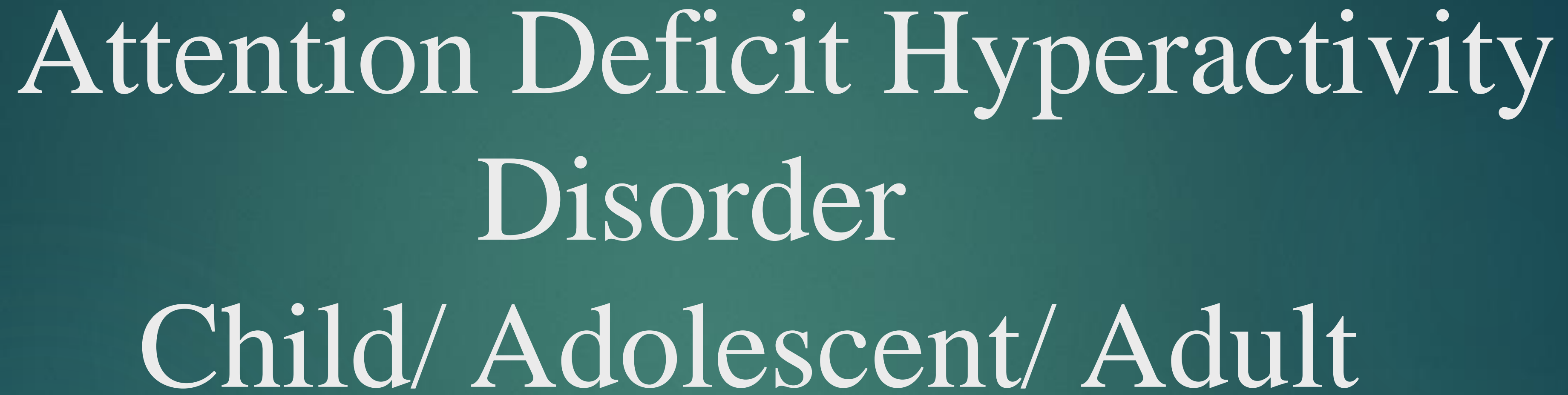


Daniel G. Orr, MD

Question 1

All the following medications have shown efficacy in the treatment of ADHD except:

A. Guanfacine ER
B. Lisdexamphetamine
C. Amitriptyline
D. Modafinil
E. Bupropion

Question 2

Co-Morbid disorders associated with ADHD include:

A. Substance Abuse
B. Smoking
C. Depression
D. Oppositional Defiant Disorder
E. Tic Disorders

Question 3

Which statement is False?

A. ADHD is over diagnosed.
B. ADHD is under diagnosed.
C. Adult ADHD generally is de novo without childhood deficits.
D. Inattentive subtype ADHD is more common in girls than boys.
E. Inattentive subtype ADHD is common in Adults.

Question 4

Which statements are True about ADHD:

A. Divergence of a patient's stimulant medication is common.
B. 33% of all ADHD patients abuse their medication.
C. ADHD is best treated with a combination of medication and support/counseling for school/ work/ and socially.
D. ADHD is one of the most common statistically heritable psychiatric disorders.

ADHD
What is it ?

Disease

Disorder

Syndrome

Variant of normal brain function

Neurologic disorder

Behavioral disorder

Personality type

ADHD Labels

Bad Kids
Lazy
Stupid
Unmotivated
Irresponsible
Defiant
Doesn't Listen

Absent Minded
Daydreamers
Immature
Wild
"Just a boy"
Doesn't care

ADHD
DSM - 5

Symptoms occur in two or more settings and interfere or reduce quality of function.

Do not occur exclusively or better explained by another psychiatric or learning disorder.

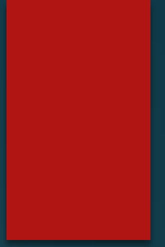
ADD/ADHD
DSM - 5

Persistent Inattention and/or Hyperactivity/ Impulsivity that interferes with functioning and development.

Six or more symptoms of Inattention and/or Hyperactivity/ Impulsivity for more than six months.

Symptoms present before age 12 yrs.

ADHD
DSM-5



Children under 17 yrs. :	6 - 9 symptoms
Adults:	5 – 9 symptoms

ADHD Symptoms

Functional impairment must be evidenced across multiple settings i.e. School/Work/Home and be developmentally relevant.

Hyperactivity and Impulsivity are frequent symptoms seen in childhood whereas Inattention often becomes the predominant symptom in adults.

ADHD Symptoms

Symptoms generally noticed before age 12 yrs.

Residual symptoms often persist into adulthood.

As age progresses symptoms and function may improve but generally not to the level of an individual who does not suffer with ADHD.

ADHD
Through the Life Cycle

As the brain develops throughout childhood and adolescence there is an increase in control of behavior with less overt impulsivity and hyperactivity.

There is an increasing adaptation in adulthood with the development of internal and external strategies to help compensate for these deficits.

Are there degrees of ADHD ?

MILD: Does not impair normal functioning in academic, vocational or social situations.

MODERATE: Moderate impairment in these settings.

SEVERE: Marked impairment in these settings.

ADHD
Statistical Links

Brain structure / Functional abnormalities

Family / Genetic factors

Prenatal / Perinatal factors

Maternal smoking and alcohol use

Neurotoxins

Psychosocial stressors and combined factors

ADHD
Genetics

Heritability of ADHD:

50% - 75% rate in 1st degree relatives:

Parents

Children

Siblings

ADHD Epidemiology

Prevalence:

5% - 9% School Age Children

Diagnosed: Boys > Girls

Girls: Inattentive Type > Mixed > Hyperactive

4% - 6% Adults

Adults: Inattentive Type > Mixed > Hyperactive

ADHD Epidemiology

High Rates ADHD in those Incarcerated:

45% Male youth offenders

30% Adult offenders

10% Female offenders

Note: ADHD is both over diagnosed as well as under diagnosed !

ADHD Circuitry

At least four sub-circuits of the Cortico-Striatal-Thalamic-Cortical (CSTC) tracts show altered function in ADHD:

Anterior Cingulate Cortex — Selective Attention Dysfunction

Dorsolateral Prefrontal Cortex — Sustained Attention Dysfunction

ADHD Circuitry

Prefrontal Motor Cortex	Hyperactivity
Orbitofrontal Cortex	Impulsivity

ADHD

Primary clinical symptoms:

- Inattention
- Hyperactivity
- Impulsivity

Subtypes:

- Predominantly Hyperactive
- Predominantly Inattentive
- Mixed: Hyperactive and Inattentive

- Poor sustained attention
- Careless errors
- Does not listen
- Hard to finish tasks
- Forgetful
- Difficulty prioritizing
- Avoids tasks requiring sustained mental attention
- Paying attention to details
- Easily distracted
- Lacks follow through with instructions
- Difficulty organizing
- Loses important items
- Poor concentration

ADHD
Hyperactivity / Impulsivity

Fidgeting/Tapping/Squirming
Not able to stay seated
Runs and climbs excessively
"On the go"/ Driven by motor
Talks excessively
Blurts out answers
Finishes peoples sentences
Difficulty waiting turn

Interrupts / Intrudes in others conversations or games etc.
Drives too fast
Impulsive job changes

ADHD

Pre School:

Behavioral Disturbances

Hyperactivity

School Age:

Behavioral Disturbances

Academic Problems

Difficulty with Social Interactions

Self Esteem Issues

ADHD
Frequent Associations

Adolescents:

Academic Problems

Difficulty with Social Interactions

Self Esteem Issues

Legal Issues

Smoking

Frequent Injuries / Accidents

Substance Abuse

ADHD Symptoms

College Age:

Academic Failure

Occupational Difficulties

Self Esteem Issues

Relationship Problems

Substance Abuse

Injuries /Accidents

Legal Issues

ADHD Symptoms

Adults:

- Occupational Failure
- Self Esteem Issues
- Relationship Problems /Marital Problems
- Injuries /Accidents
- Substance Abuse
- Legal Issues

ADHD
Co-morbidity

Co-morbid disorders are commonly seen with ADHD.

Presence of Co-morbid Disorders often prevent the correct diagnosis of ADHD by masking or resembling the symptoms of ADHD.

ADHD Comorbities

Learning Disorders	25%	
Mood Disorders	20%	
Anxiety Disorders	30%	
Substance / Alcohol Abuse	15% - 30%	Adolescents
	35% - 55%	Adults
Cigarette Smoking	20%	

ADHD Comorbities

Oppositional Defiant Disorder (ODD)	40%
Conduct Disorder	20%
Tic Disorders (simple or complex)	5% - 20%

ADHD
Developmental History (adults)

Were you a very active child?
Did parents and/or teachers complain you were difficult?
Are you accident prone?
How did you do academically?
Did you ever fail a grade?
Were you ever labeled as having a learning disability?
Did you need special help at school?
Were you ever suspended or expelled?
Were you an underachiever?
Was your performance at school variable or unpredictable?

ADHD
Adult Questionaire

Do you have problems with rage attacks?
How many jobs have you had?
How many times have you been fired? Why?
What kinds of things give you problems at work?
Do you have trouble living with others?
How many car accidents have you had?
How many traffic tickets or speeding tickets?
Have you had problems parenting in the way you'd like?
What do you enjoy doing with your spare time?
Do you have trouble with money? Housework? Being ontime?
Do you feel addicted to anything? Gambling? Computers? Games?

ADHD
Screening and Rating Scales

Presently there are no lab tests or imaging studies to diagnose ADHD

Symptoms assessed in more than one setting:

- Home
- School
- Work

Screenings / rating scales performed by:

- Patient
- Teacher
- Parent
- Spouse

ADHD
Screening Tools

Conner's

Vanderbilt

Wender (Child and Adult forms)

Adult Self Report Rating Scale (NYU)

CAARS (Adult)

Multiple Others

There is no diagnostic test for ADHD

ADHD Medications

Established Treatments

- Psychostimulants (1st line)
- Atomoxetine (1st line)
- Bupropion (2nd line)
- Guanfacine extended release (Intuniv) and Clonidine extended release (Kapvay) (2nd line line) for age 6-17
- Tricyclic antidepressants (TCAs: 3nd line)

Probable Efficacy

- Modafinil

ADHD Psychostimulants

Mechanism of Action:

Increases pre-synaptic release of Dopamine and Norepinephrine in key areas of the brain in particular the frontal and prefrontal lobes.

Inhibits the reuptake of Dopamine and Norepinephrine in key areas of the brain.

ADHD Psychostimulants

70% - 85% Response rate.
Individual response may vary between the different classes of stimulants.

Rule of 3rds
1/3 respond better to amphetamines
1/3 respond better to methylphenidates
1/3 respond about equally to either

ADHD Psychostimulants (Pro's)

Rapid response:

Response within 1-2 hrs. after ingesting but duration of action short lived particularly with IR forms and often require BID or TID dosing. Lisdexamphetamine may last up to 10 – 12 hrs.

ADHD Psychostimulants (Pro's)

Improves:

- Focus
- Concentration
- Attention Span

Reduces:

- Hyperactivity
- Impulsivity
- Fidgeting

ADHD Psychostimulants (Con's)

- Irritability
- Headache
- "Zoned Out" effect
- Sleep Problems
- Diversion
- Slowed height rate
- Sudden cardiac death
- Stomachache
- Dysphoria
- Appetite suppression/ weight loss
- Short lived with IR forms
- Abuse potential
- Tic's
- Psychosis/ Hallucinations

ADHD Psychostimulants (Cons)

Height:

Rate of growth may be slowed but ultimate adult height does not seem to be effected.

Addiction and abuse:

Less likely with ADHD treated individuals.
More likely when diverted to their friends.
Lisdexamphetamine may be harder to abuse.
Concerta may be harder to abuse

ADHD
Psychostimulants (Con's)

Tics:

5% - 20% of school age children with ADD/ADHD will experience simple or complex tics prior to initiating any stimulant medicine.

9% will develop transient stimulant induced tics.

< 1% will develop chronic stimulant induced tics.

ADHD
Tics

Tics are usually transient

Rarely do patients develop a chronic tic disorder

When tics do occur or are worsened:

- Decrease dose
- Switch to another stimulant
- Add adjunctive drug to treat tics such as clonidine/guanfacine
- Try non-stimulant medication:
- Atomoxetine, Intuniv, Kapvay
- Modafinil

ADHD Psychostimulant (Cons)

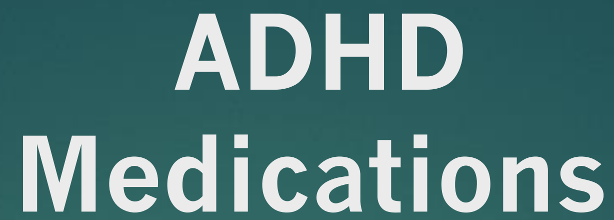
Sudden Cardiac Death:

Most cases seen in individuals with pre-existing cardiac conduction abnormalities.

Inquire about history of tachycardia, syncope, family history of sudden cardiac death, and cardiac work up.

Psychosis/ Hallucinations:

Only about 30 cases reported.



Dose: start low, go slow, and keep going until you can determine optimal risk/benefit ratio

Measure outcome: continue to use ADHD rating scales with the patient as a psychoeducational tool

Teach patients to find observational anchors they can use to

ADHD Immediate/Extended/Combination

Know when patient “needs” the psychostimulant (i.e.)

Mornings and Afternoons for school/work

Afternoons and evenings for homework and peer relations

Weekends

Patient and parent (for children) preferences for specific formulations.

Train parents to observe efficacy and side throughout the day.

ADHD
Stimulants

- Common Errors in Dosing:

Failure to increase dose slowly to maximum if no side effects.

Beginning with a dose that is too high. “Start low and go slow.”

Not assessing the duration of action (may need multiple doses esp. with IR form)

Failure to use another psychostimulant if the first or second trial fails.

Failure to use input from school/ home.

ADHD Medications

Stimulants:

- Methylphenidates
- Amphetamines

Non stimulants:

- Atomoxetine
- Bupropion
- Modafinil
- Armodafinil

Adult ADHD Medications

Most adults will tolerate larger doses than children:

60 – 80 mg	Amphetamine
70 mg	Lis-dexamphetamine (Vyvanse)
80 – 100 mg	Methylphenidate
120 mg	Atomoxetine

ADHD Methylphenidates

	Duration	
Immediate Release (IR)	2-4 hrs.	Methylphenidate (d,l)
		Ritalin (d,l)
		Methylin (d,l)
		Focalin (d)
Sustained Release (SR)	4 hrs.	Methylphenidate (SR)
		Ritalin (SR)
		Methylin (SR)

ADHD
Stimulants (Methylphenidates)

	Form	Age	Duration	Dosing
Generic/Ritalin/Methylin	IR (d,l)	6 yrs.	2-4 hrs.	BID
Focalin	IR (d)	6 yrs.	4-6 hrs.	BID
Generic SR / Ritalin SR	SR	6 yrs.	4-6 hrs.	BID
Methylin SR / Metadate ER	SR	6 yrs.	4-6 hrs.	BID

ADHD
Stimulants (Methylphenidates)

	Form	Age	Duration	Dosing
Metadate CD	Long acting	6 yrs.	8 hrs.	1/day
Ritalin LA	Long acting	6 yrs.	8 hrs.	1/day
Concerta	Long acting	6 yrs.	12 hrs.	1/day
Quillivant XR	Long acting	6 yrs.	12 hrs.	1/day
Daytrana patch	Long acting	6 yrs.	12 hrs.	1/day
Focalin XR (d)	Long acting	6 yrs.	8-10 hrs.	1/day

ADHD
Stimulants (Methylphenidates)

IR/SR/ER Forms	Dosing		
Generic/Ritalin/Methylin	(C)	2mg-4mg/Kg/day	Max 60mg/day
	(A)	Start 20mg-30mg/day	Max 60mg/day
Focalin	(C)	1mg-2mg/Kg/day	Max 30mg/day
	(A)	Start 10mg-15mg/day	Max 30mg/day

ADHD
Stimulants (Methylphenidates)

Long Acting Forms	Dosing	
Ritalin LA	Start 20mg/day	Max 60mg/day
Metadate CD	Start 20mg/day	Max 60mg/day
Focalin XR	(C) Start 5mg/day	Max 30mg/day
	(A) Start 10mg/day	Max 40mg/day
Concerta	Start 18mg/day	Max 72mg/day
Quillivant XR	Start 20mg/day	Max 60mg/day
Daytrana Patch	Start 10mg/day	Max 30mg/day

ADHD
Methylphenidate Formulations

Ritalin/Generic	Tablets: 5mg/ 10mg/ 20mg
Methylin	Tablets / Chewable: 2.5mg/ 5mg/ 10mg
	Solution: 5mg/tsp. and 10mg/tsp.
Methylin ER	Tablets: 10mg/ 20mg
Ritalin SR	Tablet: 20mg
Ritalin LA	Capsules: 10mg/ 20mg/ 30mg/ 40mg
Metadate ER	Tablet: 20mg
Metadate CD	Capsules: 10mg/ 20mg/ 30mg/ 40mg/50mg/ 60mg

ADHD
Methylphenidate Formulations

Focalin/ Generic	Tablets: 2.5mg/ 5mg/ 10mg
Focalin XR	Capsules: 5mg/ 10mg/ 15mg/ 20mg/ 25mg/30mg 35mg/ 40mg
Quillivant XR	Suspension: 25mg/tsp.
QuilliChew ER	Chewable: 20mg/ 30mg/ 40mg
Concerta	Capsules: 18mg/ 27mg/ 36mg/ 54mg
Daytrana	Transdermal Patch: 10mg/ 15mg/ 20mg/30mg Remove patch after 9 hrs.

ADHD
Stimulants (Amphetamines)

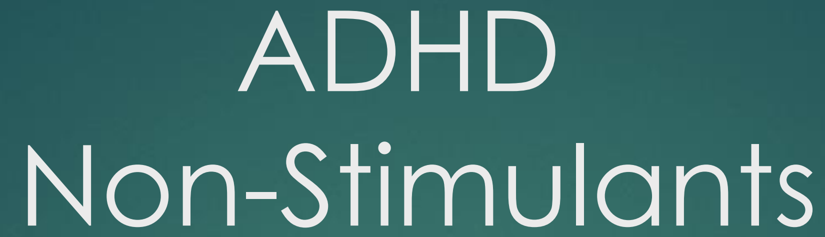
	Form	Age	Duration	
DosingGeneric/Adderall	IR (d,l)	3 yrs.	3-4 hrs.	BID
Dexedrine tablets	IR (d)	3 yrs.	3-6 hrs.	BID
Generic ER/Adderall XR (2 phase)	Long acting	6 yrs.	6-8 hr.	1/day
Mixed Amphetamine XR (3 phase)	Long acting	13 yrs	14 hrs.	1/day
Dexedrine spansules	Long acting	3 yrs.	6-8 hrs.	1 /day
Lisdexamphetamine	Long acting	6 yrs.	10-12 hrs.	1 /day
Mixed Amphetamine XR (3 phase)	Long acting	13 yrs.	14-16 hrs.	1 /day

ADHD
Stimulants (Amphetamines)

IR Forms		Dosing
Generic/Adderall	3-6 yrs. Consult Psychiatry	
	> 6 yrs. Start 5mg BID	Max 40mg/day
	(A) Start 5mg-10mg BID	Max 60mg/day
Dexedrine tabs	3-6 yrs. Consult Psychiatry	
	> 6 yrs. Start 5mg BID	Max 40mg/day
Long acting Forms		
Generic ER/Adderall XR	> 6 yrs. Start 10mg/day	Max 40mg-60mg/day
Amphetamine Salts (3 phase)	> 13 yrs.	Max 50mg/ day
Dexedrine spansules	As above for Dexedrine tablets	Max 40mg/day
Lisdexamphetamine	> 6 yrs. Start 30mg/day	Max 70mg/day

ADHD
Amphetamine Formulations

Adderall/ Generic	Tablets: 5mg/7.5mg/10mg/12.5mg/15mg/20mg/30mg
Dexedrine/ Generic	Tablets: 5mg/ 10mg
Adderall XR/ Generic	Capsules: 5mg/ 10mg/ 15mg/ 20mg/25mg/ 30mg
Dexedrine (SR) Spansule	Capsules: 5mg/ 10mg/ 15mg
Vyvanse	Capsules: 20mg/ 30mg/ 40mg/ 50mg/ 60mg/ 70mg
Mydayis	Capsules: 12.5mg/ 25mg/ 37.5mg/ 50mg



Atomoxetine (NRI) / Strattera

Potent NE reuptake inhibitor.

Enhances NE and DA transmission in frontal and prefrontal cortex.

Children 6 yrs. and older.

May take 6-8 weeks to see maximum effect.

ADHD
Non-Stimulants

Atomoxetine

Dose children < 70 kg.	Start	0.5 mg/kg/day
	Max	1.4mg/kg/day or 100mg/day whichever is less.
Dose adults	Start	40mg/day
	Max	100mg/day

ADHD
Non-Stimulants

Atomoxetine

Do not use if severe cardiovascular disorder.
Do not use if closed angle glaucoma exists.
May increase HR and BP.
Reduce dose with decreased hepatic function.
Suicidality warning up to age 24 yrs.
Potent CYP 450 2D6 inhibitors may increase levels:
(Paroxetine/Fluoxetine/Quinidine)

Common Side Effects: Dizziness/ Drowsiness/ Dyspepsia/ Decreased appetite

ADHD
Non-Stimulants

Bupropion IR/SR/ER (Wellbutrin) IR/SR/XL

Inhibits NE and DA reuptake.

May have use with co-morbid depression / substance abuse / smoking.

Not approved if < 18 yrs. but often used.

Off label use in ADHD.

Do not use in Bulimia/Anorexia/Seizure disorder/Alcoholism

Dose: Most often in ER/XL form 1/day

(C) Max dose 300mg/day (A) Max dose 450mg/day

ADHD Medications

Non stimulants:

Clonidine ER (Kapvay)

Guanfacine ER (Intuniv)

Non stimulants:

Tricyclic Antidepressants (TCA's)

ADHD
Non-Stimulants

Clonidine ER/ Kapvay

- Alpha-2a agonist
- Monotherapy or adjunctive to stimulants.
- Approved 6yrs-17 yrs. Off label use in adults.
- Start 0.1mg/day in BID dosing. Max 0.4mg/day
- Monitor BP and HR for Hypotension and Bradycardia
- Caution: severe CAD/ recent MI/ Cerebral ischemia
- Common side effects: Drowsiness/ Dizziness/ Dyspepsia
- May have efficacy for Tics/ Tourette's/ ODD/ Conduct disorder

Taper slowly to avoid reflex hypertension.

ADHD
Non-Stimulants

Guanfacine ER/ Intuniv

Alpha-2a agonist
Monotherapy or adjunctive to stimulants
Approved 6 yrs-17yrs. Off label use in adults.
Start: 1mg/day Max. 4mg/day
Less Hypotension/ Bradycardia than clonidine/kapvay but monitor.
Caution: severe CAD/ recent MI/ Cerebral ischemia
Common side effects: drowsiness, dizziness, dyspepsia
May have efficacy for Tics/ Tourette's/ ODD/ Conduct disorder

Taper slowly to avoid reflex hypotension

ADHD
Non-Stimulants

Tricyclic Antidepressants (TCAs)

3rd or 4th line

Efficacy shown for Imipramine, Desipramine, Nortriptyline

These TCA’s have strong NE activity.

Side effects and risks limit use.

ADHD
Non-Stimulants

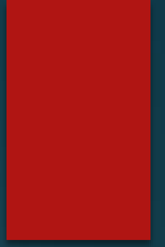
Modafanil

Submitted to FDA in 2006 for Pediatric and Adult ADHD.

2 studies showed efficacy.

Rejected due to safety concerns of possible Stevens-Johnson Syndrome.

ADHD
Issues in pharmacologic management



What % of rx's in mental health are not filled or taken improperly?

Why is psychological management important?

Ambivalence of both parent and child/teen regarding need for medication.

Inadequate parental surveillance of adherence.

Misunderstanding of doses, serum levels, and onset of effects.

Internet information and misinformation.

ADHD
Issues in pharmacologic management

How do we explain the nature of their child’s illness?

How can we develop a therapeutic alliance ***with patient and family?***

How can we develop a supporting alliance with patient’s school and community?

ADHD Medications

Provide the patient with information on medication

Review the “Bio-Psycho-Social” nature of ADHD and any comorbid psychiatric disorders

Explore patient apprehensions such as: “This is a crutch,”
“It will change my personality”

Choose medications based on efficacy duration of action comorbidities, patient/family preference, family history, patient medication history and risk of abuse.

Adult ADHD Psychotherapies

Cognitive – Behavioral Therapy

Learning new strategies to compensate for deficit

Patient Empowerment:

ADD.org
CHADD.org
NAMI.org

Legal Rights of the Student and Obligations of Colleges (adapted from Robin, 1998)

- Section 504 of the Rehabilitation Act of 1973

  This spirit of the law entitles student to classroom modifications in the mainstream college classroom

- Americans with Disabilities Act (1990): Prevents discrimination against students with ADHD

- For excellent up-to-date discussions of special education laws:

  www.schwablearning.org

The PCP should obtain specific school history at each visit.

Inquire about strengths, challenges and school connections.

Ask about specific classroom modifications and whether a 504 or individualized education plan (IEP) exists.

Resources:

- www.chadd.org
- www.add.org
- Parents Helping Parents (www.php.com)
- NAMI (www.nami.org)
- www.aacap.org (Amer Acad of Child & Adol Psychiatry: Facts for Families)
- www.parentsmedguide.org (antidepressants)

Question 1

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- C. Depression
- D. Oppositional Defiant Disorder
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Which statement is False?

A. ADHD is over diagnosed.

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C. Adult ADHD generally is de novo without childhood deficits.

D. Inattentive subtype ADHD is more common in girls than boys.

E. Inattentive subtype ADHD is common in Adults.

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Which statements are True about ADHD:

A. Divergence of a patient's stimulant medication is common.
B. 33% of all ADHD patients abuse their medication.
C. ADHD is best treated with a combination of medication and support/counseling for school/ work/ and socially.
D. ADHD is one of the most common statistically heritable psychiatric disorders.

Answers

- Question 1: C
- Question 2: ABCDE
- Question 3: C
- Question 4: ACD

Vignette #1

- A 19 male patient of your whom you have seen since childhood complains of increased anxiety and an inability to stay focused on his classes at college. In high school he had been an A-B student and is now a freshman at Lafayette College where he is struggling to get C's and is failing one of his courses. He tells you that as an adolescent he waited until the night before to study for exams and do term papers and this never caused any problems.
- You perform a PHQ, which is normal and a GAD which is moderately elevated. You perform an ADH Screen, which shows a lot of inattention but little hyperactivity. He tells that on occasionally he smokes marijuana to turn his mind off so he can sleep. But this is nothing new since he started doing this when he was 16. He is a member of the rugby team and they have an occasional beer party after a match whether they win or lose. He rarely has more than 2 beers at these events.
- He is one of 4 children and a younger brother has been identified with ADHD. You do a cursory exam and labs and all findings are normal.
- What are your next steps?

Vignette #2

- A 35 yr. old pharmaceutical representative who is notoriously late for her physician meetings and lunch dates is particularly anxious today since her district manager gave her one month to prove that she can be more organized and arrive at her meetings on time. She relates to you that her son was diagnosed with ADHD about 6 months ago and that she took one of her Adderall yesterday and for about 4 hrs. she felt more organized, focused and motivated. In fact, she even finished 6 of her reports during that time which she had been procrastinating for 2 wks. to get done. Presently she has no family physician and asks for your guidance.
- What do you do?