ANXIETY

Allison Kennedy, MD

Phillip Brown, MD

EPIDEMIOLOGY

- **Most common psychiatric disorder in primary care**
- **$42 billion in health care costs / lost productivity[1,2]**
- **More than 70% of patients diagnosed have a comorbid psychiatric disorder**
- **Jama Pediatrics 8/2021, child and adolescent depression and anxiety sx affecting as many as 25.2% and 20.5% of youth globally, double since pre-pandemic levels[3]**
- **MMWR 4/2021, 2020–February 2021, the percentage of adults with recent symptoms of an anxiety or a depressive disorder increased from 36.4% to 41.5%, and the percentage of those reporting an unmet mental health care need increased from 9.2% to 11.7%.[4]**

DEFINITIONS AND DIAGNOSIS

Anxiety: "on edge," excessive worrying, nervousness

Screening: GAD-7

- **Based on DSM-5 criteria for GAD**
- **Can use first 2 questions for screening**
  - **How often in the last two weeks have you felt bothered by feeling nervous, anxious or on edge?**
  - **How often in the last two weeks have you felt bothered by not being able to stop or control worrying?**
- **Sensitive for panic disorder, GAD, social anxiety disorder**

- Somatic presentation is more common than mental

IS ANXIETY ALWAYS PATHOLOGIC?

Feelings are your friends!

- Anxiety helps us respond, motivates action

May be hard to differentiate pathologic anxiety from anxiety as a normal human emotion, could ask (focus on avoidance)

- What have you given up because of your symptoms?

- How does the anxiety or nervousness change your every day life?

Can focus on social impairment (withdrawal from family, friends), Occupational impairment (inefficiency, lack of promotion, losing job), impairment with ADL (going out in public, shopping, etc.)

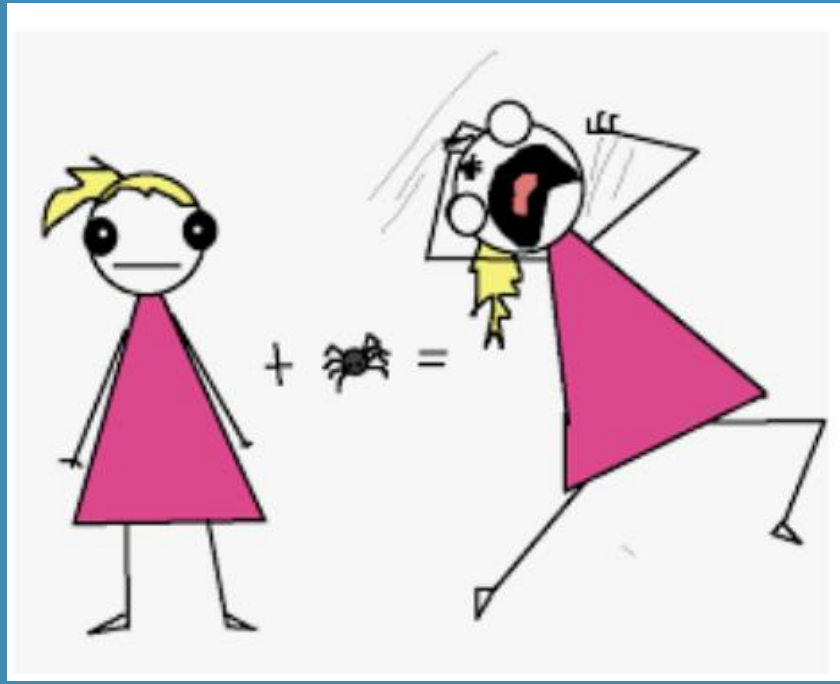
ANXIETY DISORDERS

Situational Trigger present

1. **Social anxiety disorder**
2. **Agoraphobia**
3. **Specific Phobia**

Situational Trigger absent

1. **Panic Disorder**
2. **Generalized Anxiety Disorder**



SOCIAL ANXIETY DISORDER

Most prevalent of all anxiety disorders, strong family history

Fear of embarrassment or humiliation in front of others that is out of proportion for the situation, is persistent (at least six months) and causes distress and loss of function (missing gatherings, avoiding promotions, dropping out of school, etc.).

- Could be limited to public speaking

- Fears of offending others, being rejected

- Onset usually in teenage years, usually pt with >15 years of sx before seeking tx

- Tx: pharmacotherapy (can consider propranolol if only public speaking), and/or CBT

AGORAPHOBIA

Avoidance of places including stores, trains, buses, places with crowds, etc.; specifically places where patients perceive it may be hard to leave if they had a panic attack, needed help, or had another severe symptom

Diagnosis requires 2 or more situational triggers

Some patients may become homebound or require someone to go with them into social settings

Tx: CBT

SPECIFIC PHOBIA

Severe, disproportionate anxiety related to a trigger i.e. flying, spiders, heights, enclosed spaces, blood, needles

Can be manifest by extreme sympathetic nervous system activation, vasovagal reaction, etc.

Onset usually in childhood, may start as developmentally appropriate

Tx: CBT

PANIC DISORDER

Recurrent panic attacks, initially unexpected but usually can identify a trigger (life stressor, etc.) in preceding time

Although attack itself is distressing, results in maladaptive anxiety over the next attack, possible avoidance of certain situations, persistent worry

- For diagnosis, should have >1 month of persistent concern about having a panic attack / maladaptive change in response to it

More common in women than men, younger populations

Tx: pharmacotherapy and / or CBT

PANIC ATTACK

Not an anxiety disorder itself, but can be seen frequently in multiple anxiety disorders and is a requirement for the diagnosis of panic disorder.

Typically symptoms peak in 10 minutes, don't last longer than 1 hour.

Panic attack specifier (added to other mental disorder) if > 4 of the following: palpitations, sweating, trembling / shaking, SOB, choking, chest pain, nausea / abdominal discomfort, dizziness / lightheadedness, chills / flushing, paresthesias, derealization or depersonalization, fear of losing control, fear of dying

GENERALIZED ANXIETY DISORDER

Anxiety disorder without a particular trigger

Characterized about ruminations about trivial matters, most days

Watch for comorbid conditions including insomnia, patients may present with somatic symptoms

Minimum sx > 6 months, should include at least 3 of the following: restlessness, fatigue, poor concentration, irritability, muscle tension, sleep disturbance

Tx: pharmacotherapy and/or CBT

TREATMENT

Rule out medical cause

- Consider TSH, EKG, CMP, CBC, Utox depending on presenting sx

Establishing Trust

- Consider that your patient may have been suffering for years before presenting

- Be empathetic; try to put yourself in your patients shoes

- Verbally acknowledge and legitimize emotions

Pharmacotherapy = CBT short term but > CBT long-term

- Not a lot of benefit shown for combining therapy and medication except in panic disorder

COGNITIVE BEHAVIORAL THERAPY (CBT)

Brief psychotherapy often involving homework / exercises for patient

Premise is that patients have distorted thoughts which then lead to negative emotions and patterns of avoidance

Therapy focuses on identifying the cognitive distortions through a process of cognitive restructuring and replacing those thoughts with more accurate, reality-based and adaptive explanations; challenges all or nothing thinking and catastrophizing

May also include exposure interventions so that patients may revisit previously feared situations and apply their new techniques

PSYCHOPHARMACOLOGY

SSRIs

Mechanism: Inhibit the reuptake of serotonin by pre-synaptic neurons thus increasing serotonin availability to post-synaptic neurons

Advantages

- **Good safety profile**
- **Relatively fewer side effects**

Disadvantages

- **Side Effects: weight gain, insomnia, agitation, GI sx (nausea, constipation, diarrhea), headache, sexual sx (delayed ejaculation, delayed orgasm), GI bleeding, hyponatremia**
- **Weak Inhibitors of Cytochrome P-450 (but rarely clinically significant)**
  - **Warfarin**

"Of course you feel great. These things are loaded with antidepressants."

PSYCHOPHARMACOLOGY

Preferred SSRIs – START LOW AND GO SLOW!

- **Sertraline (Zoloft)**
  - **Starting dose 12.5 - 25mg, up-titrate up to 50mg - 200mg qday; improved absorption with food**
  - **Side effects: GI**
- **Escitalopram (Lexapro)**
  - **Starting dose 2.5 - 5mg, up-titrate up to 10-20mg qday**
  - **QT prolongation but determined by FDA to not be clinically significant**
  - **Side effects: Insomnia, activating**
- **Fluoxetine (Prozac)**
  - **Starting dose 10mg, up-titrate up to 20-60mg**
  - **Very long half life so need to taper off, may be a good option in patients who forget pills, may be activating**

PSYCHOPHARMACOLOGY

Less preferred SSRIs

- **Citalopram (Celexa)**
  - **Starting dose 10mg, up-titrate to 20-40mg; shouldn't go above 20mg in patients >age 60 per FDA**
  - **Black box warning QT prolongation**
- **Paroxetine (Paxil)**
  - **Should avoid; short half life, more likely to cause discontinuation syndrome, weight gain, sedation, medication interactions**

OVERALL SSRI SIDE EFFECTS

Sexual Side Effects

SSRI + NSAID = 9 x GI bleed risk vs SSRI alone

Suicidal Ideation for those 25 and under

Increased risk of first onset stroke in younger patients (recent concern but limited data)

PSYCHOPHARMACOLOGY

SNRIs – comparable efficacy but more discontinuation syndrome

- **Venlafaxine (Effexor)**
  - **Starting dose 37.5mg, titrate up to 225mg**
  - **Can help with chronic pain but also increase BP; small increase in GI bleeding**
  - **Short half life so if not taken at the same time daily patient can experience discontinuation syndrome**
- **Duloxetine (Cymbalta)**
  - **Starting dose 30mg, up-titrate up to 120mg**
  - **Less effect on BP; avoid in patients with CrCl <30 / ESRD, hepatic impairment**

PSYCHOPHARMACOLOGY

Buspirone (Buspar)

- FDA approved for GAD only; not other anxiety disorders

- Often as an adjunct to SSRI, not great as a PRN

- Activity on Serotonin receptors, pre-synaptic agonist, post-synaptic partial agonist

- Lacks abuse potential, not sedating

- Narrow spectrum of efficacy, delay in therapeutic effect for several weeks

- Dosing: 7.5mg BID x 1 week, then 15mg BID up to 30mg BID

PSYCHOPHARMACOLOGY

Mirtazapine (Remeron)

- Off label for anxiety but can help, especially good if comorbid depression

- Sedating, off label ppx for headaches, can act as an appetite stimulant

- 15mg daily, titrate up weekly up to 45mg daily

  - Dose reduction for kidney impairment, Beers criteria in older adults (can worsen SIADH → hyponatremia)

PSYCHOPHARMACOLOGY

Hydroxyzine

- Studied only for GAD

- 2010 Cochrane review – more effective than placebo but small number of studies, not first line

- May be a PRN bridge while waiting for SSRI to take effect

  - Caution that it may cue patients that they need a medication to make their anxiety get better

- Dosing: 25mg q6h PRN

PSYCHOPHARMACOLOGY

Propranolol

- Not FDA approved

- Possible benefit in panic disorder

- Some benefit in performance anxiety

PSYCHOPHARMACOLOGY

Benzodiazepines

- Should not be prescribed in primary care setting for treatment of anxiety; reserved for psych who may prescribe if severe sx otherwise uncontrolled.

- When refusing to prescribe benzos it may not be useful to make blanket statements like "I never prescribe them" or "Its against my policy due to addiction;" instead describe specific, personalized risks as possible (addiction, sedation, respiratory depression, predisposition to falls, rebound anxiety)

- May be used in specific phobia (flying) in limited quantities

PSYCHOPHARMACOLOGY

Benzo Taper

- No universal formula but long tail is better!

- 4 – 24 weeks

- If a patient runs out too quickly, taper them sooner

- CURES!!!

SPECIAL POPULATION: INSOMNIA

SSRI/SNRI may make it worse

Can consider Hydroxyzine and pregabalin (although not approved)

Two studies showed adding trazodone to another SSRI helped

SPECIAL POPULATION: ELDERLY

Sertraline and Escitalopram have better safety profile in elderly

Postural Sway / Gait Impairment with elderly on SSRI

SNRI especially venlafaxine can raise BP (HTN risk)

Pregabalin can lead to sleepiness, dizziness, falls

SPECIAL POPULATION: REPRODUCTIVE CONSIDERATIONS

Category C: SSRI / SNRI (except D for paroxetine) however these meds may increase risk of post-partum hemorrhage, premature delivery and other post-natal complications

Category D: Benzos (cleft palate) and paroxetine (atrial septal defect)

SPECIAL POPULATION: BIPOLAR DEPRESSION AND GAD

GAD more common in bipolar depression than unipolar depression

Don't use antidepressants in rapid cycles (more than 4 episodes per year).

For the bipolar depression aspect use: lithium, quetiapine, lamotrigine, lurasidone

For anxiety: hydroxyzine, pregabalin, or benzo

SPECIAL POPULATION: PTSD

Prazosin for nighttime (nightmares) and daytime issues (disturbed awakenings) hyperarousal, irritability

Avoid benzodiazepines

SWITCHING FROM SSRI TO ANOTHER SSRI/SNRI

Conservative switch: • the first antidepressant is gradually reduced and stopped • there follows a drug-free washout interval of five half-lives of the first antidepressant • the new antidepressant is started according to its dose recommendation	Most appropriate for general practice. The risk of drug interactions is very low but discontinuation symptoms may occur.

SWITCHING FROM SSRI TO ANOTHER SSRI/SNRI

Moderate switch: • the first antidepressant is gradually reduced and stopped • there follows a drug-free washout interval of 2–4 days • the new antidepressant is started at a low dose	Also recommended for use in general practice. The risk of drug interactions is low but discontinuation symptoms may occur.

GENERAL TIPS & CAUTION

Anti-depressants have black box warning for pediatric and adolescent increased suicidality

- see your pediatric patients weekly, be sure to advise and DOCUMENT!

Counsel patients that anti-depressants are not PRN medications and that there are delayed therapeutic effects and long-term treatment is often indicated, also that there will be gradual titration

Patients can feel more anxious / activated after starting, this should go away in a few weeks; start low, go slow!

GI disturbance is common and should also go away in a few weeks.

Can add sildenafil or bupropion for sexual side effects.

Refer if diagnostic uncertainty, significant comorbidities, prior treatment failures, CBT, close follow up not feasible, severe agitation or suicidal ideation

CASE #1

22 year old female presents for CPE, screens positive for anxiety and depression at intake

- PHQ-9 score of 15 (severe), GAD-7 score of 12 (moderate)

- AMPS – anxiety, mood, psychotic, substance use

- Screen for suicidality (will cover more in future lecture)

- Referral for CBT, recommendation for "Feeling Good" book

- Pharmacology: Zoloft (start 12.5mg, up-titrate weekly to 50mg), Lexapro (start 2.5mg, up-titrate weekly to 10mg)

- Follow-up: consider 1-2 weeks, black box warning for increased suicidal thinking in young adults, advise and document!

CASE #2

28 year old female, opiate use disorder, just d/c'd from rehab on Robaxin, Seroquel, Hydroxyzine; reports headaches, insomnia, anxiety

- PHQ-9 score of 2, GAD-7 score of 16 (severe)

- AMPS – anxiety, mood, psychotic, substance use

- Screen for suicidality (will cover more in future lecture)

- Referral for CBT, recommendation for "Feeling Good" book

- Pharmacology: taper Robaxin, taper Seroquel, continue hydroxyzine but discuss temporary basis, start Mirtazapine 15mg qHS → 45mg qHS

THANK YOU!