

Reducing the Angst and Anxiety of Adolescent Anxiety and Depression

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Disclosure

I have no financial interest or other relationships with any vendor, manufacturer, or company of any product. I will be discussing off-label use of antidepressants in pediatric populations.

Objectives

- Describe common presentations and epidemiology
- Discuss common screen tools and how to diagnosis
- Review overall treatment options
- Discuss specifics of antidepressant management

Epidemiology, Risk Factors, and Clinical Presentation



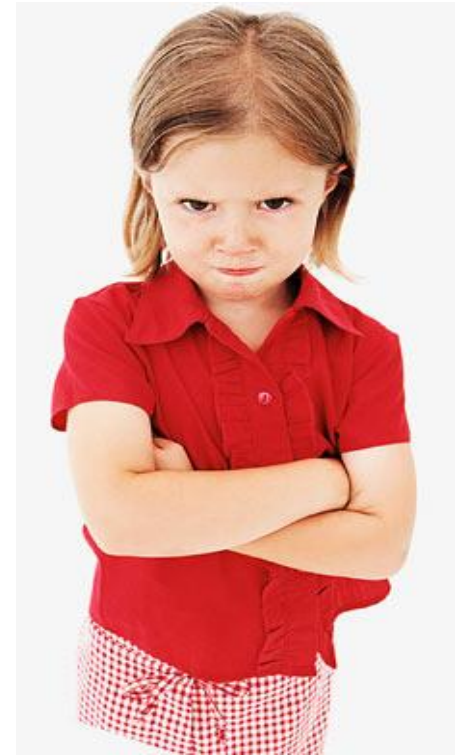
Anxiety Epidemiology

- Most common psychopathology in youth
- Prevalence rates from 6-30%
 - Specific phobias>social phobia>generalized anxiety disorder>separation>panic>OCD
- Girls>boys
- Average age of onset unclear



Depression Epidemiology

- Prepubertal Children
 - 2-3% depression prevalence
 - Female:male ratio 1:1
- Postpubertal Adolescents
 - 6-18% prevalence
 - Female:male ratio 2:1
 - Only half diagnosed before adulthood



Morbidity and Mortality

- Suicide attempts and completion
- Educational underachievement
- Substance abuse and legal problems
- Impaired social relationships
- Increased morbidity of chronic illness
- Increased risk of anxiety or depressive disorders in adulthood

Risk Factors

- Genetic heritability
- Temperamental style
- Parental anxiety
- Parenting styles and attachment
- Other psychiatric disorders
- Trauma
- Chronic medical illness
- Social media



Social Media Use

- Social relationships
 - Less time hanging out with friends
 - Increased loneliness
 - Fear of missing out “FOMO”
 - Comparisons
- Less sleep
- Cyber bullying



Common Presentations

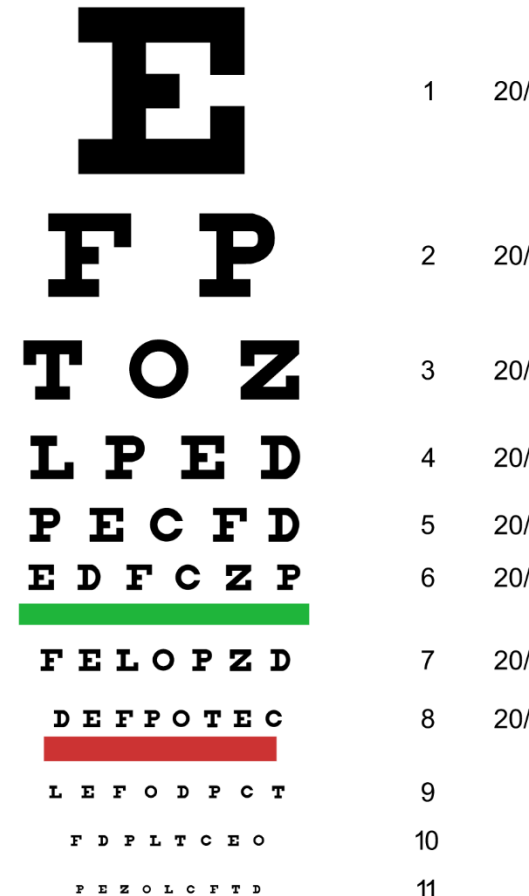
- Children
 - Somatic complaints
 - Psychomotor agitation
 - School refusal
 - Phobias / separation anxiety
 - Irritability
- Adolescents
 - Irritability
 - Substance use
 - Change in weight, sleep, grades
 - Psychomotor retardation / hypersomnia
 - Aggression / antisocial behavior
 - Social withdrawal

Screening and Assessment



Screening

- Broad measures
 - Strength and Difficulties Questionnaire
 - Pediatric Symptom Checklist
 - Pediatric PROMIS
 - Bright Futures Checklists
- Disease-specific measures
 - GAD-7
 - SCARED
 - Spence Children's Anxiety Scale
 - PHQA
 - Beck Depression Inventory
 - Moods and Feeling Questionnaire



GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems?

(Use “✓” to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

(For office coding: Total Score T = + +)

Patient Health Questionnaire (PHQ-A) (page 1 of 1)

Today's Date: _____ Patient's Name: _____ Date of Birth: _____

Are you currently: ☐ on medication for depression ☐ not on medication for depression ☐ not sure? ☐ in counseling

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, irritable, or hopeless	0	1	2	3
3. Trouble falling/staying asleep, sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself, — or that you're a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as school work, reading, or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed, or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
Total each column				

10. If you are experiencing any of the problems on this form, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult

11. In the **past year**, have you felt depressed or sad most days, even if you feel okay sometimes? ☐ YES ☐ NO

12. Has there been a time in the past month when you have had serious thoughts about ending your life? ☐ YES ☐ NO

13. Have you ever, in your whole life, tried to kill yourself or made a suicide attempt? ☐ YES ☐ NO

Diagnosis

- Direct interviews with patients and families using DSM-5 criteria
- Assessing functional impairment and co-morbid psychiatric disorders

Differential Diagnosis

- Psychiatric Disorders

- Anxiety / Depression
- Bipolar disorder
- Oppositional defiant disorder
- Adjustment disorder
- Substance abuse
- ADHD
- Learning disabilities

- Medical Disorders

- Hyper or hypothyroidism
- Autoimmune diseases
- Hypoxia / asthma
- Mononucleosis

- Medications

- Steroids
- AEDs
- Caffeine / Stimulants
- Isotretinoin
- Contraceptives

Treatment



Overall Treatment

- Usually involves therapy +/- medications
- Treatment planning should consider:
 - Severity of illness
 - Age of patient
 - Provider availability / affordability
 - Child and family attitudes



Therapy

- Cognitive behavioral therapy
 - Most empirical support
 - Psychoeducation, skills training, cognitive restructure, controlled exposure
- Psychodynamic therapy
- Supportive therapy
- Parent-child work
 - Especially with younger children
 - Focused on attachment and temperamental factors

Medications

- SSRIs medication of choice
 - Less efficacy in younger ages
 - Suspect fairly equal efficacy
- Other medication to consider
 - SNRIs
 - Bupropion, mirtazapine
 - Benzodiazepines
 - TCAs
 - Buspirone

Depression Placebo-controlled RCTs

Medication	Positive Trials	Negative Trials
Fluoxetine	3	0
Sertraline	1	0
Citalopram	1	1
Escitalopram	?1-2	?0-1
Paroxetine	?0-1	?2-3
Mirtazapine	0	1
Nefazodone	1	0
Venlafaxine	1	2

Anxiety Placebo-controlled RCTs

Medication	Positive Trials	Negative Trials
Fluoxetine	1	1
Sertraline	1	0
Citalopram	0	0
Escitalopram	0	0
Paroxetine	1	0
Fluvoxamine	1	0
Duloxetine	1	0
Venlafaxine	1	1

Treatment: TADS study

- RCT sponsored by NIMH,
 - 12-wk placebo-controlled
 - 36-wk observation
- 439 patients with MDD, ages 12-17
- Randomized to 4 groups
 - CBT and fluoxetine
 - Fluoxetine alone
 - CBT alone
 - Placebo

TADS Study Results

Depression response rates at given study time:

	12 weeks	18 weeks	36 weeks
CBT and fluoxetine	71%	85%	86%
Fluoxetine alone	61%	69%	81%
CBT alone	43%	65%	81%
Placebo	35%		

Ref: March, JAMA (2004); March, Arch Gen Psych (2007)

TADS Study Results

- Combination treatment with best response
- Medication improved response time
- More severely depressed had larger effect size of meds
- Higher SES more helped by CBT
- CBT reduces adverse effects of medication

Treatment: TORDIA Study

- 12 week RCT conducted at 6 clinical sites
- 334 patients with MDD, ages 12-18
 - Had not responded to 2-month initial treatment with an SSRI
- Randomized to 4 treatment strategies
 - Switch to different SSRI (paroxetine / citalopram or fluoxetine)
 - Switch to different SSRI + CBT
 - Switch to venlafaxine
 - Switch to venlafaxine + CBT

TORDIA Study Results

- CBT + switch to either medication regimen showed a higher response rate
- No difference in response rate between venlafaxine and a second SSRI
- Treatment with venlafaxine resulted in more side effects and less robust response with severe depression and SI
- Poorer response predicted by severity, SI, substance abuse, sleeping medication, and family conflict

Treatment: CAMS study

- RCT sponsored by NIMH,
 - 12-wk placebo-controlled
- 488 patients with separation, GAD, or social phobia, ages 7-17
- Randomized to 4 groups
 - CBT and sertraline
 - Sertraline alone
 - CBT alone
 - Placebo

CAMS Study Results

- Percent improved in anxiety:

CBT and sertraline	81%
CBT alone	60%
Sertraline alone	55%
Placebo	24%
- Adverse events uncommon; less in the CBT groups, but equal between sertraline and placebo
- Medication response may be quicker

Depression Treatment

- In milder depression:
 - Therapy alone, including “active support”
- In moderate to severe depression:
 - CBT and /or an SSRI
 - Combination treatment seems to be optimal
- In resistant depression
 - Switch to a different SSRI and add therapy

Anxiety Treatment

- Therapy is gold standard
- In younger children and milder anxiety:
 - Therapy alone, involving parent
- In older children and more severe anxiety:
 - CBT +/- SSRI
 - Combination treatment seems to be optimal
 - Family involvement

Management of Antidepressants



Risks of Antidepressants

- Side effects are common
 - GI symptoms (nausea, diarrhea)
 - Appetite changes (wt gain, anorexia)
 - Sleep changes (drowsiness, insomnia)
 - Headache
 - Sexual dysfunction
- Adverse effects are rare

Antidepressant Adverse Responses

	Symptoms	Incidence	When occurs
Suicidality	Self-harm acts/ thoughts	2%	1-4 weeks
Activation	Inner restlessness, irritability, agitation	3-10%	2-6 weeks
Mania	euphoria, decreased need for sleep	1-5%	2-4 weeks
Discontinuation	Nausea, insomnia, irritability, parasthesias	4-18%	1-7 days of stopping
Serotonin syndrome	Confusion, restlessness, fever, hyperthermia, hypertonia	<1%	Adding serotonergic medication

Antidepressants and Suicidality

- Black Box Warning (2004)
 - Warning of increased risk of suicidality in pediatric pts taking antidepressants.
- FDA Analysis of short-term RCTs
 - Average risk of spontaneous suicidal thinking / behavior on drug was 4% vs. 2% on placebo
- Toxicology studies
 - 0-6% of suicides had antidepressants in blood
 - 25% had active prescriptions for antidepressants
- Epidemiological Studies
 - Regional increases in SSRI use associated with decreases in youth suicide rates

Antidepressants: Which to choose?

- **1st - SSRI** (fluoxetine, sertraline, fluvoxamine, citalopram, escitalopram)
 - Side effect profile
 - Drug-drug interactions
 - Duration of action
 - Positive response to a particular SSRI in first-degree relative
- **2nd - Another SSRI** (above + paroxetine OR duloxetine?)
- **3rd - Alternative antidepressants or antianxiolytic**
 - Duloxetine, venlafaxine, buspirone, benzodiazepines

SSRI Comparison Chart

Medication	Half-life	Drug interaction potential	More common side effects
Citalopram	35 hrs	low	sexual SE, long QT
Escitalopram	30 hrs	low	perhaps fewer
Fluoxetine	2-4 days	high	agitation, nausea
Fluvoxamine	16 hrs	high	agitation, insomnia
Paroxetine	20 hrs	high	sexual, weight gain, sedation, anticholinergic
Sertraline	26 hrs	moderate	diarrhea, nausea

Commonly Used Antidepressants

Medication	FDA indication in Youth
Citalopram	
Escitalopram	≥ 12 years with MDD
Fluoxetine	≥ 8 years with MDD ≥ 7 years with OCD
Fluvoxamine	≥ 8 years with OCD
Paroxetine	
Sertraline	≥ 6 years with OCD
Duloxetine	≥ 7 years with GAD
Venlafaxine	

Antidepressant Dosing Chart

Medication	Starting Dose (mg/d)	Increments (mg)	Effective Dose (mg)	Maximum Dose (mg)
Citalopram	10	10	20	40
Escitalopram	5	5	10	20
Fluoxetine	10	10-20	20	60
Fluvoxamine	25	25	50-100	200
Paroxetine	10	10	20	60
Sertraline	25	12.5-25	50-100	200
Duloxetine	30	30	60	120
Venlafaxine	37.5	37.5-75	150	225

Pharmacogenetics Testing

- Different labs test for different genes, use different methods, and use different interpretation guidelines
- Do not take indication/ use into account
- Do not take drug interactions into account
- Based on single gene interactions only
- No evidence that use of these tests include clinical outcomes

Action	Drug Impacted	Clinical Interpretation	Gene	Genotype	Phenotype
✓	Antipsychotics: Aripiprazole (Abilify®), Brexpiprazole (Rexulti®), Iloperidone (Fanapt®), Pimozide (Orap®)	NORMAL RESPONSE EXPECTED	CYP2D6	*4/*10	Intermediate Metabolizer
✓	Antipsychotics: Haloperidol (Haldol®)	NORMAL RESPONSE EXPECTED	CYP2D6		
✓	Antipsychotics: Perphenazine	NORMAL RESPONSE EXPECTED	CYP2D6		
Action	Drug Impacted	Clinical Interpretation	Gene	Genotype	Phenotype
✗	Antipsychotics: Risperidone (Risperdal®)	CONSIDER ALTERNATIVES (e.g., quetiapine, olanzapine, clozapine)	CYP2D6	*4/*10	Intermediate Metabolizer
✗	Antipsychotics: Thioridazine (Mellaril®)	CONSIDER ALTERNATIVES	CYP2D6	*4/*10	Intermediate Metabolizer
✗	Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs): Venlafaxine (Effexor®)	CONSIDER ALTERNATIVES (e.g., citalopram, sertraline)	CYP2D6	*4/*10	Intermediate Metabolizer

Initial Treatment

Titrate SSRI to effective dose

After 6-8 weeks

Partial Improvement

Increase med to max dose

Add therapy

Explore poor adherence,
comorbidities

Consider augmentation

No Improvement

Reassess diagnosis

Add therapy

Switch to another SSRI

Improvement

Continue meds for 6-12 months after resolution

When to Consult Psychiatry?

- Diagnosis unclear
 - High comorbidities
 - Concern for bipolar or psychosis
- Treatment failure
 - Failure of two SSRIs (and/or SNRI)
 - Adverse reactions

Take Home Points

- Anxiety and depression are common in youth.
- Presentation includes irritability, somatic complaints, school avoidance or withdrawal.
- Therapy (CBT) is first line treatment.
- Antidepressants (SSRI and SNRI) are effective.
- Combined therapy and antidepressants seem to most effective.
- Benefits of antidepressants clearly outweigh the risks in more severe illness and older ages

Resources

www.aacap.org

www.aap.org/commpeds/doch/mentalhealth/