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Review Article

A REVIEW ON ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD)

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Abstract:

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopment disorder of childhood and often continues into adulthood. Children with ADHD may experience difficulty in sustaining attention, hyperactivity and impulsive behaviour. Children with ADHD may also struggle with low self-esteem, troubled relationships and poor performance in school. Symptoms sometimes lessen with age. However, some people never completely outgrow their ADHD symptoms. ADHD is often associated with co-occurring disorders including disruptive behaviour, moods, anxiety and substance abuse. ADHD not only affects the child's life but also has an impact on the parents and siblings causing disturbances in family and marital functioning. The major concerning factor in families is the increased healthcare costs for patients and their family members. Certain strategies can be applied to manage the condition and be successful in daily life. This involves a multimodal treatment which includes educating the family and the individual by providing supportive care, psychotherapy and medications that improve ADHD. Pharmacotherapy including stimulants, noradrenergic agents, alpha agonists and anti-depressants play a fundamental role in the long term management of ADHD but age specific treatment regimens have to be followed. Therefore, early diagnosis and treatment can make a big difference in outcome and also helping the families learn how to handle an ADHD child.

Keywords: ADHD, hyperactivity, anxiety, neurodevelopment disorder, disruptive behaviour.

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INTRODUCTION:

Attention-deficit/hyperactivity disorder (ADHD) is a complex, chronic, heterogeneous developmental, neurobehavioral disorder known to typically begin in childhood and persist into adulthood. ⁽¹⁾ ADHD is the third most common psychiatric disorder. It affects 3.4% of children and adolescents, after depression and anxiety. ⁽²⁾ It is a disorder that severely impacts an individual's personal, social, academic and professional functioning and development. ⁽¹⁾ The difficulties due to ADHD impact in education, difficulty interacting with peers, increased rates of motor vehicle accidents, unintentional injuries, and substance abuse. ⁽³⁾ It is seen that 50% of children with ADHD will develop ADHD symptoms during adolescence and adulthood. ⁽²⁾

Types of ADHD:

Children with ADHD are categorised by symptoms of inattention, hyperactivity and impulsivity. Following the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), ADHD can be categorised into 3 subtypes: ADHD predominantly inattentive subtype (ADHD-I), ADHD predominantly hyperactive/impulsive subtype (ADHD-H), and ADHD combined subtype (ADHD-C). ⁽⁴⁾ The symptoms of inattention, hyper-attention and impulsivity should be present for minimum of 6 months or longer and must be noticed in at least 2 settings (such as at home, school or work; with friends or relatives; in other activities). ⁽⁵⁾

Epidemiology:

The American Psychiatric Association (APA) has estimated that the prevalence of ADHD has been increasing by an average of 5% annually, with approximately 6.4 million children and adolescents in the United States with lower prevalence in adults. ⁽⁶⁾ From a nationally representative data in the United States, there is apparent increase of ADHD diagnosis

in 2 decades from 6.1% in 1997-1998 to 10.2% in 2015-2016 in children and adolescents. ⁽⁷⁾ Centres for Disease Control and Prevention (CDC) recently found that 6.1 million American children (9.4%) between the ages of 2-17 years had been diagnosed with ADHD in which approximately 50% were belonging to 12-17 years. ⁽⁸⁾ Few gender differences are to be considered when diagnosing ADHD with more males being diagnosed when compared to females (2:1) in which males are more likely to show hyperactive/ impulsive symptoms, while females are more likely to have inattentive symptoms. ⁽¹⁾

Risk Factors:

Multiple risk factors have been identified with the heterogeneity of ADHD listed in **Table 1**. There is a noticeable increase in the genetic predisposition in an affected individual as observed in multiple family and twin studies. ⁽⁹⁾ A recent meta-analysis reported on 12 independent genome-wide significant loci and found that FOXP2 in chromosome 7 correlates with ADHD but these loci don't have any identified diagnostic or clinical utility results. ⁽¹⁰⁾ Use of substances such as cigarettes and alcohol is one of the known risk factors which is related to maternal health during pregnancy, though the evidence is inconclusive due to uncertain nature and level of exposure in-uterus and the outcomes of having an offspring with ADHD. Exposure to toxins such as heavy metals like lead, mercury and chemicals (organophosphate pesticides) has been implicated with growing evidence of strong linkage with ADHD. The role of nutrition has been widely studied with increased supportive literature of zinc levels and omega-3 fatty acid levels found in ADHD individuals, which could be one of the causes. ⁽⁹⁾ Other causes among adolescents were observed as internet addiction, increased media usage, poor sleep-wake cycles and internet gaming have all been associated with ADHD. ⁽¹¹⁾

Table 1. Risk factors associated with ADHD symptoms

| | |
|--|--|
| <ul style="list-style-type: none"> Genetic risk factors | <ul style="list-style-type: none"> -Dopamine receptor genes (DRD4, DRD5) -Dopamine transporter gene (DAT1) -Gene encoding O methyl transferase (COMT) |
| <ul style="list-style-type: none"> Non-genetic/environmental risk factors <ul style="list-style-type: none"> a) Adversity | <ul style="list-style-type: none"> -Low socioeconomic status -Victimization -Child-parent attachment -Family discord -Intra/interpersonal violence exposure |
| <ul style="list-style-type: none"> <ul style="list-style-type: none"> b) Toxin exposure | <ul style="list-style-type: none"> -Lead -Organophosphate pesticides -Polychlorinated biphenyls |
| <ul style="list-style-type: none"> <ul style="list-style-type: none"> c) Prenatal Exposure | <ul style="list-style-type: none"> -Maternal cigarette smoking -Maternal alcohol use -Maternal stress -Maternal use of illicit drugs |
| <ul style="list-style-type: none"> <ul style="list-style-type: none"> d) Perinatal Risk Factor | <ul style="list-style-type: none"> -Prematurity -Low birth weight |
| <ul style="list-style-type: none"> <ul style="list-style-type: none"> e) Nutritional over use | <ul style="list-style-type: none"> -Sugar -Zinc -Food colourings - Magnesium -Polyunsaturated fatty acids (omega-3) |

Etiopathogenesis: ADHD is a disorder that has multiple aetiologies with combinations of genetic, neurological, and environmental factors that contribute to the pathogenesis and its heterogeneous phenotype. ⁽¹²⁾ ADHD is a highly hereditary, polygenic disorder that was strongly suggested by the evidence from family, adoption and twin studies and is 2 to 8 times more common in persons who have a first degree relative with the condition. Gene variants that are important for brain development, cell migration and encoding for catecholamine receptor and transporter genes also predict the risk for ADHD. ⁽¹³⁾ Ongoing pharmaco-genetics research aims to identify genes that are involved in medication response with ADHD.

Neurological factors affecting brain development which is not inherited or resulting in brain injury

have been implicated in ADHD pathogenesis. Strong evidence supports greater ADHD risk following in utero exposure to alcohol or tobacco and low birth weight even though the contribution of pregnancy and birth complications are mixed. Hypoxic-anoxic brain injury, epilepsy disorders and traumatic brain injury also contribute to ADHD risk. Also, exposure to environmental toxins (lead, organophosphate pesticides and polychlorinated biphenyls) has been linked to the symptoms. ⁽²⁾

Clinical Presentation of ADHD:

According to DSM-5 diagnostic criteria, there are 18 symptoms divided into 9 symptoms each for inattention and hyperactivity-impulsivity listed in the **Table 2** below. Criteria includes that several symptoms must have been present before the age of 12 years.

Table 2. DSM-5 Criteria of 18 symptoms for ADHD

| | |
|--|---|
| <ul style="list-style-type: none"> • <u>Hyperactivity and impulsivity</u> | <ol style="list-style-type: none"> 1. Fidgets excessively 2. Cannot stay seated when required (i.e., classroom, work) 3. Feels restless 4. Cannot play quietly 5. Always “on the go”; seems to be “driven by a motor” 6. Talks excessively 7. Impatiently blurts out answers without finishing question 8. Cannot await turn 9. Interrupts, intrudes, or takes over others’ doing |
| <ul style="list-style-type: none"> • <u>Inattention</u> | <ol style="list-style-type: none"> 1. Fails to pay attention to details, makes careless mistakes 2. Cannot sustain attention in work or play 3. Does not seem to listen when spoken to 4. Cannot follow instructions, fails to complete work 5. Cannot organize tasks and activities 6. Avoid tasks that require concentration like reviewing lengthy papers 7. Loses things needed for tasks and activities 8. Gets distracted by extraneous stimuli like unrelated thoughts 9. Forgetful in daily activities such as paying bills and keeping appointments |

All symptoms must be present in at least 2 settings (such as at home, school or work; with friends or relatives; in other activities) and must impact functioning clearly. In adolescence, the presentation may vary and the most noticeable symptom: hyperactivity tends to decrease during their developmental period, though the symptoms of inattention, impulsivity, restlessness and disorganisation persist and become more obvious. ^(1, 14)

The core symptoms of hyperactivity and impulsivity tend to decline between childhood and young adulthood in both boys and girls, while inattention tends to persist. Inattentive symptoms are worse on average in boys than in girls throughout childhood, adolescence, and young adulthood. ⁽¹⁴⁾ Due to inaccurate recall of ADHD symptoms at younger age and later presenting inattentive manifestations, the criterion of age of onset for ADHD symptoms was increased from age 7 to 12 years. ⁽¹⁵⁾ Inattention and impulsivity can be difficult to distinguish from typical age appropriate behaviour. ADHD can affect function at home, school, social gathering, extracurricular and job settings. With academic impact, adolescents with ADHD are at risk of not graduating high school or college and will have difficulty sustaining good relationship with peers. ⁽¹⁾

Diagnosis:

ADHD remains challenging to diagnose because specific biomarkers and symptoms specificity are lacking, there’s no specific test to diagnose. It can be diagnosed based on questionnaires such as:

i) ADHD self report scale (ASRS),

- ii) Behavior Assessment System for Children (BASC-3), designed for people aged 2 to 21 years,
- iii) Conners Comprehensive Behavior Rating Scale (CBRS), intended for ages 6 to 18 years) and
- iv) Other screening tools can be used to gather diagnostic information from multiple informants. ^(2, 16)

Obtaining a diagnosis of ADHD in preschoolers and adolescents can be complicated. Only the Conner’s Comprehensive Behaviour Rating scale and the ADHD Rating Scales IV have been validated in this age group. ⁽²⁾

- i) The Conners Comprehensive Behaviour Rating Scale (CBRS) is a tool used to gain a better understanding of academic, behavioural and social issues that are seen in young children between ages 6 to 18 years old. ⁽¹⁷⁾
- ii) The ADHD Rating Scale-IV (ADHD-RS) rates the 18 symptoms of ADHD as defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) on a four-point (0 to 3) scale from “never” to “always”. ⁽¹⁸⁾

1. Assessment Scales/ Checklists :

ADHD specific scales are also referred to as a) narrow band scales as its focus is mainly on the ADHD core symptoms. One of the widely used tools is the Conners rating scale found to be reliable and valid in rating ADHD symptoms and in identifying comorbid conditions like oppositional defiant disorder. ⁽¹⁹⁾ The ADHD global scales are also referred to as b) broadband scales are used as a

wider assessment including possible internalizing and externalizing behaviours. Compared to narrow band scales, the broadband scales have lower sensitivity and specificity in establishing the diagnosis, hence not a strong recommendation by the AAP. Although some studies concluded that broadband scales like Child Behaviour Checklist (CBCL) which covers the variable facets of childhood ADHD psychopathology, can be used for accurate diagnosis of ADHD. ^(19, 20) The various scales are listed in **Table 3**.

Table 3. List of various Narrow band and broad band scales

| ADHD Rating Scale | Year Published | Applicable Age Groups |
|------------------------------------|----------------|---|
| 1. Specific/narrow-band | | |
| a) ADHD-RS-V by DuPaul et al. | 2016 | 5 to 18 years |
| b) ADDeS-4 by McCarney and Arthaud | 2013 | 4 to 18 years |
| c) CRS-3 by Conners | 2008 | 3 to 18 years Self-report (12–18 years) |
| 2. Global/broad band | | |
| a) BASC-3 by Reynold and Kamphaus | 2015 | 2 to 21 years |
| b) chenbach/CBCL by Achenbach | 2001 | 6 to 18 years |

2. Electroencephalography (EEG): Since ADHD is a known neurodevelopmental disorder, analyzing the brain's electrical activity was thought to be promising. Almost 80 years ago, children found to be hyperactive, impulsive and highly variable were found to have particular EEG findings in the fronto-central sensors. ⁽¹⁰⁾ This is not routinely recommended in ADHD diagnosis, although the US Food and Drug Administration did approve a medical device called Neba, that uses EEG testing in diagnosing children and adolescent's ages 6 to 17 years. ^(1, 13)

3. Neuroimaging: Magnetic resonance imaging (MRI) has been used in determination of brain findings in ADHD. ⁽²⁾ One recent study found widespread differences in terms of lower surface area and thickening in the frontal cortical areas of children with ADHD, but not in affected adolescents and adults. Majority of these findings have been described from male population, with very limited longitudinal studies looking into the neurobiology of females. ^(6, 14)

4. Differential Diagnosis: The DSM-5 lists 16 conditions or groups of conditions to be distinguished from ADHD, many of which can also

occur as co morbidities. The 16 conditions differentiated from ADHD are:

1. Anxiety disorders
2. Autism spectrum disorder
3. Childhood bipolar disorder
4. Childhood depression
5. Conduct disorder
6. Disruptive mood dysregulation disorder
7. Intellectual disability
8. Intermittent explosive disorder
9. Learning disorder
10. Neurodevelopmental disorders (e.g., autism)
11. Neuroendocrine abnormality (e.g., hyperthyroidism)
12. Oppositional defiant disorder
13. Physical abuse or neglect
14. Reactive attachment disorder
15. Schizophrenia
16. Substance use disorder

Beginning with disorders considered to be psychiatric, ADHD is often grouped with externalizing conditions associated with visible, often disruptive, and aggressive behaviours such as oppositional defiant disorder (ODD) and intermittent explosive disorder; a disruptive behaviour can be mistaken for hyperactivity or impulsive reactivity. Unipolar internalizing disorder may be mistaken for inattentive presentation, while mood disorders with mood swings and poor emotional regulation, disruptive mood dysregulation can mimic all the symptoms of ADHD. ^(2, 8) Children with a specific learning or language disorder may show inattention and disruptive symptoms, when their specific area of difficulty is the focus of the class or homework assignments. The movements associated with autism spectrum disorders and other neuro-developmental disorders may be mistaken for hyperactivity. ⁽²⁾ The prevalence of ADHD in children with epilepsy is two to three times higher than in the general population and is typically inattentive presentation. ⁽²¹⁾ Many genetic conditions such as fragile X chromosome, turner syndrome, tuberous sclerosis, neurofibromatosis, 22q11 deletion syndrome and other developmental symptoms show a higher prevalence of ADHD than the general population. ⁽²⁾

Management of ADHD: The main categories of ADHD treatment are pharmacologic and non-pharmacologic treatments including counselling, behavioural and environmental modification strategies. Behavioural therapy and parent behavioural training can potentially address core symptoms and functional impairments that occur in children with ADHD. Pharmacological therapies can

be useful in managing core symptoms of ADHD including reducing distractibility, improving sustained attention, reducing impulsive behaviours, and improving activity level all of which can allow for improved performance across settings. Pharmacological agents used to treat ADHD can be divided into two main classes: stimulant and non-stimulant medications. ⁽⁶⁾ The medications are listed below in **Table 4**.

1. Stimulants:

Stimulants work to enhance the arousal in the prefrontal cortex. Preparations of methylphenidate and amphetamine act to boost norepinephrine and dopamine neurotransmission in the prefrontal cortex. Methylphenidate exerts its effect from inhibiting presynaptic dopamine transporters of central adrenergic neurons. ⁽⁶⁾ It also inhibits norepinephrine transporters to a much lesser degree. This increases synaptic cleft concentration of dopamine, amplifying the dopaminergic neurotransmission. Amphetamine is a competitive inhibitor of dopamine, acting directly on dopamine transporter and norepinephrine transporter binding sites as a pseudo-substrate. ^(6, 23)

2. Non-Stimulant Medications: Atomoxetine

Atomoxetine is a selective norepinephrine reuptake inhibitor, which causes increased concentrations of norepinephrine and dopamine in the prefrontal cortex. It does not cause increased norepinephrine or dopamine in the nucleus accumbens and lacks abuse

potential. In children and adolescents with ADHD treated with atomoxetine, initial response may be slower than that seen with stimulant medications. ADHD symptoms may respond over the course of several weeks and after the dose is titrated up to the maximum daily dose; symptom improvement may continue over 2 months. Atomoxetine should not be used in children and adolescents taking monoamine oxidase inhibitors within 14 days. The drug is contraindicated in children and adolescents with glaucoma, history of pheochromocytoma, or any severe cardiac or vascular disorders in which the condition would be expected to worsen with increase in the heart rate. ^(6, 23)

3. Non - Psychostimulant Medications: Alpha-2-Agonists

Clonidine stimulates alpha-2 adrenoceptors in the brain stem activating inhibitory neurons, which results in reduced sympathetic outflow from the central nervous system. The reduced sympathetic outflow produces decreased peripheral resistance, renal vascular resistance, heart rate and BP. In treatment of ADHD, the exact mechanism of action is unknown. Alpha-2 agonists should not be used in children and adolescents with history of significant depression as their physiologic effects may worsen depression symptoms. A hypersensitivity to the medication or component of formulation is a contraindication to Clonidine or Guanfacine use. ^(6, 23)

Table 4. List of Medications for ADHD

| Drug Brand | Formulation(mg) | Dosing | Duration (hrs) |
|----------------------------|--|--|----------------|
| Ritalin (methylphenidate) | Tablet 5, 10, 15 | Initial: age 3-5 yr, 1.25 mg BD; age >6, 0.3 mg/kg/dose BD. Titration increase by 0.1 mg/kg/dose or 5-10 mg/week. Max 2mg/kg/day or <50 kg, 60 mg/day; 50kgs+, 100 mg/day. | 2-4 |
| Methylin (methylphenidate) | Tablet 5, 10, 20; chewable: 2.5, 5, 10; solution : 5, 10 mg/mL | Initial: age 3-5 yr, 1.25 mg BD; age >6, 0.3 mg/kg/dose BD. Titration increase by 0.1 mg/kg/dose or 5-10 mg/week. Max 2mg/kg/day or <50 kg, 60 mg/day; 50kgs+, 100 mg/day. | 2-4 |
| Adderall (amphetamine) | Tablet: 5, 7.5, 10, 12.5, 15, 20, 30. | Initial: age 3-5 yr, 2.5 mg daily; age >6 yr, 5 mg daily or BD. Titration: age 3-5 yr increase 2.5 mg/week; age >6 yr increase 5 mg/day. Max 40mg/day | 4-6 |
| Strattera (atomoxetine) | Capsule: 10, 18, 25, 40, 60 | Initial: <70 kg, 0.5 mg/kg; >70 kg, 40 mg daily. Titration: <70 kg increase after 1 week to 1.2 mg/kg as single or divided dose: >70 kg, increase to 80 mg over 1 week as single or divided dose. Max: 1.4 mg/kg/day upto 100 mg/day | 10-12 |
| Kapvay (alpha-2-agonist) | Tablet: 0.1, 0.2 | Initial: 0.1 mg/day at bedtime. Titration: 0.1 mg/week and divided BD. Max: 0.4 mg/day divided BD | 12-24 |
| Intuniv (alpha-2-agonist) | Tablet: 1, 2, 3, 4 | Initial: 0.05-0.08 mg/kg/dose or 1 mg daily. Titration: no more than 1 mg/week. Max: 6-12 yrs, 4 mg/day. | 12-24 |

Clinical Approach to Pharmacotherapy

STEP 1: Extended release stimulant medications such as methylphenidate ER (methylphenidate tablet 10, 20 mg OD), metadate ER (methylphenidate tablet 10, 20 mg OD) are first line in pharmacologic management of ADHD symptoms. In general, stimulants improve core ADHD symptoms equally but a child or adolescent may respond better to one stimulant over another. Stimulant medications (methylphenidate, amphetamine) are approximately equivalent in efficacy and side effects but some children and adolescents respond better to one over another.

STEP 2: Starting with the first stimulant medication chosen, increased titration of dose should occur until maximum symptom benefit is achieved without significant side effects or to the dose at which side effects are tolerable and benefit outweighs risk.

STEP 3: If one stimulant medication (either methylphenidate or amphetamine) does not work at the highest appropriate dose, a medical practitioner should then consider trying the other stimulant medication. Similarly, increased titration of dose of the other stimulant medication should occur until maximum symptom benefit is achieved without significant side effects.

STEP 4: If both (methylphenidate and amphetamine) stimulants have been tried without producing benefit in ADHD symptoms or are not tolerated due to side effects, the next step in ADHD medication management should be to consider trying non-stimulant medications. It is recommended that systematic rating scales be used to measure symptoms at baseline and throughout treatment to monitor symptoms, performance and potential side effects. ^(6, 20)

Age Related Considerations: **a) Pre-School Aged Children:** Management of ADHD in preschool-aged children (4-5 years) should start first with behavioural therapy. There is some evidence that preschool-aged children with moderate to severe dysfunction may benefit from pharmacologic therapy. In order for a clinician to consider initiation of stimulant medication, the following criteria should be met: symptoms that have persisted at least 9 months, dysfunction that is present in both the home and another setting such as day care and dysfunction that has not responded adequately to behaviour therapy. ⁽⁹⁾ Dextroamphetamine is the only medication approved by the US FDA for use in children younger than 6 years. There is reasonable evidence regarding safety and efficacy of methylphenidate for use in preschool aged children, however, it is not specifically

approved by the US FDA for use under the age of 6 years. The initial dose chosen should start low and be increased in smaller increments. ^(23, 24)

b) Adolescents 12 Years and Older: Prior to initiating stimulants for adolescents with newly diagnosed ADHD, clinicians should assess for symptoms of substance use and when substance use is identified, treatment of the underlying disorder should be evaluated and treated. Medical practitioners should monitor for signs of misuse or diversion of stimulants. ⁽⁶⁾ Atomoxetine (initially, 40 mg once a day). The dose is increased after a minimum of 3 days to a total daily dose of 80 mg as a single dose in the morning or divided in 2 doses), extended-release Guanfacine (initially, 1 mg once a day and later adjusted), or extended release Clonidine (initially, 0.1 mg once a day, given at bedtime and later adjusted) may be considered when misuse of stimulant medication is a concern. ⁽²⁵⁾

Co-Morbid Conditions and ADHD: Up to half of children with ADHD may also have coexisting or comorbid psychological and development disorders. Learning disabilities, disruptive behaviour disorders, anxiety and mood disorders are the most common comorbid conditions in children with ADHD. It can also co-occur with autism spectrum and other neurodevelopmental disorders such as foetal alcohol syndrome, Tourette syndrome or another genetic syndrome. ⁽⁶⁾ Previously, ADHD and autism spectrum disorder could not be diagnosed together, but the DSM-5 now allows diagnosing both of the conditions. Anxiety occurs in approximately 30% of the patients with ADHD. Children with co-morbid (attention deficient) AD/ADHD present with more school fears, inattention, poorer social skills, and greater symptom severity compared with ADHD without AD. ⁽²⁾ Oppositional defiant disorder (ODD) and conduct disorder (CD) comprise the disruptive behaviour disorders, which are characterised by externalizing and aggressive behaviours. Studies report the frequency of ODD/CD comorbidity with ADHD to be as high as 90%. ^(2, 6) Learning disorder is the most common comorbid condition with approximately one-third of children with Specific learning disorder (SLD) alone can present with symptoms of inattention because they do not understand what is being taught. Specific skills that may be affected include word reading accuracy, spelling, grammar, or calculation. Difficulties with these skills often cause problems in learning subjects such as history, math, science and social studies and may impact everyday activities and social interactions. A careful psychoeducational assessment can help determine whether the child has SLD as a

primary diagnosis or whether the two disorders, ADHD and SLD are comorbid. ⁽²⁾

CONCLUSION:

It is critical that the environment is aware of the effects of the condition and responsive to the requirements of children with ADHD. To lessen parental stress, it's crucial to provide focused parenting guidance and support in addition to medical care of ADHD to the child. Therefore, health care providers have a crucial role in delivering accurate and affirming information about ADHD and in understanding the needs of affected people and their families.

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REFERENCES:

1. Maria Demma I. Cabral, Stephanie Liu, Neelkamal Soares, Attention-deficit/hyperactivity disorder: diagnostic criteria, epidemiology, risk factors and evaluation in youth, *Transl Pediatr* 2020;9(Suppl 1):S104-S113, doi: 10.21037/tp.2019.09.08.
2. Stacey A. Bélanger, Debbi Andrews, Clare Gray, Daphne Korczak, ADHD in children and youth: Part 1—Etiology, diagnosis, and comorbidity, *Paediatrics & Child Health*, 2018, 447–453 doi: 10.1093/pch/pxy109.
3. Erskine HE, Ferrari AJ, Polanczyk GV, Moffitt TE, Murray CJ, Vos T, Whiteford HA, Scott JG. The global burden of conduct disorder and attention-deficit/hyperactivity disorder in 2010. *J Child Psychol Psychiatry*. 2014 Apr;55(4):328-36. doi: 10.1111/jcpp.12186.
4. Gibbins C, Weiss MD, Goodman DW, Hodgkins PS, Landgraf JM, Faraone SV. ADHD-hyperactive/impulsive subtype in adults. *Ment Illn*. 2010 Sep 9;2(1):e9. doi: 10.4081/mi.2010.e9.
5. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th edition. Arlington, VA., American Psychiatric Association, 2013.
6. Brown KA, Samuel S, Patel DR. Pharmacologic management of attention deficit hyperactivity disorder in children and adolescents: a review for practitioners. *Transl Pediatr*. 2018 Jan;7(1):36-47. doi: 10.21037/tp.2017.08.02.
7. Xu G, Strathearn L, Liu B, Yang B, Bao W. Twenty-Year Trends in Diagnosed Attention-Deficit/Hyperactivity Disorder Among US Children and Adolescents, 1997-2016. *JAMA* Netw Open. 2018 Aug 3;1(4):e181471. doi: 10.1001/jamanetworkopen.2018.1471.
8. <https://www.cdc.gov/ncbddd/adhd/data.html>
9. Thapar A, Cooper M, Jefferies R, Stergiakouli E. What causes attention deficit hyperactivity disorder? *Arch Dis Child*. 2012 Mar;97(3):260-5. doi: 10.1136/archdischild-2011-300482.
10. Demontis D, Walters RK, Martin J, Mattheisen M, Als TD et al., Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder. *Nat Genet*. 2019 Jan;51(1):63-75. doi: 10.1038/s41588-018-0269-7.
11. LeBourgeois MK, Hale L, Chang AM, Akacem LD, Montgomery-Downs HE, Buxton OM. Digital Media and Sleep in Childhood and Adolescence. *Pediatrics*. 2017 Nov;140(Suppl 2):S92-S96. doi: 10.1542/peds.2016-1758J.
12. Akutagawa-Martins GC, Rohde LA, Hutz MH. Genetics of attention-deficit/hyperactivity disorder: an update. *Expert Rev Neurother*. 2016;16(2):145-56. doi: 10.1586/14737175.2016.1130626.
13. Faraone SV, Mick E. Molecular genetics of attention deficit hyperactivity disorder. *Psychiatr Clin North Am*. 2010 Mar;33(1):159-80. doi: 10.1016/j.psc.2009.12.004.
14. Philip Asherson, Iris Manor & Michael Huss, Attention-deficit/hyperactivity disorder in adults: update on clinical presentation and care, *Neuropsychiatry* (2014) 4(1), 109–128
15. Vande Voort JL, He JP, Jameson ND, Merikangas KR. Impact of the DSM-5 attention-deficit/hyperactivity disorder age-of-onset criterion in the US adolescent population. *J Am Acad Child Adolesc Psychiatry*. 2014 Jul; 53(7):736-44. doi: 10.1016/j.jaac.2014.03.005.
16. <https://www.medicalnewstoday.com/articles/321867#adhd-rating-scale>
17. Conners, C.K., Pitkanen, J., Rzepa, S.R. (2011). Conners Comprehensive Behavior Rating Scale. In: Kreutzer, J.S., DeLuca, J., Caplan, B. (eds) *Encyclopedia of Clinical Neuropsychology*. Springer, New York, NY. https://doi.org/10.1007/978-0-387-79948-3_1536
18. [https://en.wikipedia.org/wiki/Conners_Comprehensive_Behaviour_Rating_Scale#:~:text=The%20Conners%20Comprehensive%20Behaviour%20Rating,deficit%20hyperactivity%20disorder%20\(ADHD\).](https://en.wikipedia.org/wiki/Conners_Comprehensive_Behaviour_Rating_Scale#:~:text=The%20Conners%20Comprehensive%20Behaviour%20Rating,deficit%20hyperactivity%20disorder%20(ADHD).)
19. Thorell LB, Chistiansen H, Hammar M, Berggren S, Zander E, Bölte S. Standardization and cross-cultural comparisons of the Swedish Conners 3[®] rating scales. *Nord J Psychiatry*. 2018 Nov;72(8):613-620. doi: 10.1080/08039488.2018.1513067.

20. Chang LY, Wang MY, Tsai PS. Diagnostic Accuracy of Rating Scales for Attention-Deficit/Hyperactivity Disorder: A Meta-analysis. *Pediatrics*. 2016 Mar;137(3):e20152749. doi: 10.1542/peds.2015-2749.
21. Williams AE, Giust JM, Kronenberger WG, Dunn DW. Epilepsy and attention-deficit hyperactivity disorder: links, risks, and challenges. *Neuropsychiatr Dis Treat*. 2016 Feb 9;12:287-96. doi: 10.2147/NDT.S81549.
22. https://www.wikidoc.org/index.php/Attention-deficit_hyperactivity_disorder_differential_diagnosis
23. Felt BT, Biermann B, Christner JG, Kochhar P, Harrison RV. Diagnosis and management of ADHD in children. *Am Fam Physician*. 2014 Oct 1;90(7):456-64.
24. <https://www.mayoclinic.org/drugs-supplements/dextroamphetamine-oral-route/side-effects/drg-20071795?p=1#:~:text=Dextroamphetamine%20works%20in%20the%20treatment,are%20easily%20distracted%20and%20impulsive>.
25. <https://www.mayoclinic.org/drugs-supplements/atomoxetine-oral-route/proper-use/drg-20066904>