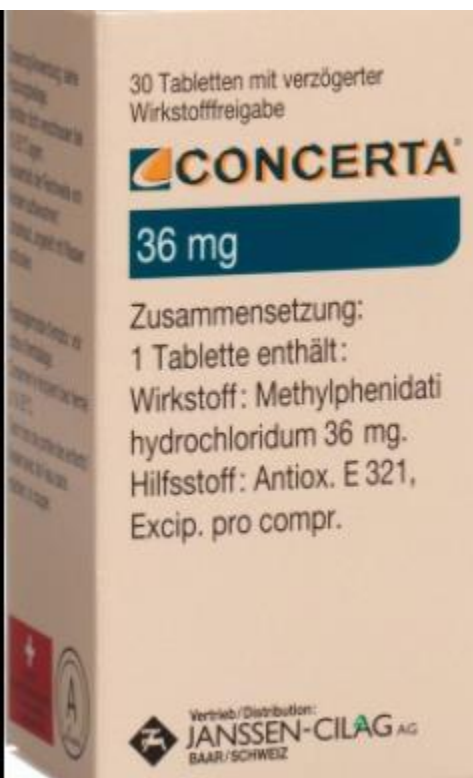


Attention-Deficit/ Hyperactivity Disorder



cause?

Low LEVELS

↓

Symptoms of **ADHD**

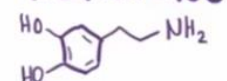
ATTENTION DEFICIT HYPERACTIVITY DISORDER

INATTENTIVE ~ not paying attention

HYPERACTIVE / IMPULSIVE ~ overly active & impulsive

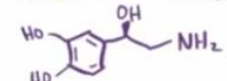
CAUSE: Environmental + Genetic Factors

DOPAMINE

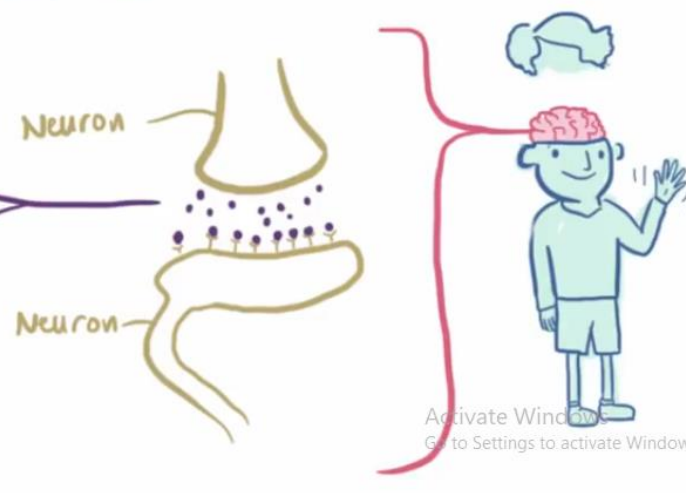


- reward, risk,
impulsiveness

NOREPINEPHRINE



- attention &
arousal



Abdulsalam Halboup

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LEARNING OBJECTIVES

Upon completion of the chapter, the reader will be able to:

1. Explain accepted criteria necessary for the diagnosis of attention-deficit/hyperactivity disorder (ADHD).
2. Recommend a therapeutic plan, including drug selection, initial doses, dosage forms, and monitoring parameters, for a patient with ADHD.
3. Differentiate among the available pharmacologic agents used for ADHD with respect to pharmacology and pharmaceutical formulation.
4. Recommend second-line and/or adjunctive agents that can be effective alternatives in the treatment of ADHD when stimulant therapy is less than adequate.
5. Address potential cost–benefit issues associated with pharmacotherapy of ADHD.
6. Recommend strategies for minimizing adverse effects of ADHD medications.

Introduction

- ADHD is the most common neurobehavioral disorder that affects children.
- Attention-deficit/hyperactivity disorder (ADHD) is characterized by a persistent pattern of inattention and/or hyperactivity-impulsivity.
- It can have a severe impact on a patient's ability to function in both academic and social environments.
- Early diagnosis and appropriate treatment are essential to compensate for areas of deficit.

EPIDEMIOLOGY AND ETIOLOGY

- This disorder usually begins in young children and must occur before 12 years of age to meet current diagnostic criteria.
- ADHD occurs more than twice as often in school-aged boys than girls.
- Although ADHD generally is considered a childhood disorder, symptoms can persist into adolescence and adulthood.
- problems associated with ADHD (eg, social, marital, academic, career, anxiety, depression, smoking, and substance abuse problems) increase with the transition of patients into adulthood.

PATHOPHYSIOLOGY

- The exact pathologic cause of ADHD has not been identified.
- Dysfunction of the neurotransmitters is thought to be key in the pathology of ADHD.
 - Norepinephrine is responsible for maintaining alertness and attention;
 - Dopamine is responsible for regulating learning, motivation, goal setting, and memory.
- Genetics appears to play a role because a child who has a parent with ADHD has a 50% chance of developing ADHD.

Clinical presentation and diagnosis

- All patients 4 to 18 years of age presenting with inattention, hyperactivity, impulsivity, academic, and/or behavioral problems should be evaluated for ADHD.
- The most useful diagnostic criteria for ADHD is the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5)*.
- The **DSM-5** defines **three presentations of ADHD**:
 - (a) predominately **inattentive**;
 - (b) predominantly **hyperactive-impulsive**; and
 - (c) **combined**, in which both inattentive and hyperactive or impulsive symptoms are evident.

Clinical presentation and Diagnosis

- Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (eg, overlooks or misses details, work is inaccurate.)

- Is often forgetful in daily activities (eg, doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).

- Often has difficulty sustaining attention in tasks or play activities (eg, has difficulty remaining focused during lectures, conversations, or lengthy reading).

- Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).

Inattention

(≥6 symptoms for at least 6 months to a degree that is negatively impacts directly on social and academic/occupational activities:

- Often does not seem to listen when spoken to directly (eg, mind seems elsewhere, even in absence of any obvious distraction).

- Often loses things necessary for tasks or activities (eg, school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).

- Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workspace (eg, starts tasks but quickly loses focus and is easily sidetracked).

- Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (eg, schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).

- Often has difficulty organizing tasks and activities (eg, difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).

Clinical presentation and Diagnosis

Hyperactivity and impulsivity:

(≥ 6 symptoms for at least 6 months to a degree that is negatively **impacts directly** on **social** and **academic/occupational** activities:

- Often fidgets with or taps hands or feet or squirms in seat.
- Often leaves seat in situations when remaining seated is expected (eg, leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).
- Often runs about or climbs in situations where it is inappropriate. (Note: In adolescents or adults, may be limited to feeling restless.)
- Often unable to play or engage in leisure activities quietly.
 - Is often "on the go," acting as if "driven by a motor" (eg, is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).
- Often talks excessively.
- Often blurts out an answer before a question has been completed (eg, completes people's sentences; cannot wait for turn in conversation).
- Often has difficulty waiting his or her turn (eg, while waiting in line).
- Often interrupts or intrudes on others (eg, butts into conversations, games, or activities; may start using other people's things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).

ADHD diagnosis

Clinical Presentation and Diagnosis of ADHD

General

Patients with ADHD can present with inattention, hyperactivity-impulsivity or both. ADHD is typically encountered with comorbid conditions.

Diagnostic Criteria

- Must exhibit at least 6 diagnostic symptoms before 12 years of age that persist for at least 6 months
- Symptoms must be present in two or more settings and adversely affect functioning in social situations, school, or work
- Must meet the diagnostic criteria in DSM-5 for ADHD
- Symptoms cannot be better explained by another mental disorder (eg, autism)

ATTENTION DEFICIT HYPERACTIVITY DISORDER

DIAGNOSTIC & STATISTICAL MANUAL:
for MENTAL DISORDERS ~ Fifth ed.

- STARTED between 6-12 yrs.
- (1) INATTENTIVE ~ not paying attention
6 / 9 symptoms for at least 6 months
↳ careless mistakes, not listening, easily distracted, etc.
 - (2) HYPERACTIVE / IMPULSIVE ~ overly active & impulsive
6 / 9 symptoms for at least 6 months
↳ fidget, squirm around, get up often, etc.
 - (3) BOTH ~ most common

6× 6 before 12

TREATMENT

Desired Outcomes:

- The primary therapeutic objectives in ADHD are to:
 - ✓ improve behavior and increase attention or response inhibition;
- secondary goals of treatment are to:
 - ✓ • Improve interpersonal relationships and academic performance
 - ✓ • Decrease disruptive behavior
 - ✓ • Increase independence
 - ✓ • Minimize adverse effects of therapy

Nonpharmacologic (Behavioral) Therapy

a reward/consequence system.

- Behavioral therapy can be useful; however, it is generally **not recommended as first-line monotherapy** except in preschool-aged children (4–5 years of age). Pharmacotherapy is superior to behavioral intervention

Behavior therapy and environmental changes that can be used by **parents or teachers** to shape the behavior of children with ADHD include:

- Maintaining a **daily schedule**
- Keeping **distractions to a minimum**
- Providing specific and logical places for the child to keep his or her schoolwork, toys, and clothes
- Setting small, **reachable goals**
- Rewarding positive behavior (eg, with a "token economy")
- Identifying unintentional reinforcement of negative behaviors
- Using **charts and checklists** to help the child stay "on task"
- Limiting choices
- Finding activities in which the child can be successful (eg, hobbies, sports)

Pharmacologic Therapy

- The proposed mechanism of ADHD pharmacotherapy is to **modulate neurotransmitter function** in order to improve academic and social functioning.

❖ *Stimulants:*

- Psychostimulants (eg, **methylphenidate** and **amphetamines**) are **the most effective agents** in treating ADHD.
- Following diagnosis of ADHD, a stimulant medication should be considered **first-line therapy** in **patients 6 years of age or older**.
 - Stimulants theoretically exert their primary effect by **blocking the reuptake of dopamine and norepinephrine**.
- In preschool-aged children, **methylphenidate** can be added to the patient's treatment if behavioral modification monotherapy is not sufficient.
- Generally, a trial of at least 3 months on a stimulant is appropriate, and this includes dose titration to response as tolerated.

- If treatment with the first stimulant formulation fails, it is recommended to switch to a different stimulant formulation.
 - For example, if the patient was started on methylphenidate but could not tolerate the side effects, switching to dextroamphetamine with or without amphetamine is appropriate.
- If the patient fails two adequate trials of different stimulant medications, a third stimulant formulation or second line nonstimulant such as atomoxetine, guanfacine, or clonidine can be considered.
- Generally, stimulants should not be used in patients who have glaucoma, severe hypertension or cardiovascular disease, hyperthyroidism, severe anxiety, or previous illicit or stimulant drug abuse.



Stimulants

(Methylphenidate 18–54 mg,
Dexmethylphenidate,
Dextroamphetamine)

Amphetamine

Short Acting

Methylphenidate,
Dextroamphetamine

Intermediate Acting

Long-Acting
(Concerta)

Adverse effect of stimulants:

- Serious side effects (eg, hallucinations and abnormal movements) require discontinuation of medication.
 - To avoid potential drug–food interactions and absorption issues, stimulants should be given 30 to 60 minutes before eating.
- Growth suppression or delay is a major concern for parents of children taking stimulants. Growth delay appears to be transient and to resolve by mid-adolescence,
- Another concern is risk of substance abuse with stimulant use.
- Most side effects can be managed by changing the dosing routine (ie, giving with food, dividing daily dose, or giving the dose earlier in the day).
- GI upset, Insomnia, Headache, Tics are also documented.

Nonstimulants:



❖ **Atomoxetine:**

- Atomoxetine is approved for the treatment of ADHD in both children and adults.
- Atomoxetine may be used as a second- or third-line medication for ADHD.
- Atomoxetine selectively **inhibits the reuptake** of adrenergic neurotransmitters, principally norepinephrine.
- **Onset** of therapeutic effect of atomoxetine may **take up to 2 to 8 weeks**, significantly longer than with stimulants.
- Atomoxetine's labeling includes warnings about **severe hepatotoxicity** and increased association with suicidal thinking. Common
- side effects (**headache, decreased appetite, decrease growth, HTN, insomnia**) of atomoxetine are **similar to those of stimulants**.
- One big disadvantage of atomoxetine is **cost** compared with other ADHD medications, despite a generic being

❖ Clonidine and Guanfacine:

- Clonidine and guanfacine are **central 2-adrenergic agonists** that inhibit the release of norepinephrine presynaptically.
- Both of these agents are **less effective than stimulants** in treating ADHD but typically are **used as adjuncts to stimulants** to control disruptive or aggressive behavior and alleviate insomnia.
- Common side effects with clonidine and guanfacine are low blood pressure and sedation. Sedation generally subsides after 2 to 3 weeks of therapy.
- **Bupropion is no longer available as a treatment option.**

OUTCOME EVALUATION

- effectiveness of treatment can be assessed by
 - (a) family and social relationships,
 - (b) disruptive behavior,
 - (c) completing required tasks,
 - (d) self-motivation,
 - (e) appearance, and (f) self-esteem.
- Assess **eating and sleeping patterns, height, weight, pulse, and blood pressure** at baseline and after initiation of pharmacotherapy every 2 to 4 weeks to determine efficacy of treatment and potential effects on growth and cardiac system. Then every 3 months (assess height and weight, and screen for possible adverse)
- Counsel patients and their families that **treatment generally is long term.**

Patient Encounter Part 1

Rorin, an 8-year-old boy with combined type ADHD comes to your clinic. Three months ago, Rorin's dose of generic Concerta increased from 18 mg to 36 mg daily. At school he still often is in trouble for not listening to teachers, losing interest easily, not remaining seated, talking excessively, blurting out answers, interrupting others, not participating in groups, being disruptive and easily distracted, and hitting other children. The beneficial effects of generic Concerta wear off by 4 PM and no adverse effects have occurred.