Attention-Deficit/Hyperactivity Disorder (ADHD) in Children

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Attention deficit hyperactive disorder is a developmental condition of inattentiveness and easy distractibility with accompanying episodes of hyperactivity. The disease affects about 8-12% of children in the world, while the worldwide adulthood prevalence is 4-5%. The disease arises from genetic mutations that may occur due to toxin exposure or hypoxic-ischemic brain injury in the perinatal period. These etiologies cause neurotransmitter deficiencies or structural changes in the brain areas involved in the control of attention and mood.

Definition

It is a neurodevelopmental disorder characterized by problems of paying attention, excessive activity, and inappropriate behavior for the person's age. In simple terms, as the name suggests, patients are hyperactive with short spans of attention.

The disease is characterized by three variations in the symptomatic presentation:

1. Deficient attention to activities where a person frequently veers off the tasks
he/she engages in. The main problem is a lack of focus and not defiance or incomprehension of instructions.

2. Hyperactivity/impulsiveness where the patient is restless becomes fidgety and cannot remain still as needed.
3. A variety of patients have combined hyperactivity and inattentiveness.

These patients usually act quickly without thinking, they have trouble concentrating in school/learning institutions, while the impulsiveness and talkative behavior leads to social segregation.

The magnitude of neurodevelopmental derangement is so severe that it leads to a compromised social, economic, and educational impact.

Epidemiology of Attention-Deficit/Hyperactivity Disorder

The disease affects about 8–12 % of children in the world, while the worldwide adulthood prevalence is 4–5 %. It is a disease of childhood with the hyperactive subtype being the most common in those aged 7–12 years. 15–20 % of the children will carry the disease into adulthood. **Boys are more affected than girls with a male: female ratio of 5:1** seen in the occurrence of the disease.

**The combined subtype of the disease is the most common form**, the inattentive subtype is more common among girls, while the hyperactive subtype is more common in boys.
In the United States, the incidence was 11 % in the year 2011, with a constant rise in the prevalence of the disease that has been seen over the last decade. Literature shows that it is a disease of school-going children.

Risk Factors for Attention-Deficit/Hyperactivity Disorder

**The risk of developing the disease increases with:**

1. The presence of a first-degree relative who had a similar disease.
2. Exposure to toxins, such as lead in pipes and paints.

**Environmental risk factors:**

- Low socioeconomic status
- Parental mental disorder
- Foster care
- Low birth weight or prematurity
- Acquired traumatic brain injury

Etiology of Attention-Deficit/Hyperactivity Disorder

The disease arises from exposure to risk factors mentioned above leading to slow development of the disease. **It also arises due to genetics:** Attention deficit hyperactive disorder is thought to be a familial disease where children have 2–8 times the
risk of developing the disease if born to affected parents. The genetic mutations that are incriminated, include genes that encode for dopamine receptors such as DRD4, DRD5, DAT, DRH, 5-HTT, and 5 HTR 1B.

**Genetic syndromes with ADHD:**
- Klinefelter
- Turner
- Fragile X
- NF type 1
- Williams syndrome
- DiGeorge syndrome

Intrauterine **toxin exposure to mutation inducing toxins, such as chemicals in food additives and cigarette smoke** taken by the mother, predisposes the fetus to toxin exposure thus leading to DNA damage and possible mutations that cause an alteration in neurobehavioral development.

Perinatal hypoxic/ischemic brain injuries that damage the neurohormonal mechanisms of the brain. **Personality factors that naturally predispose some children to suffer from the disease.** Toxin exposure at a young age, such as lead in water and soils, leading to neurohumoral brain damage.

**Pathophysiology and Embryological Rotation of the Gut**

Significant impairment in functioning in at least 2 settings due to impulsivity, inattention and/or hyperactivity.

<table>
<thead>
<tr>
<th>Combined type</th>
<th>Inattentive type</th>
<th>Hyperactive-impulse type</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Most common</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Difficulty with attention and focus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Some hyperactive/impulsive behavior</td>
<td></td>
<td></td>
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<tr>
<td>• 2nd most common</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Difficulty with attention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• No significant hyperactive or impulsive behavior</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Less difficulty with attention</td>
<td></td>
<td></td>
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<tr>
<td>• More common in preschoolers</td>
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Several theories have been put forward to explain the cause of Attention Deficit Hyperactive Disorder with **a majority of them having little or no scientific evidence to prove the association.**

**Neurotransmitter deficiency:**

The theory states a deficiency of neurotransmitters, such as dopamine and norepinephrine, in areas of the brain which are responsible for attention and control of activity and behavior (frontal and prefrontal cortex). The **lack of message transmission causes problems of initiating and maintaining resistance.** Evidence to support this theory includes:

- A positive response is seen with the administration of drugs that increase the levels of neurotransmitters in the brain. These include stimulant drugs such as methylphenidate.
- Functional MRI studies and positron emission tomography studies of these brain areas that show reduced neurotransmission thus reduced brain activity.
Structural changes in the basal ganglia nuclei (Globus pallidus and putamen) and cerebellum

These are the areas that control attention, behavior, and emotions. Thus, structural derangements cause reduced brain activity, difficulty in performing some tasks, impaired attention, and unstable emotions. The cause of structural changes can be:

- A perinatal hypoxic-ischemic injury that destroys the converging glutaminergic neurons.
- Fetal circulatory insufficiency that predisposes to a loss of autoregulation of fetal blood supply and ischemic injury of secluded sites such as the striatum.

Deficiency in cognitive function

Neurophysiological deficits seen in cognitive functions are seen even at rest and impair one’s ability to regulate and maintain attention since the involved brain areas are deficient in task processing ability.

Classification of Attention-Deficit/Hyperactivity Disorder

Attention deficit hyperactive disorder is classified into three major subtypes:

1. **Predominantly inattentive:**
   The patient is deficient in attention to activities where a person is disorganized and veers off the tasks he/she engages in. The main problem is a lack of focus and not defiance or incomprehension of instructions.

1. **Predominantly hyperactive/impulsive:**
   The patient is restless and becomes fidgety with tapping and restlessness. The person cannot remain still. The person bursts into impulses and talks a lot.

1. **A variety of patients have combined hyperactivity and inattentiveness:**
   These patients have a variety of symptoms from both inattentiveness and impulsivity.

Clinical Features of Attention-Deficit/Hyperactivity Disorder

Presentation of attention deficit hyperactive disorder (ADHD) is described by the following findings:

Patients suffering from ADHD present with symptoms such as:

- Inability to remain still, concentrate
- Squirming
- Louder than expected and expression of extreme anger
- Loss of appetite
- Tics of new-onset
- Increased anxiety and depression due to episodes of low mood
Mental status examination (MSE) reveals:

- Appearance is one of a fidgety, impulsive, and restless person
- Mood may be elevated with periods of low self-esteem with alternating periods of irritability
- The thought process is usually normal but has a direction towards the goal
- Loud due to hallucinations and delusions
- Loss of concentration and short-term memory

Summary: presentation of ADHD

<table>
<thead>
<tr>
<th>Preschool Age</th>
<th>Elementary school</th>
<th>Adolescence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hyperactive</td>
<td>• Struggles with listening in class</td>
<td>• Academic demands become overwhelming</td>
</tr>
<tr>
<td>• Impulsive</td>
<td>• Poor organizational skills</td>
<td>• Struggles with attention, learning, executive functioning</td>
</tr>
<tr>
<td>• Not flexible</td>
<td>• Struggles with social interaction</td>
<td></td>
</tr>
<tr>
<td>• Maybe aggressive with peers</td>
<td>• Difficulty functioning independently</td>
<td></td>
</tr>
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Diagnostic Criteria for Attention-Deficit/Hyperactivity Disorder

The diagnostic and statistical manual of mental illnesses (DSM 5) describes the diagnosis of ADHD by identification of at least 6 symptoms that should have lasted for at least 6 months.

The symptoms that make up the criteria for each subtype are as follows:

**Predominant inattentiveness:**

- The person makes careless mistakes in daily activities, such as school work, due to a lack of attention to details
- Failure to sustain attention
- The person does not listen to the speaker
- Failure to complete tasks and follow instructions but lacks defiance, oppositional behavior, or incomprehension of the instructions
- Disorganized tasks and functions
- The person dislikes activities that demand high levels of concentration and attention such as schoolwork
- Similarly, the person is easily distracted by any form of extraneous stimuli
- He is forgetful when it comes to daily activities

**Predominant hyperactivity:**

Identification of at least 6 of the following symptoms for at least 6 months gives the diagnosis:

- The person gets fidgety hands and restless feet
- He/she squirms on the seat
- In addition to restlessness, the person cannot remain seated for long and leaves unceremoniously or rises when he/she is expected to remain seated
- Upon rising, the person runs about in a manner unexpected for his/her age or level of development
- The person has difficulty in engaging in activities
- Uncomfortable with remaining still, especially for long periods
- Excessive periods of outbursts, such as shouting out answers before the completion of the question
- Excessive talking
- Interrupting/intruding others in their activities

**Other symptoms that reinforce the diagnosis:**

- Onset before 12 years of age
- Occurrence in two or more set-ups, such as school, home, or work
- The symptoms cause significant impairment of social, academic, and economic dysfunction
- The disorder may occur concurrently with another mental disorder which cannot account for all the symptoms

**Investigations of Attention-Deficit/Hyperactivity Disorder**

The diagnosis of the attention deficit hyperactive disorder **is made based on the clinical presentation and rarely requires further investigations.** The diagnosis is made on a presentation of a 6–12-year-old child with inattentiveness and hyperactivity mostly diagnosed by the teachers at school.

A comprehensive history of the child’s behavior is compiled to establish the existence, frequency, and impact of the symptoms on daily life. Interviews on the same topics should be done with teachers, relatives, and caregivers.

**Note:** A thorough medical examination to rule out medical illnesses should be done.

**Differential Diagnosis of Attention-Deficit/Hyperactivity Disorder**

<table>
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<tr>
<th>Disorder</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Depression</strong></td>
<td>Due to associated low mood and problems in tolerating frustration</td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td>The condition shows a low mood and an inability to cope with expectations</td>
</tr>
<tr>
<td><strong>Bipolar disorder</strong></td>
<td>Further investigation to differentiate it from ADHD due to the associated period of low mood</td>
</tr>
<tr>
<td><strong>Tourette syndrome</strong></td>
<td>It can be a cause of new-onset tics</td>
</tr>
<tr>
<td><strong>Oppositional defiant disorder</strong></td>
<td>Children suffering from this disorder show negative hostile and defiant behavior towards those in authority such as teachers and parents. They have normal behavior when around their peers.</td>
</tr>
<tr>
<td><strong>Antisocial behavior</strong></td>
<td>Due to the inability to cope with friends and the expression of violence and aggression against others</td>
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</tbody>
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**Treatment of Attention-Deficit/Hyperactivity Disorder**

**Treatment is mainly supportive management** since the disease presents a lot of difficulties in its management. For example, there are few/no approved medications to treat the disease and the physicians have limited experience in the management of the
disease. However, some positive results have been seen in local trials with:

**Medical treatment**

Stimulants such as methylphenidate are the mainstay therapy and considered first-line drugs in the treatment of the disease. These drugs enhance the brain function and mental ability thus, they control the lack of attention and distractibility. They work by increasing the levels of dopamine and norepinephrine level in the involved brain areas.

Non-stimulants, such as atomoxetine and bupropion, are considered second-line medications. They have adverse effects of cardiotoxicity and sudden death.

<table>
<thead>
<tr>
<th>Stimulants</th>
<th>Nonstimulants</th>
<th>α2-agonists</th>
</tr>
</thead>
<tbody>
<tr>
<td>• First-line therapy</td>
<td>• Atomoxetine</td>
<td>• Clonidine and guanfacine</td>
</tr>
<tr>
<td>• Short or long-acting per behavioral pattern</td>
<td>• Less effective</td>
<td>• No tic exacerbation, better for sleep disturbance, cause sedation, dry mouth</td>
</tr>
<tr>
<td></td>
<td>• Perhaps better for those with tics/anxiety which worsens with stimulants</td>
<td>• Take daily, do not stop abruptly</td>
</tr>
<tr>
<td></td>
<td>• Side effects: fatigue, somnolence, irritability</td>
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**Psychosocial therapy**

Behavioral patient therapy (BPT) and Behavioral Classroom Training (BCT) are methods that ensure that the patient has a conducive environment to control the lack of attention and periods of outbursts. The method is very effective and should be considered as a first-line method of treatment, especially in children.

**Metacognitive therapy**

This enhances time management and the capability to control anxiety and depression.

**Dietary modification**

The change of diet entails the cessation of intake of foods with causative toxins, such as food color and food preservatives. The reduction of these toxins helps to reduce the occurrence of symptoms. Dietary stimulants, such as caffeine, tend to increase the occurrence of symptoms and should be avoided. Vitamin and mineral supplements have been shown to reduce the rate of symptom occurrence.

**Exercises and physical activity**

Engagement of ADHD patients in various activities helps them focus on activities training the person to concentrate and avoid distractions.

**Alternative medicine**

These include yoga and meditation that enhance relaxation and the person’s ability to concentrate on activities. Herbal remedies have shown some control of symptoms.

**Neurofeedback mechanisms**

The patient is trained to couple the EEG wave with certain tasks and thus encourage the
presence of brain activity in all the brain areas, especially the frontal and prefrontal cortex.

Complications of Attention-Deficit/Hyperactivity Disorder

The disease is associated with:
- Increased incidence of drug and substance abuse
- The tendency to have low mood and self-esteem
- The occurrence of suicidal and homicidal tendencies
- More frequent accidents in childhood due to hyperactivity
- Compromised social relations and the children becoming social misfits
- Compromised educational life with poor performance in school

Course and Prognosis of Attention-Deficit/Hyperactivity Disorder

Morbidity and mortality in attention deficit hyperactivity disorder (ADHD) is connected to higher incidences of substance abuse which leads to suicidal tendencies.

The presence of comorbid psychiatric conditions leads to difficulty in treatment and chronicity of the disease. Otherwise, the disease runs a rather predictable course.

References


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