Differential Diagnosis of Adult Patients with ADH

A Training program

Making Education Easy

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About the Reviewer



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Dr Umesh Jain completed medical school at Dalhousie University in 1986 and his psychiatry and child psychiatry training between Dalhousie and the University of Pittsburgh during1986-1991.

He is Board Certified in psychiatry in Canada and the US. He completed his PhD at the University of Toronto in 2002 and M.Ed. from The University of Toronto in 2007, at which he currently holds the position of Associate Professor of Psychiatry.

Dr Jain is an internationally recognised scientist and teacher in the area of ADHD across the lifespan. He has participated in numerous grants including CIHR, OPGF, OMHF and contract research. He has written over 125 peer reviewed papers, books, book chapters, academic poster and invited speaker presentations. He has been on the Scientific Boards of the Canadian and American Academies of Child and Adolescent Psychiatry and on the National Executive of the Canadian Academy. He started CADDRA, an affiliation of all Canadian specialists practicing in the ADHD arena. CADDRA produces the Canadian ADHD Guidelines for Practice, which he was the Managing Editor until 2011.

Dr Jain has won the Naomi Rae Grant Award for Professional Excellence and the Canadian Academy of Child Psychiatry Education Award for his work on ADHD. His production company, TotallyADD.com has created a new model of information dissemination for people with ADHD. He is also working as a consultant for child psychiatry projects throughout the world. He lives in Toronto with his wife, a neonatal specialist, and their four children.

About Expert Forums

Expert Forum publications are designed to encapsulate the essence of a local meeting of health professionals who have a keen interest in a condition or disease state. These meetings are typically a day in duration, and will include presentations of local research and discussion of guidelines and management strategies.

Even for local events it is not always possible for everyone with a similar therapeutic interest to attend. Expert Forum publications capture what was said and allows it to be made available to a wider audience through the Research Review membership or through physical distribution. Welcome to this review of the recent Adult Attention-Deficit Hyperactivity Disorder (ADHD) Workshop held in Auckland. ADHD in adults remains clinically very challenging and whilst

great strides have been attempted in further understanding, recognition and therapeutics of its treatment, there is considerable work still to be done to help attain meaningful outcomes for patients, parents, carers and healthcare professionals. To this end, Dr Jain presented an interactive training workshop looking at the differential diagnosis and treatment of adult patients with ADHD. Dr Jain has been instrumental in putting together the TotallyADD Training Manual, a continuing medical education program and has developed a website full of useful resources on this difficult area of psychiatry (<u>www.totallyadd.com</u>). The content of the Training Manual is evidence-based as much as possible, but also incorporates consensus-based information from key opinion leaders.

This workshop, sponsored by Eli Lilly, was the first of its kind and the sponsors welcome any feedback.

Dr Jain introduced the Forum by explaining that adult patients with ADHD are easy to treat, but that such treatment must involve a holistic agenda. This means lifestyle management using a multimodal intervention strategy involving medications and behavioural, psychological, occupational and educational interventions. He pointed out that after treatment, these patients will feel better than they did before and that this phenomenon is quite different from many other areas of psychiatry where the best that can be done is to get the patient to a pre-morbid level of functioning. This phenomenon is what makes treating ADHD very satisfying.

Dr Jain directed clinicians to the CADDRA (Canadian ADHD Resource Alliance) website (<u>www.caddra.ca/</u>) where the CADDRA 2011 Practice Guidelines can be downloaded to assist clinicians with assessing and treating patients with ADHD.

Why doctors don't like assessing and treating ADHD

Some clinicians have negative biases against patients with ADHD because such patients are often late to appointments (or do not show up at all), can be annoying, dependant, demanding, emotional, have short attention spans, have a need for immediacy, exhibit poor follow through (often ignoring clinicians suggestions or requests), can be very concrete in their understanding and are often pessimistic of treatment resolve. Sometimes these patients blame others for their problems and deep down may even blame their doctor for not 'fixing' them. They may act in immature ways and appear as if they have a personality disorder. Often the patient seems child-like and the physician runs the risk of becoming the idealised parent in the doctor–patient relationship, with associated issues of dependency.

Helpful hints for managing adult ADHD patients

Dr Jain stressed that while the behaviour of a patient with ADHD may be irritating, once you understand them they can be very likeable. He made some suggestions for managing patient appointments and pointed out that clinicians can adjust the way that they schedule their appointments so that there is more opportunity to juggle things to accommodate this group. Sending patients a reminder of their upcoming appointment can be very helpful. He also advised that patients fill out any questionnaires at the doctor's office rather than risk having them taken home and not returned.

A suggested approach to the management of patients with ADHD is to remember that they are trapped in their childhood. It is important to feel empathy for them, instead of contempt. When they challenge you be firm, but avoid being authoritarian or defensive. Let the patient know that you are not perfect and that together you can make their situation better. Trust and the therapeutic alliance is the critical factor in treating these patients and they need to be reminded that they will not see immediate results from their treatment.

The first visit: taking a patient history

Dr Jain would normally put aside 45 minutes for the first appointment. A video clip of Dr Jain interviewing a new patient (Bill Smith aged 45 years) was shown to demonstrate a typical first interview. During the interview, Bill talked excessively and was over inclusive, a feature common in adults with ADHD. This type of nervous banter does not have the pressure of speech seen in individuals with bipolar disorder, the loose associations seen with schizophrenia or the disorganised thinking of a thought disorder. Individuals with ADHD seem to feel the need to give more information than is asked for and a circumstantial type of speech may be observed. Dr Jain explained that if you encounter such a patient during an initial assessment and you find that you are having trouble controlling the interview, ADHD should be considered. You will need to take a more interrogative and interrupting approach in order to control the interview.

How prevalent is ADHD?

In Ontario, the prevalence of ADHD in school-aged children is estimated to be 3-9%,¹ and in adults in the US to be approximately 4.4%.² Faraone et al suggest a New Zealand ADHD prevalence rate of 3-5%.³ It is thought that the actual rate in New Zealand may be more than double that rate. Interestingly, Ukraine is estimated to have an ADHD prevalence rate of 20%.³

It is estimated that approximately 60% of children with ADHD will continue their impairment into adulthood.^{4,5} For those who appear to have 'lost' their ADHD it is most likely that as an adult they have adapted sufficiently for their symptoms to no longer constitute a disorder. This phenomenon supports the value of non-medical approaches to treatment.

While more boys than girls are diagnosed with ADHD, the adult male-to-female ratio is close to 1:1.⁶ Girls with ADHD often go undiagnosed, mainly because they exhibit the inattentive subtype. Also, girls exhibit different coping strategies and cultural expectations suppress the symptoms of this disorder.

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Most common reasons for referral

One of the most common reasons for referral is having a child diagnosed with the condition. The parent will often realise that they have the same symptoms. Often too, the patient or their partner may have seen a documentary or have read about the condition. In fact, after the screening of the documentary *ADD and Loving It?!*, the rate of referral increased in the US. Frequently, it will be a spouse who has identified the symptoms. Sometimes the patient may be in trouble at work or in trouble with the law.

Identifying the chief complaint

Dr Jain played a video clip of the second part of his interview with Bill. In the interview, Bill explained that his wife had insisted that he make the appointment and that his son had recently been diagnosed with ADHD. He talked about having previously been divorced, having had more jobs and career changes in the past decade than most people have in a lifetime, and that while he always thought of himself as carefree, his sister-in-law considers him to be one of the most anxious people she has met. He explained that he always has unpaid bills and is constantly in crisis management mode, although never really managing. He reported that he felt like his life was in chaos and that he had felt like that all his life. He said that while his situation was depressing, he didn't think he was depressed and didn't think he had any thing psychologically wrong with him. He reported that when things get really bad he just makes up jokes, which others think are juvenile. To some extent his wife defends him saying he has a big heart.

From this interview we get the impression that this patient's life is spinning all the time, and any clinicians first instinct would tell them that this patient is suffering from anxiety and depression. Dr Jain stresses that with such a presentation, ADHD must be considered.

Key statements suggestive of ADHD

A patient with ADHD may report the following:

- · 'My child was diagnosed with ADHD and I think I have the same symptoms.'
- 'I have never felt well.'
- 'I am not meeting my potential.'
- · 'I have anxiety/depression that simply doesn't seem to be getting better.'
- 'I just can't focus on anything for very long.'
- 'I used some of my child's/friend's medication and frankly I felt better.'
- 'I talk the talk but can't do the walk.'
- 'I am incredibly disorganised.'
- 'I'm in trouble with'

Dr Jain pointed out that so many of his new patients have tried their child's ADHD medication that he now just directly asks them 'So how did you feel when you took your child's medication?' He says that this is often a segway to help him get to the story faster.

Where to from here?

If, during the first patient visit, ADHD is on your radar, then Dr Jain suggests arranging a second visit and directing the patient to the Virtual Doctor on the TotallyADD.com website. He suggests that the patient prints out their generated profile and brings it to their next appointment and that they watch the video on informed consent on the TotallyADD.com website. These could be watched at the doctor's office. He also suggests giving the patient the relevant questionnaires (including the Adult Self-Report Scale-V1.1 [ASRS-V1.1] Screener) from the CADDRA Canadian ADHD Practice Guidelines to be filled out before they leave the office.

Identifying the core impairing symptom

There are many clinical symptoms that present with ADHD, but it is important to identify the core impairing symptom/s. In the case of Bill presented above, the two core symptoms coming through in his initial assessment were impulsivity and poor organisational skills.

Symptoms associated with ADHD include the following:

- Impulsivity
- Inattention
- · Motor restlessness (hyperactivity)
- Associated symptoms
 Low self-esteem
 Procrastination
 Lack of organisational skills
 - Poor time management

More information on each of these symptoms can be found in the DSM-IV-TR $^{\odot}$ Diagnostic and Statistical Manual of Mental Disorders.⁷

Visual representation of how these symptoms impact on the daily life of an individual with ADHD can be viewed in the many videos on the TotallyADD.com website. Watching these videos is an effective way for patients to connect with the information. Dr Jain says that the videos are especially useful for adolescents with ADHD, a group that is difficult to reach.

ADHD classifications – DSM-TR

There are three subtypes of ADHD:

- Predominantly Combined Subtype (ADHD-C)
- Most common ($\approx\!60\%$ of cases) though likely to move to inattentive subtype by adulthood

- Predominantly Inattentive Subtype (ADHD-I)
 - Probably underreported (${\approx}35\%$ of cases)
 - Females likely not showing robust symptoms in early childhood
- Predominantly Hyperactive-Impulsive Subtype (ADHD-HI; ≈5% of cases) – Higher prevalence in the prison population
- May result from congenital abnormality or head injury

Age-dependent decline and change of ADHD symptoms

Data from a longitudinal study of children growing up with ADHD support the clinical observation that hyperactivity and impulsivity symptoms decline with age at a higher rate than inattention symptoms.⁸ Because the hyperactive-impulsive symptoms of ADHD tend to internalise as the individual moves through adolescence and into adulthood, these symptoms are not as relevant to the diagnosis of adult ADHD. To this end, it is essential that a childhood history be taken to look for evidence of these symptoms. If one looks only at the adult symptoms, where hyperactivity and impulsivity may be absent, ADHD may be overlooked in the diagnosis. It is also easy to misdiagnose the inattentive symptoms (which tend to plateau and persist) as loss of concentration due to depression.

The ways in which the three main symptoms of ADHD change from childhood to adulthood are listed in **Tables 1-3**. Often an adult with ADHD will have a huge pile of unattended paper work on their desk, with numerous unpaid bills. Dr Jain joked that paperwork is like kryptonite to these individuals. Sometimes patients may appear to cope well in their professional life and may have chosen careers that fit with their traits, but often if you dig deeper you will find a history of a very dysfunctional personal life. Dr Jain used the example of a successful attorney who is on his third marriage, has been bankrupt and has a list of traffic violations.

Table 1. Inattention: child to adult symptom changes

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Childhood DSM-IV-TR® symptoms7	Common adult symptoms ⁹
Difficulty sustaining attention	Difficulty sustaining attention to reading or paperwork
Does not listen	Easily distracted and forgetful
Difficulty following instructions	Poor concentration
Cannot organise	Poor time management
Loses things	Difficulty finishing tasks
Easily distracted/forgetful	Misplaces things

Table 2. Hyperactivity: child to adult symptom changes

Childhood DSM-IV-TR® symptoms7	Common adult symptoms ⁹
Squirms and fidgets	Inner restlessness
Runs or climbs excessively	Overwhelmed
Cannot play or work quietly	Self-selects active jobs
'On the go,' driven by a motor	Talks excessively
Talks excessively	Fidgets when seated

Table 3. Impulsivity: child to adult symptom changes

Childhood DSM-IV-TR® symptoms7	Common adult symptoms ⁹
Blurts out answers	Impulsive job changes
Cannot wait his or her turn	Drives too fast, has traffic accidents
Intrudes on or interrupts others	Irritability or quickness to anger

Establishing the childhood symptoms

A second interview with the patient Bill Smith was shown exploring his childhood history. During the interview, Bill describes an early childhood living in the country and spending all day playing outside. He explained that he was always getting in trouble and doing stupid things and no matter how many times his mother told him to stop and think he would do it again. When he was very young he was tied into a chair so that he would finish his meal. His mother had to put him on a leash when they went out to town. He reported that he gave his mother hell. She reported that it was not until his younger brother was born that she realised there was something wrong with Bill's behaviour. He was born two weeks late and was late to talk. His temper tantrum twos never stopped. His teacher had referred to him as having 'ants in his pants' and had told his parents that he needed to learn to raise his hand to talk. At school he was a charmer and got away with things by making a joke. He was the class clown. He was never invited to birthday parties or sleepovers. He hated schoolwork and homework, and used to daydream that he was Calvin from the Calvin and Hobbes comic strip. If he liked a topic he would get totally involved in it. He had been prescribed medication for his behaviours, but his mother declined to give it to him until he was older. Bill reported that his father drank a lot and was abusive. He also reported that he himself got into fights at school. He liked to set fire to things but never got in serious trouble.

Obtaining an accurate childhood history is vital to the diagnosis of adult ADHD and is the critical component of ADHD investigation. Dr Jain suggests asking the patient to bring in their school reports and any results of childhood psychological testing to their next visit. He also suggests

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obtaining their permission to talk to their mother and/or other relatives to get a clear picture of their childhood history. He says that there is always a story that can be found with regard to the patient's childhood behaviours. He adds that he does anything to get that story. He will phone parents up halfway around the world. He cannot emphasise enough that the core aspect of the diagnosis for the adult patient will come out of the context of childhood symptoms.

To aid the patient to go back to earliest memories, use associations. Ask them to describe their house, people and events from their childhood. It is necessary to eliminate major trauma (sexual and physical abuse) as the symptoms of this can mimic ADHD in childhood. Investigate any separation issues. Try to establish a chronological history with an emphasis on the ages between 2½ to 6 years, as this time happens to be very similar to the cycles of adolescence and midlife (adolescent rebellion, midlife crisis). Ask yourself if you could eliminate the family history would this patient still have symptoms of ADHD today. It is often difficult to tease out abuse and hypervigilance from ADHD.

Family factors are relevant

ADHD is a highly genetic disorder.¹⁰ In fact, if one or both of your patient's parents do not have symptoms your patient's diagnosis should be questioned. A good start line is 'Who in the family remindes you of you?' Also ask 'Were your parent's opposite in their personalities?' It is generally recognised that hyperactive-impulsive men tend to gravitate towards highly obsessional women.

Social history and global domains – establishing impairment

An adult with ADHD may be doing well in most aspects of their life. In order to ascertain if a patient needs treatment, impairment must be determined. As already mentioned, even if a patient is high functioning in their job, they often have impairments in many domains. You need to ask about the following: driving record, substance abuse, relationships, education, career opportunities, parenting, and financial issues.

Adult ADHD can lead to serious consequences. Such individuals are more than twice as likely to have been arrested, are 47% more likely to have received >1 speeding tickets in a 12-month period, are 78% more likely to be addicted to tobacco, are twice as likely to have been divorced and are 78% more likely to be currently unemployed.^{11,12} A driving performance study by Barkley et al revealed that young adults (aged 17 to 28 years) with ADHD had significantly more total traffic citations, speeding citations and license suspensions or revocations than controls.¹² Furthermore, individuals with ADHD were involved in significantly more cashes.¹²

With regard to education, individuals with ADHD are far more likely to have dropped out of school or college, been expelled or suspended, or been held back a year.¹³ With regard to employment, individuals with ADHD chop and change careers frequently either due to boredom or job related mistakes (they are more likely to have been fired) and are often referred to as being a 'jack of all trades and master of none.'¹³ Furthermore, adults with ADHD may have a lower household income than those without ADHD.¹⁴

At the end of the first visit:

- · Set next appointment
- Arrange for collateral source (ideally patient's mother).
- Request school reports
- Arrange psychological tests
- · Questionnaires (fill out now, not at home)
- Direct patient to '<u>www.totallyadd.com</u>' website to review 'Sponsored Videos'

Visit 2: collateral

During the second interview, which would normally be about 30 minutes in duration, Dr Jain aims to take a collateral story. Sometimes it is hard to find a reliable collateral source, but the gold standard is the mother. One needs to be sensitive of privacy issues so having the patient arrange this interview is important. If you are not sure how to conduct the interview, refer to the CADDRA template (available from <u>www.caddra.ca</u>).

Mock interviews

Dr Jain asked for a volunteer from the audience to do a mock interview while he played the role of the mother of Bill, the patient with ADHD with the **hyperactive/impulsive subtype**. The aim with this interview was to establish a history from pregnancy to 6 years. The existence of possible risk factors for ADHD such as smoking, drug or alcohol use during pregnancy (foetal alcohol syndrome or effects), small birth weight (intrauterine growth retardation), prematurity, difficult temperament, post-partum depression, delayed speech, other learning disabilities and difficulty with fine motor coordination should be determined.¹⁵⁻¹⁷ These items are not necessarily considered to cause ADHD, but are highly associated with the disorder. Dr Jain believes that ear infections and atopy may also be associated with ADHD.

Another volunteer was asked to interview Dr Jain while he played the role of the mother of a 30-year-old woman with ADHD with the **inattentive subtype**. In this interview the 'mother' gave a history of an anxious and clingy child who had a difficult time falling asleep and was lost in her own world. She was difficult to motivate and was very forgetful. Her organisational skills were non-existent. All of her teachers liked her, but she did have some learning disabilities. She would always procrastinate over doing her school projects, attending to them at the last minute. The 'mother' reported that she herself was similar as a child and that there was a lot of depression in her family (including herself). Her son was diagnosed with mild ADHD and her brother had similar symptoms.

Screening questionnaires

Once you suspect that your patient has ADHD, you need to apply some sort of screening questionnaire. While these questionnaires are not diagnostic, they aid in deciding the clinical direction that you will take. The World Health Organisation adult ADHD self-report scale (ASRS) is a useful screener, especially for the hyperactive/inattentive subtype and is downloadable from the TotallyAdd.com website. Another useful tool is the DSM-IV checklist, which is also downloadable from the website. Functional rating scales can be found at the CADDRA website. It is often enlightening to get the patient's partner to fill in the self-assessment questionnaires for the patient.

Assessment algorithm

An assessment algorithm for adult ADHD is outlined in **Figure 1.** Dr Jain says that the items falling in the 'diagnosis' box are all that are really necessary to cover, and that the most important part is the childhood onset. The childhood history helps to differentiate the comorbidities.

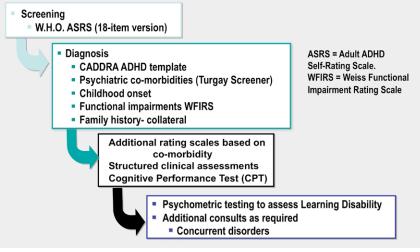


Figure 1. Assessment algorithm for adult ADHD.

Overlap with anxiety/depression

A video interview with Bill was played in which he described being in a continuous funk. He reported that he goes through the motions, but never really feels alive. He gets bored with things easily and does not finish things, which is depressing. He reported that he has three beers a night maximum and smokes a joint to help him sleep. He described himself as the eternal optimist and stated that he had never thought about taking his own life. He said that he felt like a fraud.

Dr Jain pointed out that with Bill there is a sense of helplessness and hopelessness, but that he does not meet the criteria for true depression or anxiety. If his life was functional then he would not feel this way. These symptoms are secondary to his ADHD and it is therefore important to treat that core symptom which is driving the secondary symptoms of anxiety and depression. Without knowledge of his childhood history it would be easy to mistake his symptoms for true anxiety and depression.

Comorbidities

Comorbidity is the rule, not the exception and likely occurs in over 70% of cases of ADHD. Numerous outcome studies show the likelihood of complex adult presentations.¹⁸⁻²¹ The following are the typical comorbidities associated with ADHD.

Anxiety and depression

Anxiety and depression are at the top of the list of comorbidities with ADHD and in fact it is estimated that approximately 1 in 3 adults with ADHD have one or more coexisting anxiety disorders. This secondary anxiety tends to occur during adolescence when the individual becomes aware of their impulses and tries to control them. There is a frequent overlap of anxiety and inattention and individuals with generalised anxiety disorder (GAD) may look like the inattentive subtype of ADHD, but they are not the same. Those with ADHD do not exhibit the hypervigilance of GAD. One needs to be careful

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in treating patient with ADHD with secondary anxiety, as stimulant medications may aggravate the anxiety. In such patients, it is best to use the lowest possible dose of stimulants or use non-stimulant medications.

Depression, as a symptom, is common in ADHD due to the natural exposure of low-level negativism inherent in the way an ADHD child presents with others around them. It is important that children with ADHD are not constantly told what not to do, but rather are given instructions on desired behaviour. Adults with ADHD tend to have an internal optimism and do not exhibit the consistent negative mood seen in mood disorders. They experience lack of motivation, not anhedonia.

Bipolar disorder

Many of the symptoms of ADHD and bipolar disorder overlap so it is difficult to understand which symptom truly is discriminating. There is no dispute with regard to bipolar I disorder as patients with ADHD do not get manic. Although, some researchers have speculated that that ADHD is a catch-all diagnosis in childhood and that some patients might evolve into bipolar I in time.²² Dr Jain says that the best strategy is to either use an atypical neuroleptic or mood stabiliser to regulate what seems to be cyclical changes and then to evaluate the left-over symptoms.

One discriminating factor between ADHD and bipolar disorder may be the way in which an episode of rage ends. In a child with ADHD, a rage episode will often end abruptly as if nothing happened, while in someone with bipolar disorder the episode typically ends with depression.

Learning disabilities

Learning disabilities usually manifest themselves in Grade 1, 4, 7 or entry to college and >40% of those with ADHD have such a disability.²³ Adults with ADHD will often exhibit an inability to do mental calculations and exhibit a need for frequent repetition. They often experience problems understanding, remembering and following instructions. Psychometric testing is useful.

Substance use disorders

Recent evidence suggests that up to 50% of adults with ADHD have a substance use disorder.^{24,25} Such individuals tend to gravitate towards anything that is catecholaminebased. Agents of abuse include energy drinks, caffeine, nicotine, cannabis and cocaine. There are two schools of thought as to whether or not to treat for ADHD while substance abuse is occurring. Dr Jain recommends concurrent disorder treatment, but to pick non-stimulant medications in cases where you fear abuse or diversion potential. Individuals with the impulsive subtype of ADHD and substance abuse are a little more difficult to treat, as they will tend to require stimulant medications.

A show of hands revealed that less than half of attendees would opt to treat a patient with ADHD while they had a substance use disorder. Dr Jain says that in clinical practice he has seen cocaine users benefiting from the use of psychostimulants, but that it takes a lot of courage to treat a cocaine-addicted ADHD patient with a stimulant.

Cannabis use is a little more difficult to tackle because it is more common and patients are often not willing to quit even in the face of ADHD management. Dr Jain tends to allow his patients to continue to use cannabis as long as they agree to not consume the agent during the day while their ADHD medications are having their peak effect. He informs his patients that they must not use more than 1 g per day and that he would rather they quit totally. He says that if he takes the hard line with these patients they would tend to not come back to him for treatment. It is important to establish a strong therapeutic alliance with your patients.

Studies have shown that adolescents medicated for ADHD have a significantly decreased risk of substance use at 4-years follow-up compared with unmedicated ADHD.²⁶ In that study, pharmacotherapy was associated with an 85% reduction in the risk for substance use disorder.²⁶

Personality disorders

If a personality disorder is present, one needs to consider the possibility of ADHD. Not everyone with a personality disorder will have ADHD, but in Dr Jain's clinic at least 73% of his ADHD patients have a concurrent personality disorder. These patients are stuck in childhood. He says that the personality disorders tend to cosegregate: cluster B personalities (borderline, narcissistic, histrionic) tend to be seen in those with the hyperactive/impulsive subtype, while cluster C personalities (obsessive, avoidant, dependent) are more frequently seen in those with the inattentive subtype.

Dr Jain says that while it is commonly considered that individuals with ADHD tend to have antisocial personality, he does not see this as a strong association. He sees a gamut of personality disorders associated with ADHD including borderline personality disorder, which is apparent in both men and women. He stresses that clinicians need to be careful that they are not idealised by these patients who often expect to be 'saved' by their doctor. Instead, facilitate a partnership, empowering the patients to take charge of their clinical symptoms.

A problem in treating ADHD is separating out the personality issues, as treatment for ADHD will not necessarily resolve a personality disorder. Dr Jain uses the Temperament and Character Inventory (TCI) in order to separate out personality disorders in his patients. The form is available from: http://tinyurl.com/7kkjg3r

Eating disorders

There is emerging literature on eating disorders and ADHD.²⁷ Bulimia and obesity have strong ADHD connections particularly in people who have core impulsiveness. Adequate treatment for ADHD has a strong influence on body mass regulation and internal self-control. This issue needs to be addressed appropriately.

At the end of the second visit:

- · The presumptive diagnosis should have been established.
- Make sure that the patient understands that you are both partners in the management of their ADHD and that you do not have all the answers.
- Dispel the myths surrounding ADHD.
- Emphasise that their ADHD diagnosis is not all doom and gloom (have them watch the video featuring Jake Wetzel, a successful athlete who has ADHD [<u>http://totallyadd.com/jake-wetzel]</u>). Inform them that a lot of very successful people have ADHD.
- · Ask the patient if they are committed to making lifestyle changes
- · Remind them that their symptoms are not going to disappear overnight
- · Begin the process of psychoeducation
 - <u>www.caddra.ca</u>
 - www.caddac.ca
 - www.totallyadd.com

Psychoeducation - problem-focused and cognitive-behavioural therapy sessions

Psychoeducation helps to reinforce the belief that patients are responsible for themselves and diminishes the propensity for creating an 'idealised' relationship with their doctor. Educating patients is important to help patients make their own decisions and to help them advocate for their needs in the future.

Dr Jain runs group patient education sessions and insists that his patients attend 14 hours of such therapy. During each 2-hour session he lectures patients on two topics and over the seven sessions covers areas such as sleep disorders, motivational problems, time management, neurobiology of ADHD and medications. Family members and friends are welcome to attend. He says that patients want this sort of education and that it helps them to get a different perspective on their situation. After the patient has attended these sessions another appointment is scheduled and the patient encouraged to say what they want to do in the treatment of their ADHD.

Dr Jain stresses that these group-based sessions are critically important and that all clinicians are capable of running such sessions. He directs clinicians to several websites, which have free and downloadable patient education videos and information (www.caddra.ca; www.caddac.ca; www.totallyadd.com). Sessions should be problem-focused therapy sessions (which could be run by a practice nurse) and cognitive-behavioural therapy sessions. Cognitive-behavioural therapy is important for changing the negative internal patient narrative to a positive one and breaking apart the lifelong history of negative thinking.

Such sessions are a dynamic atmosphere for the clinician to observe their patients and when patients hear information from others with ADHD they don't feel alone. Often these individuals continue to meet with each other after the sessions.

For problem-focused therapy Dr Jain suggests the following format:

- 1. Pick a random problem (you facilitate and keep a stop watch and note pad)
- 2. Ask each patient to give one example of how it affects them (5 minutes each). You summarise the information
- 3. Now each person finds a solution (3 minutes each). Again, summarise the information and facilitate a 10-minute open discussion as to which is the best answer. Vote and then practice the solution until next week
- 4. Option: give them some citations on the problem they have picked

For cognitive-behavioural therapy, which would ideally involve 15-20 sessions, Dr Jain suggests using either David Burn's Book, *Feeling Good*, or Ramsay and Rostain's practical clinical guidebooks.^{28,29}

Visit 3

- · Begin the process of psychoeducation (group-based management is optimal)
- · Review relevant videos in your office (based on historical information)
- If you feel that the patient has committed to the lifestyle agenda then initiate medical treatment – all the while emphasising the holistic approach

Non-medical treatment of ADHD in Adults – The holistic agenda

Medications, if used, are there to facilitate the real agenda, which is the creation of a positive lifestyle. This can be summarised into one mantra word – HABITS. In order to create good habits, one has to break bad habits. Adults with ADHD take longer to create habits because of all of the distractions and lack of internal reinforcements. The following are the habits that should be looked at:

The motherhood habits:

Sleeping properly Eating properly Exercising adequately Organisational habits:

Work and play schedules Attend to bigger tasks first



Dr Jain emphasises the importance of cognitive-behavioural therapy in helping the patient to internalise a positive voice. He often asks his patients to think of a relative such as a grandparent who may have been encouraging and try to imagine what advice they would give in certain circumstances. If patients are unable to find that positive voice, they will find the voice of their doctor. The voice of the family doctor is the strongest and patients should see their family doctor often (ideally every 3 months). The voice of the family doctor can strongly reinforce the positive internal narrative.

The neurobiology of ADHD

Arousal hypothesis

The first theory of ADHD was the arousal hypothesis purported by Satterfield et al in the 1970s.³⁰ Saterfield and colleagues explained that the ADHD individual has a much more open filter than a non-ADHD individual. They suggested that the ADHD brain is under stimulated internally and looks for more external stimulation. For example if a child is sitting in a classroom and is not very stimulated their filter will open, ultimately inhibiting the child from focusing. If the brain of such a child is stimulated with an interesting task (for example lego or TV) they can focus very well. This is where the idea of giving a patient a stimulant to stimulate the brain to a normal level in order to allow the individual to focus was developed. Stimulants that would make non-ADHD individuals euphoric and excited are able to normalise individuals with ADHD.

Inhibitory control model

This relates to the internal self-regulation that occurs when making decisions and is, in essence, a strong 'go signal' and a weak 'stop signal'. This is associated with executive functioning abnormalities.³¹ Noradrenaline-based agonists diminish the 'go signal' and dopamine-based agonists increase the 'stop signal'.

Lack of blood flow/glucose regulation

PET studies have shown that there are alterations in the right frontal lobe (and other brain regions) of individuals with ADHD, with the frontal lobe not having sufficient glucose regulation and blood flow.³²

The genetic hypothesis

The genetic hypothesis seemed more certain when the first gene (DRD4.7) was identified.³³ Other genes have since been identified, but so far only account for about 4% of the variance (the actual gene heritability is close to 79%). A genome-wide scan for loci involved in ADHD by Fisher and colleagues has revealed that there is unlikely a single major-gene effect in this disorder.³⁴

The dopamine connection

Convincing clinical evidence of stimulant responsiveness has been seen, including selfmedication with cannabis and cocaine. Most of the theories point to a dopamine connection, but the most compelling component is the normalisation of symptoms using medications that are dopamine-based. Dopamine appears to enhance the signal (versus noise), improves attention and makes the 'no' stronger. Genetic findings point to possible dopamine factors.

The noradrenaline connection

The need for high stimulation points to the noradrenaline system and this is evident by the number of individuals with ADHD who partake in extreme sports. The patient has a high need for internal or external excitement which alters their decision making. Noradrenaline changes the noise (versus signal) and affects the 'go' signalling, making it stand out. Individuals with the inattentive subtype have the same mechanism, but are distracted by internal noise rather than external noise. An individual with ADD cannot turn off the internal noise.

Dr Jain gave an example of a fireman who reported that when he drove his fire truck down the main street to a fire, the faster he went the slower it felt like the world moved around him and the more in control he felt. This is a common feeling for these individuals, the faster the world happens the slower their mind goes. Other patients have reported that if they drive at the speed limit they make more mistakes than if they exceed it. They are more focused at the faster speed with the associated increased stimulation.

MRI studies

Anatomical structures involved in movement have been found to be smaller in individuals with ADHD. These areas include the basal ganglia, cerebellum and frontal lobes (areas that are rich in dopamine receptors).³⁵

Treatment

Medications definitely work in ADHD and there is no dispute about that. The neurobiological processes are evident and there are numerous brain locations where the medicines operate. However, not everyone with ADHD needs medication. Many patients can be effectively treated with lifestyle management alone. Dr Jain says that the real agenda should be behavioural/ psychotherapy and that medication should only be used to facilitate the non-pharmacological agenda for those patients whose symptoms continue to be impairing. He says that the pala should be: psychoeducation \Rightarrow commitment to lifestyle changes \Rightarrow activation by medications. This way the patient doesn't see the medications as the cure all, but rather something that enables them to action their lifestyle changes. For those patients who do require medication, the hope is that down the track they will have learnt the skills to manage their life and no longer require such agents.

Dr Jain says that for children it is important that their 'new' behaviour is recognised and rewarded with praise. This helps to reinforce the new habits.

Treatment guidelines

Establish risk

The New Zealand Guidelines for the Assessment and Treatment of Attention-Deficit/ Hyperactivity disorder is a useful resource for clinicians.³⁶ Before any medication can be started it is important to establish any medical risks, contraindications or precautions. The patient's cardiovascular risk factors need to be assessed and the patient should not answer yes to any of the following: structural cardiac defect or arrhythmia; family history of unexplained death; unexplained syncopal attack; CV symptoms like increased blood pressure; chest pain; highperformance athlete.

Dr Jain also gives his patients a document from the CADDRA Guidelines outlining the potential cardiovascular risk of ADHD medications.

Review rare, though dangerous side effects

Inform the patient that some medications may activate aggression, psychosis, mania and anxiety. Also inform patients of any potential drug interactions.

Review medication-specific side effects

Data from medicine safety data sheets available from Medsafe. The CADDRA Guidelines include side effect management strategies for patients and inform patients on managing sleep and appetite problems.

Establish baseline symptoms

The use of systematic rating scales is highly valid and these are useful for monitoring outcome. Using any ADHD rating scale, a 25% shift from baseline would be considered a positive treatment outcome.

Monitoring

Monitor the patient every 3-6 months.

Trials off medication

Trials off medications should be considered in order to determine if the medication's utility is still valid. Medications should have been used for at least 1 year before attempting discontinuation. This is the length of time that it usually takes to get lifestyle changes in place.

ADHD medications registered for use in New Zealand

Stimulant-based

Methylphenidate hydrochloride [Ritalin[®]; Ritalin[®] SR; Ritalin[®] LA; Concerta[®]; Rubifen; Rubifen SR] Dexamphetamine sulphate [Dexamphetamine]

Non-stimulant-based

Atomoxetine [Strattera®]

These agents all have their advantages and disadvantages. Immediate-release methylphenidate is fast acting, does not last long and is reasonably priced, however, it has abuse and diversion potential, it has peaks and troughs, and requires frequent dosing. Long-acting methylphenidate has the advantage of once-daily dosing and the effect declines slowly, however, the effect has often worn off by dinnertime, there is a lack of flexibility with dosing and there is some abuse potential. Dexamphetamine has the advantage of being slightly longer acting than methylphenidate, has an antidepressant effect, targets the hyperactive motor symptoms in children and comes in smaller doses, however, the name has negative connotations, there is no long-acting formulation, it suppresses appetite, withdrawal symptoms may be evident, psychosis has been seen and there is abuse and diversion potential. Atomoxetine has the advantage of being useful in patients with the inattentive subtype of ADHD, there is no abuse potential, it has ease of dosing (can be taken once a day), it has a good side effect profile, it does not have the stigma associated with it that stimulants have, however, it can take a while to work, does not work for all patients and there is a small possibility of liver dysfunction.

Dr Jain points out that fast acting agents may not be the best alternative for patients who need to put lifestyle changes in place. If an agent takes a few weeks to start working this is a good time for those patients to start working towards making those changes.

Treatment options

The patient should be asked the following questions:

- Do you have a treatment preference?
- Can you swallow a pill? (especially relevant in children some tablets must be swallowed whole)
- What parts of the day do you feel impaired?

Treatment strategy

- Choose the right medication for your patient
- · Optimise medication dosing, but use a slow and steady approach
- Combination interventions (stimulant + non-stimulant) can be used though no systematic studies have been performed
- Review side effect profile and efficacy with each visit (ideally every 3-6 months)
- Involve the patient's family physician in the management of their ADHD

Differential Diagnosis of Adult Patients with ADHD - A Training program

Take-home messages

- Adults with ADHD have had the disorder since they were children and will not change overnight
- Individuals with ADHD are treatable
- · Getting a childhood history is important in the diagnosis of adult ADHD
- The holistic agenda is critical in the treatment of ADHD
- The holistic agenda should incorporate lifestyle management using a multimodal intervention strategy (medications, behavioural interventions, psychological intervention, occupational interventions and educational interventions)
- · Medications, if used, are there to facilitate the creation of positive lifestyle habits

References

- Szatmari P et al. Ontario Child Health Study: prevalence of attention deficit disorder with hyperactivity. J Child Psychol Psychiatry 1989;30(2):219-30.
- Kessler RC et al. The prevalence and correlates of adult ADHD in the United States: Results from the National Comorbidity Survey Replication. Am J Psychiatry 2006;163(4):716-23.
- Faraone SV et al. The worldwide prevalence of ADHD: Is it an American condition? World Psychiatry 2003;2(2):104-13.
- Faraone SV et al. The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. Psychol Med. 2006;36(2):159-65.
- Kessler RC et al. Patterns and predictors of attention-deficit/hyperactivity disorder persistence into adulthood: results from the national comorbidity survey replication. Biol Psychiatry 2005;57(11):1442-51.
- Faraone SV and Biederman J. What is the prevalence of adult ADHD? Results of a population screen of 966 adults. J Atten Disord. 2005;9(2):384-91.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th edition, text revision. Washington, DC: American Psychiatric Press, 2000. Available from: <u>http://tinyurl.com/87uw8uj</u> (Accessed April 2012).
- Biederman et al. Age-dependent decline of symptoms of attention deficit hyperactivity disorder: Impact of remission definition and symptom type. Am J Psychiatry 2000;157(5):816-8.
- Adler L and Cohen J. Diagnosis and evaluation of adults with attention-deficit/hyperactivity disorder. Psychiatr Clin North Am. 2004;27(2):187-201.
- 10.Faraone SV. Genetics of childhood disorders: XX. ADHD, Part 4: Is ADHD genetically heterogeneous? J Am Acad Child Adolesc Psychiatry 2000;39(11):1455-7.
- 11.Faraone SV and Biederman J. Presented at the 157th Annual APA Meeting; May 6, 2004; New York, NY 12.Barkley RA et al. Driving in young adults with attention deficit hyperactivity disorder: Knowledge,
- performance, adverse outcomes, and the role of executive functioning. J Int Neuropsychol Soc. 2002;8:655-72. 13. Barkley RA. Major life activity and health outcomes associated with attention-deficit/hyperactivity disorder.
- J Clin Psychiatry 2002;63 Suppl 12:10-5.
- 14.Biederman J and Faraone SV. Presented at the 158th Annual APA Meeting; May 23, 2005; Atlanta, GA
- 15.Banerjee TD et al. Environmental risk factors for attention-deficit hyperactivity disorder. Acta Paediatr. 2007;96(9):1269-74.
- 16.Raph JB et al. The influence of nursery school on social interactions. Am J Orthopsychiatry 1968;38(1):144-52.
- 17.Barkley RA. Issues in the diagnosis of attention-deficit/hyperactivity disorder in children. Brain Dev. 2003;25(2):77-83.
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CLINICALLY SIGNIFICANT WARNINGS AND PRECAUTIONS: Short-term placebo controlled studies evaluated over 2200 children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD). Among the 1357 patients on STRATTERA, there was a positive signal for suicidal thoughts (5 patients) and behaviours (1 patient) in children 12 years of age and younger compared to placebo (0/851). No suicides occurred in these trials. Anyone considering the use of STRATTERA in children must balance the risk of suicidality (suicidal thoughts or behaviours) against the clinical need. Patients who are started on STRATTERA should be closely monitored for suicidality; aggressive behavior or hostility, seizures; cardiovascular effects including sudden death; caution with pre-existing cardiovascular conditions which could be worsened by increases in blood pressure or heart rate, such as patients with hypertension, tachycardia, or cardiovascular or cerebrovascular disease*; severe liver

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- Gadow KD et al. Attention-deficit/hyperactivity disorder in adults: beyond controversy. Arch gen Psychiatry 2001;58(8):784-5.
- Fyer AJ et al. Panic disorder and social phobia: effects of comorbidity on familial transmission. Anxiety 1996;2(4):173-8.
- Murphy KR et al. Young adults with ADHD: subtype differences in comorbidity, educational, and clinical history. J Nerv Ment Dis. 2002;190(3):147-57.
- 21. Biederman J et al. Can a subtype of conduct disorder linked to bipolar disorder be identified? Integration of findings from the Massachusetts General Hospital Pediatric Psychopharmacology Research Program. Biol Psychiatry 2003;53(11):952-60.
- 22. Carlson GA and Fahim F. "George". J Affect Disord. 1998;51(2):195-8.
- Lambert NM and Sandoval J. The prevalence of learning disabilities in a sample of children considered hyperactive. J Abnorm Child Psychol. 1980;8(1):33-50.
- 24. Wilens TE. Attention deficit hyperactivity disorder and substance use disorders. Am J Psychiatry 2006;163(12):2059-63.
- Sullivan MA and Rudnik-Levin F. Attention deficit/hyperactivity disorder and substance abuse. Diagnostic and therapeutic considerations. Ann NY Acad Sci. 2001;931:251-70.
- Biederman J et al. Pharmacotherapy of attention-deficit/hyperactivity disorder reduces risk for substance use disorder. Pediatrics 1999;104(2):e20.
- 27. Levy et al 2009.
- 28. Feeling Good: The New Mood Therapy. David D Burns. William Morrow Paperbacks. 1999.
- 29. Cognitive-Behavioural Therapy for Adult ADHD: An Integrative Psychosocial and Medical Approach. J Russell Ramsay and Anthony L Rostain. Routledge Taylor & Francis Group. 2008.
- 30. Satterfield JH et al. Pathophysiology of the hyperactive child syndrome. Arch Gen Psychiatry 1974;31(6):839-44.
- 31.Schachar R et al. Deficient inhibitory control in attention deficit hyperactivity disorder. J Abnorm Child Psychol. 1995;23(4):411-37.
- Zametkin AJ et al. The neuropharmacology of attention-deficit hyperactivity disorder. Annu Rev Med. 1989;40:447-51.
- LaHoste GJ. Dopamine D4 receptor gene polymorphism is associated with attention deficit hyperactivity disorder. Mol Psychiatry 1996;1(2):121-4.
- 34. Fisher SE et al. A genomewide scan for loci involved in attention-deficit/hyperactivity disorder. Am J Hum Genet. 2002;70(5):1183-96.
- Swanson JM et al. Attention-deficit hyperactivity disorder and hyperkinetic disorder. Lancet 1998;351(9100):429-33.
- Ministry of Health. New Zealand Guidelines for the Assessment and Treatment of Attention-deficit/ hyperactivity disorder. Available from: <u>http://tinyurl.com/6vswyss</u> (Accessed April 2012).

injury, anaphylactic reactions, caution with a history of hyperthyroidism*. **OTHER PRECAUTIONS:** Pregnancy, lactation, elderly, hepatic impairment, renal impairment, allergic reactions.

INTERACTIONS: Drugs that prolong QT interval, cause electrolyte disturbance and inhibit CYP2D6; betaadrenergic receptor agonists; tricyclic antidepressants, or noradrenaline reuptake inhibitors, anti-hypertensive drugs* and pressor agents and other drugs that increase blood pressure*.

ADVERSE EVENTS:- Adults and/or children and adolescents: Palpitations, increased blood pressure and heart rate*, dry mouth, anorexia, insomnia, somnolence (including sedation), GI upset, headache, dizziness, mood swings, irritability, hallucinations, influenza, dermatitis, rash, pruritus, sweating, hot flushes, asthenia, weight loss. Adults: urinary disorders, menstrual disturbance, tics, anxiety, depression, depressed mood. Refer to full PI for complete list. Some events were more significant in CYP2D6 poor metaboliser than CYP2D6 extensive metaboliser.

DOSAGE AND ADMINISTRATION: *Children and adolescents* (≤70 kg): 0.5 mg/kg q.d.; after 3 days to 1.2 mg/kg q.d as single or divided doses. Max q.d.: 1.4 mg/kg or 100 mg. *Children and adolescents* (> 70 kg) and adults: 40 mg q.d; after 3 days to 80 mg q.d. as single or divided doses. Max q.d.: 100 mg. Dose adjustment for ESRD and hepatically impaired patients and concomitant use with CYP2D6 inhibitor. Recommence at starting dose, if interrupted for > 1 week

*Please note recent changes. Please review full Data Sheet before prescribing. Full DS is available on request from Eli Lilly and Company (NZ) Limited, PO Box 109197, Newmarket, Auckland 1149. Telephone (09) 523 9300. or www.medsafe.govt.nz. . STRATTERA is a registered trademark of Eli Lilly and Company. Based on DS dated 22 November 2011.



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