acting stimulants are second-line treatments.³ In some provinces or territories, pharmacare plans do not align with CADDRA treatment recommendations, and coverage of long-acting stimulants is restricted.⁹

With the rapid onset and fairly rapid offset of stimulant action, timing of stimulant dose administration is very important. Many patients take stimulant medication first thing in the morning after waking which affords the best chance for control of ADHD symptoms by the time school or work starts. This should be followed by a big breakfast before the appetite suppressing effects begin. If the time to onset of action of the extended-release stimulant takes longer than desired, some prescribers order a small adjunctive dose of IR stimulant to be taken at the same time as the extended-release stimulant to help shorten the delay in onset. Whether a stimulant medication is short-acting or long-acting, eventually stimulant blood levels decline and many patients experience ADHD symptom rebound as the stimulant action wears off. In these situations, ADHD symptoms can briefly return with a higher intensity and patients may become temporarily more anxious, impulsive or emotional than usual.³ Sometimes small adjunctive IR stimulant doses are prescribed in the late afternoon to extend the duration of action of long-acting stimulants longer into the evening hours or to reduce the intensity of rebound symptoms.

Caregivers or patients may ask whether stimulants can be temporarily stopped on long weekends or when out of school during holiday breaks or summer vacation. This is commonly referred to as a drug holiday. These are relatively common in practice, especially for children who experience severely reduced appetite during stimulant therapy (see below). However, it has been observed that interrupting stimulant treatment every weekend may actually increase side effects.³ Patients or caregivers should obtain approval from their prescriber before implementing drug holidays.

Non-stimulants

Non-stimulants, such as atomoxetine, guanfacine extended-release and clonidine, are

TABLE 4 - Appetite Management Tips for Patients Taking Stimulants⁽²¹⁾

- Adjust meal times to occur before stimulant onset in the morning or after wearing off in evening
- Prepare some snacks/meals in advance that can be thawed/reheated on demand when appetite perks up
- Offer a second supper (full meal with fat, protein, carbohydrates, not just a snack) to be eaten when appetite is rebounding before bedtime to help make up missed caloric intake during day
- Avoid rigid meal schedules: encourage patient to eat as much as possible, whenever they are hungry; allow "grazing" on nutritious foods made available throughout the day
- Avoid the requirement to sit at the table for meals; try allowing eating during screen time (when watching television/videos or while playing video games)
- When thirsty, instead of soda, offer nutritious fluids such as smoothies (can blend in peanut butter, protein powder or a banana), meal replacement shakes (e.g., Boost) or chocolate milk
- Switch to use of homogenized milk if possible (provides extra fat/calories)
- Engage the school in helping with nutrition intake before going outside to play at recess/lunch
- Maintain a consistent approach to nutritional intake between caregivers

also effective ADHD treatments. The percentage of patients who respond to these treatments and the degree of ADHD symptom reduction are generally smaller than with stimulants.

Non-stimulants are usually considered second-line treatments (atomoxetine, guanfacine extended-release) or third-line treatments (clonidine) by CADDRA and other ADHD practice guidelines.^{3,10} However, non-stimulants represent important treatment options, since stimulant treatment may not always be safe (e.g., patients with a family history of sudden cardiac death), tolerated (e.g., due to adverse effects on appetite, aggression or mood), or appropriate (e.g., patients with a history of stimulant use disorder). Non-stimulants may be used on their own or in combination with stimulants.^{3,10,11}

An advantage of non-stimulants is that following an initial one- to four-week delay in onset of action, they act continuously around the clock (if administered on an ongoing basis).

Other third-line treatments are occasionally prescribed by ADHD specialists (mainly in adults). These include antidepressants such as bupropion, venlafaxine or imipramine, which have properties of dopamine and/or norepinephrine reuptake inhibition.³

Stopping non-stimulants

Atomoxetine treatment may be stopped abruptly if required, as there is no known withdrawal reaction.^{12,13} ADHD symptoms return gradually following atomoxetine discontinuation as the brain adjusts. However, treatment with guanfacine extended-release and clonidine should not be stopped suddenly due to the risk of a rebound increase in blood pressure. The dosage of these medications should be tapered (gradually reduced) over one to two weeks. It is important to highlight this difference to caregivers and patients when starting these medications, especially if they have previously become accustomed to stopping long-acting stimulant treatment abruptly (e.g., for drug holidays), or if patients transition between different caregivers.

Technician's role

With knowledge of the basic underlying pathophysiology of ADHD, common ADHD comorbidities and the mechanisms of action and pharmacokinetics of the various ADHD treatments, pharmacy technicians will be well positioned to educate and support caregivers and patients living with ADHD. Technicians can help patients derive optimal benefit from their treatments, by providing education on proper timing of medication administration and by dispelling common myths about ADHD (Table 3). They can also provide tips to help manage stimulant adverse effects on appetite, aid in overcoming oral administration challenges, assist in promoting adherence to therapy and provide timely referrals to the pharmacist when needed.

Stimulant-induced appetite impairment

One of the most common stimulant adverse



effects is reduced appetite during the davtime while the stimulant is acting. Over the long term, reduced nutritional intake in stimulant-treated children can adversely affect growth in some children. Some tips to support patients and caregivers struggling with reduced appetite from stimulant treatment are shown in Table 4. Evidence shows that on average children treated with stimulants for a period of three years grew an average of 2 cm less in height, and gained 3 kg less in weight compared to age-matched stimulant non-users.^{3,14} Some patients may experience a more severe reduction in growth and switching to a non-stimulant ADHD treatment may be required.³ A longer-term follow-up study of young adults showed a mean reduction in adult height of 1.3 cm for patients who had received stimulant treatment, with up to a 4.7 cm reduction in consistent stimulant users compared to a control group.^{15,16} Drug holidays are sometimes recommended to help reduce the impact of stimulant use on growth.3 Close monitoring of height and weight over time by prescribers and caregivers is recommended for patients taking long-term stimulant treatment.³

Oral administration challenges

Oral medication administration can be challenging, especially in young children who have difficulty swallowing tablets or capsules. Currently, no liquid or oral dissolving formulations of ADHD treatments are commercially available in Canada. Some currently available ADHD medications can be administered by alternate methods, such as by opening capsules and sprinkling the medication beads contained inside on soft food (e.g., applesauce, yogurt/pudding, ice cream) prior to administration. Doing so does not affect drug absorption or duration of action; however, patients should be advised not to chew the contents of products with beaded/sprinkle formulations. Lisdexamfetamine capsules may be opened, and the powder mixed into water, orange juice or yogurt prior to administration. Other ADHD treatments must be swallowed whole to preserve the intended drug delivery system. Inadvertent splitting, crushing or chewing products intended to be swallowed whole can alter onset or duration of drug action (e.g. methylphenidate extended-release (Concerta)), or lead to an increase in adverse effects (e.g., guanfacine extended-release).17,18

Adherence

Technicians can monitor patient adherence to ADHD medication using standard methods such as looking for discrepancies between the days' supply of medication dispensed to numbers of days between refills. When identified, gentle inquiry whether there has been a change in the way the ADHD medication is being taken will often reveal what is happening. It should be kept in mind that some patients may temporarily stop taking stimulant medication during holiday periods, or even on weekends, often with their doctor's approval, so one should not make the leap to non-adherence automatically. However, suddenly stopping and/or restarting certain non-stimulant medications is not recommended, and if identified that this is occurring, patient/caregiver counselling may be required about the way these medications work, and the potential adverse reactions that may occur.

Referral to the pharmacist

Technicians should refer patients/caregivers to the pharmacist for further consultation when it is identified that patients are taking ADHD medication in a sub-optimal manner, experiencing an unexpected medication duration of action, an uncommon or severe side effect; are prescribed dosages that exceed those found in practice guidelines; or have a complex medication profile and are at risk of a drug interaction with other medications.

Summary

Pharmacy technicians can make a positive impact on the care of patients with ADHD through promotion of adherence and management of common adverse effects. A

working understanding of ADHD symptoms, comorbidities, common myths and the medications used to treat ADHD is the foundation for providing high-quality care.

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QUESTIONS

- 1. Which symptom is NOT part of one of the ADHD symptom clusters?
- a) Hyperactivityb) Impulsivityc) Aggressiond) Inattention
- 2. Executive functioning (EF) is abnormal in
- patients with ADHD. Which skill is not related to EF?
- a) Regulating behaviour and emotions
- b) Controlling attention and resisting distractions
- c) Identifying and solving problems
- d) Interpreting social cues

3. The most correct statement about the underlying cause of ADHD is:

- a) Poor parenting skills
- b) Neurological abnormalities that are present from birth
- c) High dietary gluten intake
- d) Excessive amounts of time playing video games
- 4. The main neurotransmitters involved in the pathophysiology and treatment of ADHD are:
- a) Dopamine and norepinephrine
- b) Dopamine and histamine

Please select the best answer for each question and answer online at eCortex.ca for instant results.

- c) Serotonin and norepinephrine
- d) Histamine and serotonin
- 5. Which of the following is a common comorbid condition in patients with ADHD?
- a) Schizophrenia
- b) Generalized anxiety disorder
- c) Communication disorder
- d) Type 1 diabetes

According to the 4th edition of the CADDRA ADHD practice guidelines, guanfacine extended-release is:

- a) A first-line treatment recommendation
- b) A second-line treatment recommendation
- c) A third-line treatment recommendation
- d) Not recommended

All of the following symptoms are part of the ADHD hyperactive-impulsive symptom cluster, EXCEPT:

- a) Fidgets and squirms in seat
- b) Interrupts others and blurts out answers without waiting for their turn
- c) Frequently loses notebooks, pencils or assignment papers
- d) Climbs furniture or rolls on floor frequently

- 8. What does scientific evidence tell us about the risk of development of substance use disorders (SUDs) subsequent to treatment of ADHD with stimulant medications?
- a) Stimulant treatment for ADHD lowers risk for development of SUDs
- b) Stimulant treatment for ADHD does not increase risk for development of SUDs
- c) Stimulant treatment for ADHD increases risk for development of SUDs
- d) Nothing is known about how stimulant use affects risk for development of SUDs
- 9. What does the evidence say is the typical impact on height and weight in children following 3 years of stimulant treatment compared to age-matched stimulant non-users?
- a) Height growth reduced by 5 cm, weight gain reduced by 5 kg
- b) Height growth reduced by 2 cm, weight gain reduced by 3 kg
- c) Height growth reduced by 1 cm, weight gain increased by 2 kg
- d) Height growth increased by 2 cm, weight gain reduced by 1 kg

- 10. As stimulant blood levels decline at the end of their duration of action, some patients with ADHD experience symptom rebound. Which of the following is NOT typical of symptom rebound?
- a) Increased emotionality
- b) Increased anxiety
- c) Increased impulsivity
- d) Increased physical strength
- 11. According to the 4th edition of the CADDRA ADHD Practice Guidelines, what line of treatment are long-acting stimulants considered?
- a) First-line treatments
- b) Second-line treatments
- c) Third-line treatments
- d) CADDRA guidelines do not comment on place in therapy of long-acting stimulants
- 12. Which would be an appropriate suggestion for caregivers and patients struggling with the adverse effects of stimulant medications on appetite?
- a) Cut your stimulant dosage in half for 2 weeks to see if appetite improves
- b) When thirsty, try offering/drinking smooth-

ies or meal replacement shakes

- c) Switch to using skim milk at home to improve appetite for solid foods
- d) Make candy and sugary foods available for patients to graze on throughout the day

13. Which patient/caregiver concern about ADHD medication should be referred to the pharmacist for consultation?

- a) A child has become very aggressive 3 days after starting treatment with a new long-acting stimulant medication
- b) A parent is expressing regret that their child would not have to take ADHD medications if they had just been better at parenting
- c) A child weighing 40 kg has lost 1 kg of weight 1 month after starting treatment with a new long-acting stimulant medication
- d) A child is unable to swallow a beaded formulation of a newly prescribed long-acting stimulant medication
- 14. If a patient taking methylphenidate extended-release tablets (Concerta) is not experiencing onset of ADHD symptom control within a reasonable time frame, prescribers may order:

- a) A small dose of clonidine immediate-release to be taken with methylphenidate extended-release tablets (Concerta)
- b) A small dose of methylphenidate immediate-release to be taken with methylphenidate extended-release tablets (Concerta)
- c) Wake the patient up 2 hours prior to when they usually arise to give the methylphenidate extended-release tablets (Concerta)
- d) Take a double dose of methylphenidate extended-release tablets (Concerta)
- 15. Pharmacy technicians can help caregivers and patients with ADHD to achieve optimal results from their medications by doing all of the following EXCEPT:
- a) Educating about ADHD medication timing and adherence strategies
- b) Educating about stopping all ADHD medications and following an elimination diet to control symptoms
- c) Educating about alternate administration strategies if patients can't swallow medications whole
- d) Educating about appetite management strategies for patients taking stimulant medications

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