[Saved by the Bell Theme]

CB: It's back to school time! This means schedules now have more busy time than free time. There are multiple committee meetings, mixers that have to be planned and attended, intramural sports and finding time to hit the gym, part-time work in order to be able to pay for all of this, applications to be filled out to decide what path the future holds, family and friend commitments, oh – and studying! How could I forget?

We've all been there, and the stress of living a chaotic life and realizing that you have an exam tomorrow at 9 am that you aren't prepared for is something I never want to relive.

Today's episode features a prominent problem within universities, and that is the misuse of prescription stimulants.

Welcome back to the Med Thread, your monthly dose of drug knowledge from Memorial's School of Pharmacy. I'm Cathy,

MC: and I'm Mike, and as Cathy said, we have got a good topic for you today. Just about all of us have used stimulants, perhaps even already today.

CB: Well, I'm just about to get my second coffee of the day, so you could say I'm also under the influence of a stimulant; caffeine is my saviour most mornings.

MC: Of course, many of us use caffeine, and there are still a fair number of people using nicotine, but today we are tackling the prescription stimulants, their history, their use and misuse, and some interesting facts along the way.

CB: Let's speed this up.

MC: Nice one!

History of stimulants

(Hicks, 2012, Blakemore, 2017)

CB: Stimulants do exactly what the name implies; they speed up the functions of the body. This leaves users feeling more alert. There are a wide variety of stimulants out there.

MC: Most commonly used are caffeine and nicotine, which are both derived from plants, and also amphetamines, which are synthesized in the lab.

CB: Let's look at prescription stimulants, starting with amphetamines; these were first used for nasal congestion in the 1930s and eventually went on to treat other conditions. Their side effects were found useful for obesity, depression and hyperactivity. These same side effects, mostly excitement and alertness, spread in popularity and over time they started to be abused.

MC: Part of the reason for abuse may stem from societal pressures. We are living at a much faster pace and more demanding lifestyle than previous generations. We are expected to do more, be better and do it all faster. Whether it is friends and family expectations people try to live up to,

or a supervisor or a professor, or even our own personal standards, these stimulants have been a crutch for those who are trying to achieve more.

CB: Let's go back in time and look at where these first came from…

CB: Amphetamines are relatively new on the scene in comparison to caffeine and nicotine; they first popped up in 1887 after the first amphetamine was made by accident when a German Scientist was working on a treatment for asthma. The drug sat on the lab shelf for a few decades, until the early 1930s when it was explored further.

MC: It was found to be a strong bronchodilator, hence the connection to asthma, and when it was being tested the subjects found it gave them energy and they felt almost euphoric. The researcher put these effects aside and amphetamine went on the market as the Benzedrine inhaler, used to treat colds and asthma.

CB: It didn't take long before word spread that these didn't just clear your nasal congestion, and during this time of prohibition and depression, Benzedrine became very popular for a quick fix.

MC: From there, amphetamine was developed into a tablet and used by soldiers during World War II to reduce fatigue.

CB: And they weren't the only ones using them. Drug companies marketed amphetamines for depression and as dieting aids and were taken up by people in all walks of life. Sleepy truck drivers used them to stay awake, athletes used them to perform harder and longer, women who wanted to lose extra weight, and students cramming for exams. They were easy to get, and legal to use.

MC: But that's not the case today, so what changed?

CB: By the 1960s, amphetamine addiction was noticed by many physicians and reported to the FDA, soon after, restrictions were put in place to protect people from developing such a dependency.

MC: Today prescription stimulants are only indicated for ADHD, attention deficit hyperactivity disorder and narcolepsy.

CB: But is that all they're being used for?

MC: Not at all, prescription stimulants of today are still being misused for their psychoactive properties. For both cognitive enhancement and recreational purposes, or to get high.

CB: I should mention that when we are talking about prescription stimulants we are including methylphenidate, brand name Ritalin, Biphentin and Concerta, as well as the amphetamine products, like Adderall, Dexedrine and Vyvanse.

[Matthew Good Band – Hello Time Bomb]

Epidemiology

MC: The Canadian Centre on Substance Abuse [Use and Addiction] released an article in June 2016 that looked at the use of prescription stimulants across Canada. They found that the rate of use in the general population has remained pretty consistent at about 1% since 2008 and the highest use is found in the youth demographic.

CB: Today we really want to focus on the misuse of stimulants, and by that we mean when an individual takes a prescription stimulant without a prescription, or for purposes other than prescribed.

How much of the use of prescription stimulants is actually misuse?

MC: Well between 2012 and 2013, 2.5% of Canadian students in grades 10-12 reported using stimulants to get high in that past year.

CB: And what about University students?

MC: A convenience sample taken from 32 post-secondary institutions indicated 3.7% of students had used them to get high in the last 12 months, but this isn't completely representative and other studies of post-secondary campuses indicated rates as high as 5.9%.
(CCSA, 2016)

CB: A report by the same group published in April of this year looked at the non-medical prescription use among post-secondary students; they found the prevalence rate varied between 8 and 43% in individual studies. Variability was suspected to be due to the difference in study designs and levels of anonymity. Regardless, we know that non-medical prescription stimulant use is prevalent in post-secondary students.

MC: Also, students listed prescription stimulants just second to cannabis when asked, what were the prevalent substances on campus. They also said stimulants were more appealing as their use is easier to hide, there is no smell like with cannabis, and they are perceived as safe because it is legal and 'everyone is on medication'.

CB: And they're not hard to find, 62% of students said they'd been offered prescription stimulants, most often by a friend with a prescription, at least once in their lifetime.
(CCSA, 2018)

MC: The most common source of prescription stimulants among college students are peers. Focus groups have found that they're being sold in the library during exam time and over social media.
(Benson, 2015)

CB: And it's important to mention that sometimes these stimulants are actually prescribed this way, I have clients in the community that have been prescribed stimulants to focus during studying without having a diagnosis of ADHD.

MC: Does it work this way? The picture is quite complex and the evidence is inconclusive. There are a few studies in non-ADHD people that showed better recall and recognition, but it may be limited to rote memory tasks, like memorizing a list. This is not the complex memory and learning we

strive for in education. And single dose studies have not shown significant positive benefits either.
(Lakhan, 2012, Batistela, 2016, Linssen, 2014)

CB: In addition, the laboratory conditions set up to do these cognitive tests cannot be directly transferred to real life school and work situations.

MC: And it's interesting to think very negatively about the use of performance enhancing drugs in sports but when it comes to possible cognitive enhancement, it seems to be a different story.

Actually, one university I read about has a policy stating 'the unauthorized use of prescription medication to enhance academic performance is considered cheating"
(Duke University: https://studentaffairs.duke.edu/conduct/z-policies/academic-dishonesty)

CB: So the idea of cognitive enhancement, like in the book and film Limitless, is a fairly long shot.

[Limitless Trailer 2011]

CB: This medication misuse can fly under the radar as students often think that these are safer than street drugs. There are many campaigns targeting binge drinking, street drug use, prescription pain medications, but not stimulants.

So why are we concerned about misuse? Let's look at how these drugs work and then we can showcase the potential risks of using these stimulants for focus, alertness, and wakefulness.

Pharmacology and Risks of Misuse

(Pharmacology available from DiPiro, 2017)

CB: As we mentioned, these therapies are used to treat attention disorders, and actually, ADHD is the most common paediatric neuropsychiatric disorder, affecting 4-12% of North American school-aged children. Usually symptoms present before the age of 12 and may persist into adulthood.
(Akinbami, 2011)

MC: There are 3 hallmark symptoms – inattention, hyperactivity and impulsivity – the presence and severity can vary person-to-person and the Diagnostic and Statistical Manual of Mental Disorders or DSM-5 has criteria for diagnosing it.
(American Psychiatric Association, 2013)

CB: The DSM-5 doesn't discuss symptom onset after 12 years of age, but there is increasing evidence that late-onset ADHD may occur in young adults with no childhood diagnosis, and an estimated 3-4% of adults have ADHD.

MC: Symptoms often interfere with normal development, are present in 2 or more settings, at home, work or school, and have a direct unfavourable impact on social, academic, cognitive or occupational functioning.
(Agnew-Blais, 2016)

CB: And there are different subtypes, an individual can be primarily inattentive subtype, a hyperactive/impulsive subtype, or combined subtype, which is the most common. The goals of therapy are to reduce the symptoms, and improve behavioural, academic or occupational performance. So let's look at how stimulants help these patients.

MC: Although amphetamines and methylphenidate derivatives are structurally different, they work in several, similar ways. One mechanism is by increasing the release of dopamine and norepinephrine and another is to block their reuptake into neurons, both of which increase the amount of the neurotransmitters in the communication between neurons. How this works to help ADHD symptoms is not fully understood.

CB: It is suspected that ADHD sufferers don't have enough access to dopamine and these drugs help symptoms by providing a calming effect, allowing them to focus. When they're used appropriately under the guidance of a healthcare provider, they're effective for ADHD symptoms and they're used on a daily basis. For those without an attention disorder these drugs are more likely to cause the side effects because they already have enough dopamine in the brain and they're not taking them daily, just when they feel they need them to focus.

MC: Right, we know that amphetamines travel to the brain quickly and they increase nerve cell activity and stimulate the reward center of the brain.

So what potential side effects are we talking about?

Short-term effects of stimulants include trouble sleeping, decreased appetite, elevated heart rate, elevated breathing rate and headache/dizziness, which are all likely related to increased norepinephrine. The increased dopamine can cause euphoria, or that feeling of being high, as well as nausea and vomiting.

CB: As we mentioned, some of these side effects are actually the goal effect for students who abuse these to study late at night without getting tired, to perform better at athletics, to lose weight, or to get high. But there are also long-term effects.

MC: Increasing the levels of nor-epi and dopamine long-term can cause changes in mood or behaviour and may lead to anxiety, sleep disorders, aggression and anger, suspicion and paranoia. And of course, those that are misusing stimulants are at risk of becoming physically dependent.

CB: Once dependent, a user can experience withdrawal, which is never comfortable. Withdrawal can bring upon cravings, anxiety and agitation, tiredness and sleep problems, loss of physical and mental energy, and mood changes, particularly depression. Picture one really big crash. And I should mention that the crash is bigger for those that just use these drugs on occasion to study, since they're not taking another dose when it wears off. The body has just used up a tonne of energy and now can feel exhausted and depressed.

MC: The severity of the 'crash' of withdrawal can vary depending on which stimulant was used, how much of it was used and the duration of use. For people looking to stop using stimulants, it is important to chat with a healthcare provider and get advice on how best to decrease the dose gradually.

CB: Although side effects can happen with just one dose, it is extremely important not to take high doses of prescription stimulants. This can lead to dangerously high blood pressure; thus an increased risk of heart attack and stroke, also seizures, psychotic episodes, dangerously high body temperatures and overdose.

MC: And there are drug interactions. Anything else that you take that increases nor-epinephrine or dopamine can have additive side effects. Even caffeine pills and energy drinks interact! And drugs like over the counter decongestant cold medications, and some prescription antidepressants can cause irregular heartbeat when combined with these drugs.

CB: And what do university-aged people stereotypically do more of? Drink alcohol, and this is a big problem if mixed with stimulants. They counteract the relaxing effects of alcohol and people tend to drink too much too quickly since they don't notice the effects and accidental overdose of either drug is possible.

MC: Another concern is when these agents are cycled with sleep-aids. Of course, when you're using a stimulant you may not be able to get to sleep, so then you can end up relying on a medication for sleep, which can cause you to be drowsy in the daytime, needing more stimulant, and the cycle continues!

[Smino – Amphetamine]

CB: And do they actually help us perform better? Well, the Canadian Center on Substance Use and Addiction published a report in April which states that the most common reported motivation for non-medical prescription stimulant use among post-secondary students is for academic enhancement. But there's research to suggest that those who do use stimulants have lower grades compared to those who do not use.
(CCSA, 2018)

MC: And while we talk about drugs in this podcast, it is equally important to think about the social, cultural and individual reasons for taking these drugs.

I came across one interesting article through the Canadian Public Health Association, written by a university-student at Western University. He talks about 'Why students are using study drugs and what we can do about it'. Essentially, there are a number of underlying factors and drugs are possibly used to help students cope with those issues. I'll post a link to the article on our website.
(Abelman, 2017)
(https://www.cpha.ca/why-are-students-using-study-drugs-and-what-can-we-do-about-it)

Healthier Alternatives to a potentially ineffective treatment

CB: Although students may feel extreme pressures to succeed, there are ways to study effectively, without the help of stimulants for focus, and that crash that follows.

MC: The typical tips for healthy living apply, even when in study-mode. Eating a balanced and healthy diet and getting plenty of sleep will allow you to stay engaged in the classroom to help the information be absorbed in the first place.

CB: Relaxation techniques are important to relieve the performance anxiety of test-taking or the stress of competing in academics. Yoga, and other types of exercise, are proven to reduce stress. Also, take study breaks and spend time with friends,

MC: And if you do need a coffee a day, that is a safer option of course. Safer but still a stimulant. Remember, a grown adult can handle 300-400 mg of caffeine a day. Putting that into perspective, a Medium coffee at Tim Hortons has 205 mg, and those caffeine pills average about 200 mg each.

But we could talk about coffee all day, let's move along.
(http://www.timhortons.com/ca/en/pdf/CAFFEINE-CONTENT-Canada-May2017.pdf)
(See Health Canada – Licensed Natural Health Products Database, Ingredient: caffeine)

CB: And let's not forget the evidence that students who use stimulants non-medically actually have lower grades than those that don't. One study looked at over 1200 first-year university students who reported non-medical use at baseline and found that they studied less, socialized more, and reported skipping more classes than those who didn't use stimulants, and they received lower grades at the end of the year.
(Arria, 2008)

MC: Another study looked at academic records across two years and showed no improvement in GPA in students who used stimulants non-medically. Actually, GPAs increased for those who didn't use stimulants.
(Arria, 2017)

CB: And the placebo effect may also be fooling users, students in one study were given a placebo that they believed to be methylphenidate and reported they had greater ability to focus for long periods of time
(Looby, 2011)

What I'm getting is that the use of stimulants without a medical diagnosis is dangerous and may not work for improving studying in the first place.

MC: There is, of course, a place for these therapies in medicine, and in no way do we mean to say that patients that are prescribed stimulants for the treatment of their condition are taking them irresponsibly.

CB: Absolutely, given the time of the year, we wanted to educate our listeners on prescription stimulant misuse in the university-aged population and to encourage people to always speak to a healthcare provider when determining whether or not to use any medications, prescription or otherwise, for therapeutic or recreational use.

MC: And if you have trouble with focusing and attention look up your school's student support and academic resource centre. They're always there to help you.

Memorial has a whole website and department focused on Student Support.
(https://www.mun.ca/currentstudents/student/)

CB: As always, you can find our references and notes on our webpage at www.mtsclinic.ca and if you have questions, comments or things you want to hear about, send us a message on Facebook via the School of Pharmacy or email medthread@mun.ca.

And be sure to catch us next month where we have another guest in-studio. Our friend Justin Turner from the Canadian Deprescribing Network will be here to talk about proton pump inhibitors and all that stomach acid.

MC: That's it for today! Thanks for listening!

CB: Bye for now!

[Canned Heat – Amphetamine Annie]

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Extra reading

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