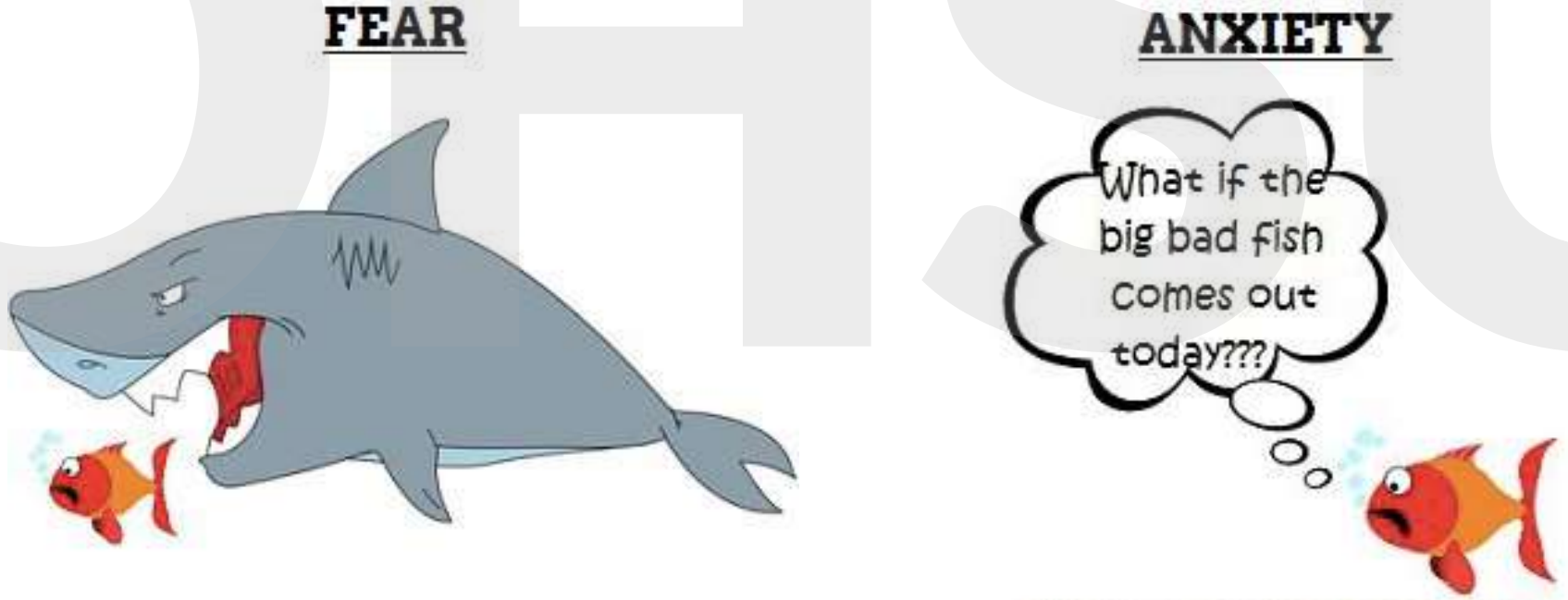
Common Presentations in Primary Care:

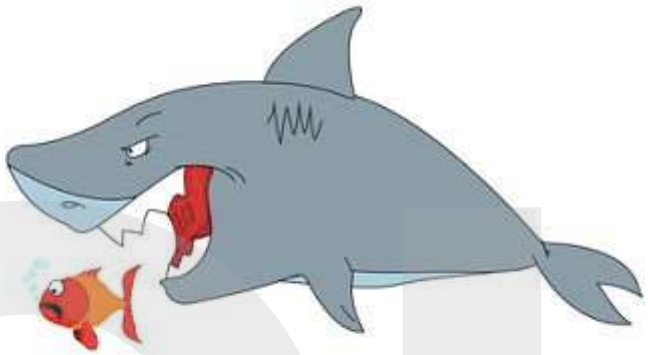
Anxiety

Test Yourself

What is the difference between fear and anxiety?



FEAR



Stress Response from Immediate Danger!

Fear
Rapid onset for instantaneous survival response
Primarily non-cognitive
Intense autonomic arousal
Brief/Discrete

ANXIETY

Stress Response just from your Thoughts!

Anxiety
Subacute onset for expected challenge
Primarily Cognitive
Less Intense autonomic arousal
Protracted

- For most people, fear and anxiety are appropriately activated/deactivated.
- For some people
  - If fear is activated the wrong time → Panic Attacks
  - If anxiety is not well modulated → Generalized Anxiety Disorder

Case – Andrew – Part 1

Generalized Anxiety Disorder

Case – Andrew – Part 1

Generalized Anxiety Disorder

18 yo male, living in Portland with parents, in last year at language magnet public high school. Enjoys music, chess, baseball. Has some good friends. Good relationship with parents and older brother. Has been accepted to several colleges, but has not committed, but knows he must decide soon.

Andrew feels an increase in worry thoughts, both about upcoming college, but also more diffuse worries – disappointing others, saying things that will make others dislike him, not living up to his potential, failing in college – which is accompanied by physical symptoms such as tension, insomnia, difficulties concentrating.

His parents are concerned when his school performance drops and he starts missing school, feeling too anxious even to attend his chess club meetings or to talk to the school counselor with whom he has a good relationship.

Case – Andrew – Part 2

Generalized Anxiety Disorder

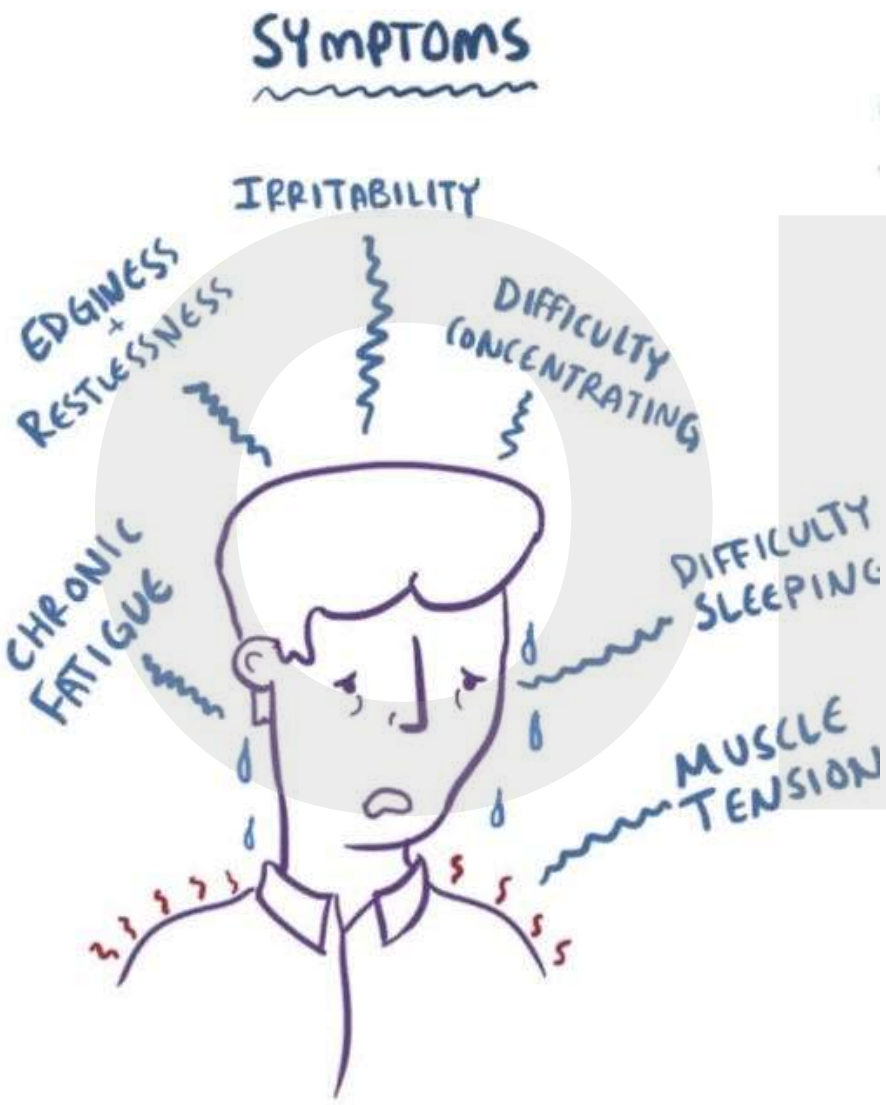
Andrew and his parents present to Andrew's PCP at the behest of his school counselor.

They describe Andrew as a very conscientious, kind, but cautious person. They mention that, even from a very young age, he was "clingier" than his brother, took a long time to warm up to others, and required more coaxing before big events. They describe 2 periods of time in early middle school where he had difficulty going to school for some days, but work with the school counselor to connect him with activities he looked forward to and that he could attend with a good friend, coupled with supportive behavioral incentives from home helped get him back into school.

Andrew is healthy physically. And, in private, he denies substance use, denies symptoms of psychosis, mania, and does not quite meet criteria for a depressive episode. He denies panic attacks or prior traumas.

He does describe multiple worries, that he carries with him at all times, in almost every setting, as he has for the past few years. He also describes muscle tension, feeling keyed up, irritable, has difficulty settling down to sleep, and as a result feels fatigued and has difficulty concentrating often.

The family notes that Andrew's mother has significant anxiety, sees a psychiatrist, and has taken paroxetine (Paxil) for many years, and that Andrew has two uncles who continue to struggle with Alcohol Use Disorder.



DSM 5 Criteria
Generalized Anxiety Disorder

- A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).
- B. The person finds it difficult to control the worry.
- C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms present for more days than not for the past 6 months).

  Note: Only one item is required in children.

  (1) restlessness or feeling keyed up or on edge
  (2) being easily fatigued
  (3) difficulty concentrating or mind going blank
  (4)irritability
  (5)muscle tension
  (6) sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. Arlington, VA: American Psychiatric Association, 2013.

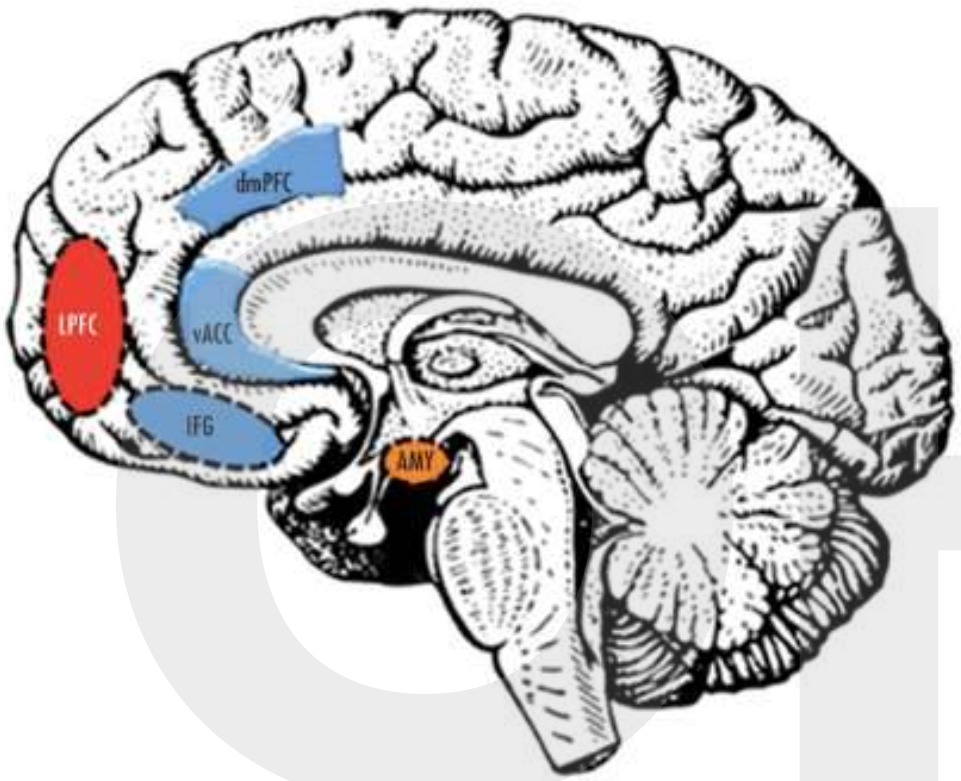
Generalized Anxiety Disorder
Epidemiology/Course

- Lifetime risk of GAD is 9% in US[1]
- Median Age of onset: ~30 years old[1]
  - But many diagnosed individuals report “anxiety for much of life” or “anxious temperament”
- Symptoms wax and wane over lifetime based on stress load, but peak in middle age[1] (45-52% experience recurrence over life[2])
- Most common worries[1]:
  - Children: school and performance
  - Adults: Family and health
- Rates of complete recovery are low (32%-58%[2])
- Genetics account for about 30% of cause of GAD[1]

1- American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders: DSM-5. Arlington, VA, USA: American Psychiatric Association.
2- Gabbard G. O., (Ed) (2014). Gabbard’s Treatment of Psychiatric Disorders (5th Ed). Arlington, VA, USA; American Psychiatric Publishing, Inc..

Generalized Anxiety Disorder

Neurobiology



Reduced Volume

- Ventral anterior cingulate cortex (assesses salience of emotional information)
- Inferior frontal gyrus (language comprehension and production, inhibition)

Hypofunction

- Dorsomedial Prefrontal cortex (predicting mental states of others)

Hyperactive

- Lateral Prefrontal cortex (moral decision making)

Overactive conscientiousness ✚ difficulty predicting others' thoughts/expectations
difficulty accurately assessesing emotional information
difficulty putting complex thoughts/words into order

Arciniegas, DB, ed., The American Psychiatric Association Publishing Textbook of Neuropsychiatry and Clinical Neurosciences, 6th Ed, Ch. 26, APPI, Washington DC, 2018

Case – Andrew – Part 3

Generalized Anxiety Disorder

The PCP discusses the diagnosis of Generalized Anxiety Disorder, a common anxiety disorder and discusses possible treatments, including Cognitive Behavioral Therapy, which will help him understand his worries and find ways to decrease their power over him. Andrew likes the sound of that. They also discuss medications, but Andrew declines at the current time.

Andrew begins seeing a therapist, with whom he builds a great rapport, and over 16 sessions finds numerous ways to understand his automatic thoughts and challenge them with alternative possibilities. This greatly decreases his worries and anxious tension, but doesn't abolish them completely.

Yet, it does allow him to complete high school successfully, and to start college.

Generalized Anxiety Disorder Treatments

Cognitive Behavioral Therapy

- Self-monitoring
- Relaxation Training
- Cognitive therapy toward negative appraisals

Achieves some sx reduction in most treatments

Achieves significant reduction enough to not meet criteria in ~50%

Medications

SSRIs (response rates 50s-80s%)

SNRIs (response rates 50s-80s%)

Buspirone

GABA-modulators (benzodiazepines and pregabalin) (response rates 40s-60s%)

- Neither CBT, nor medications are significantly more effective than the other
- No SSRI/SNRI performed significantly better than others

Gabbard G. O., (Ed) (2014). Gabbard's Treatment of Psychiatric Disorders (5th Ed). Arlington, VA, USA; American Psychiatric Publishing, Inc..

Generalized Anxiety Disorder Treatments

REVIEW Open Access

Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders

Martin A Katzman[1*], Pierre Bleau[2], Pierre Blier[3], Pratap Chokka[4], Kevin Kjernisted[5], Michael Van Ameringen[6], the Canadian Anxiety Guidelines Initiative Group on behalf of the Anxiety Disorders Association of Canada/ Association Canadienne des troubles anxieux and McGill University

Table 24 Recommendations for pharmacotherapy for GAD

First-line	Agomelatine, duloxetine, escitalopram, paroxetine, paroxetine CR, pregabalin, sertraline, venlafaxine XR
Second-line	Alprazolam*, bromazepam*, bupropion XL*, buspirone, diazepam*, hydroxyzine, imipramine, lorazepam*, quetiapine XR*, vortioxetine
Third-line	Citalopram, divalproex chrono, fluoxetine, mirtazapine, trazodone
Adjunctive therapy	**Second-line:** pregabalin **Third-line:** aripiprazole, olanzapine, quetiapine, quetiapine XR, risperidone **Not recommended:** ziprasidone
Not recommended	Beta blockers (propranolol), pexacerfont, tiagabine

CR = controlled release; XL = extended release; XR=extended release.

*Note: These have distinct mechanisms, efficacy and safety profiles. Within these second-line agents, benzodiazepines would be considered first in most cases, except where there is a risk of substance abuse, while bupropion XL would likely be reserved for later. Quetiapine XR remains a good choice in terms of efficacy, but given the metabolic concerns associated with atypical antipsychotic, it should be reserved for patients who cannot be provided antidepressants or benzodiazepines. Please refer to text for further rationale for the recommendations.

FDA Approved

Case – Andrew – Part 4

Generalized Anxiety Disorder

The summer between Andrew's first and second year of college he returns home and personally schedules an appointment with his PCP.

At the appointment Andrew requests continuation of paroxetine 40mg which was started at the student health center. He denies side effects although he had some weight gain over first couple months, which reduced when he joined a running group. He is not taking other medications, although he did note he was prescribed a small amount of clonazepam when he first started the paroxetine, but hasn't used it in months.

He reports he is doing well in school, has made some good friends, and looks forward to going back in the fall.

Case – Pandora – Part 1

Panic Disorder

Case – Pandora – Part 1

Panic Disorder

24 yo female, child of Vietnamese immigrants, originally from Virginia, started medical school in Portland 3 months ago.

Not married, no children, but in stable relationship with partner who is an electrical engineer recently hired at Intel.

Pandora presents to her PCP and expresses hope that the PCP will feel comfortable continuing her clonazepam prescription.

Pandora describes a history of panic attacks, fairly rare now (<1/mo at this time), but very problematic, characterized by rapid onset of intense fear, accelerated heart rate, sweating, feeling dizzy, numbness/tingling, fear of losing control. They come on unexpectedly, anywhere, and peak within a few minutes and can last from 20 minutes up to an hour.

Case – Pandora – Part 2

Panic Disorder

Pandora describes that her panic attacks first started as an undergraduate, around the time of her first organic chemistry final. Unfortunately, they happened in a number of locales - in the student library, in the grocery, and while driving.

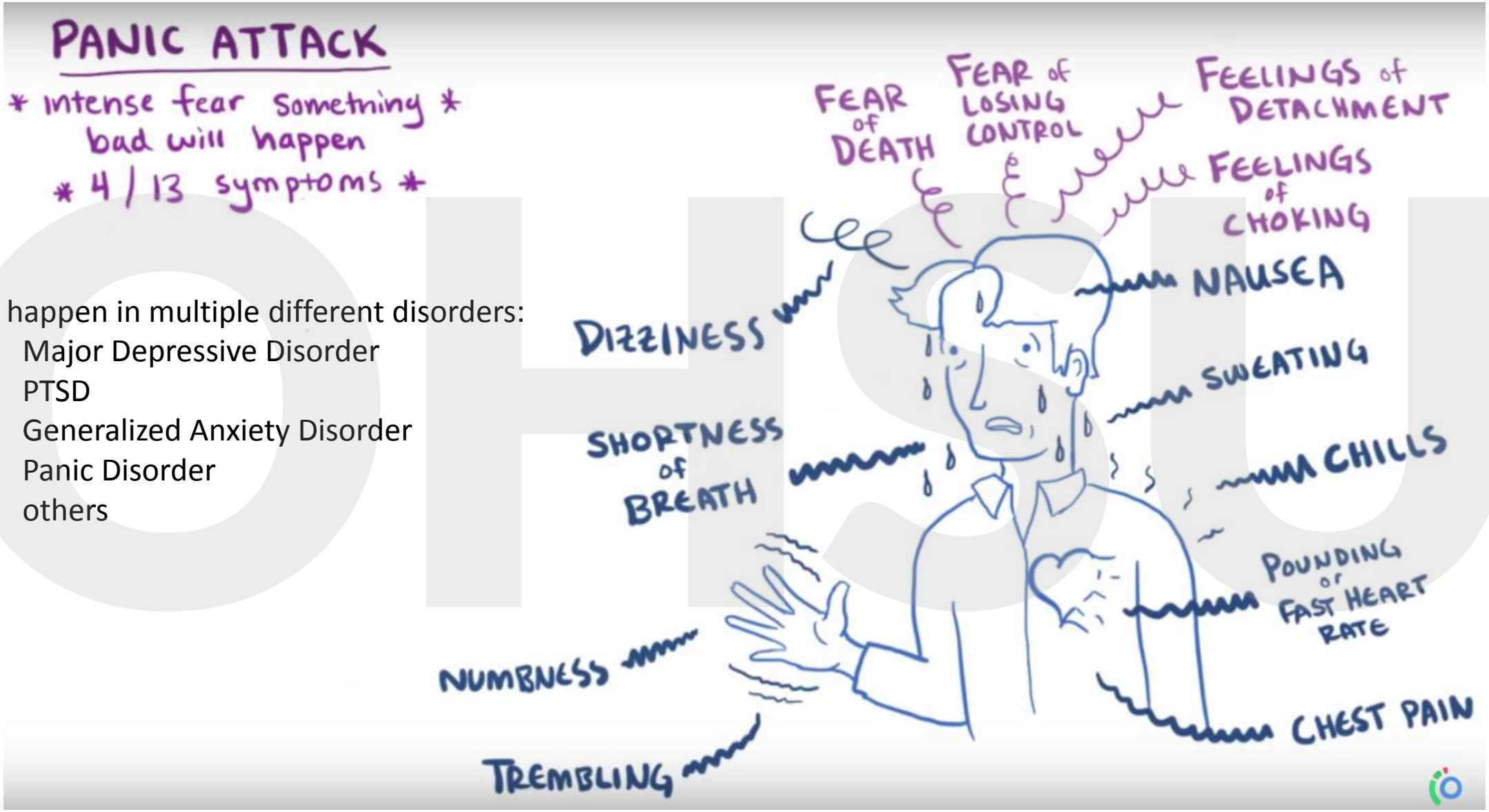
At that time, she was so affected by those first panic attacks that for months she was incredibly anxious about having another panic attack, in fact, had to suspend her organic chemistry study for an entire year, and couldn't drive for 6 months for fear of having more attacks.

Her father told her she was just "hit by the wind" (trung gio), like his sister often was. But a friend told her to go see the student health center.

While the attacks started in earnest in college, she realized after talking to the counselor that her "fearful spells" during childhood may have been early, less severe indications of vulnerability to panic attacks later.

The last time she had a panic attack was about 3 months ago. If they occur, she takes 0.5mg of Clonazepam, which stops it fairly quickly. She has even had one come on in the middle of the night, which she describes as "the worst".

Pandora notes she tried 2 SSRIs and an SNRI, but she found side effects from each even at the lowest doses. She likes to keep 7 tablets of Clonazepam on hand at any time in case they recur. She has only 2 left now, and this causes her some trepidation.



**Can happen in multiple different disorders:

- Major Depressive Disorder
- PTSD
- Generalized Anxiety Disorder
- Panic Disorder
- others

From Video “Panic Disorder” – by Osmosis – accessed at https://www.youtube.com/watch?v=YxELZyA2bJs

DSM-V criteria

PANIC DISORDER

(1) Recurrent & unexpected PANIC ATTACKS

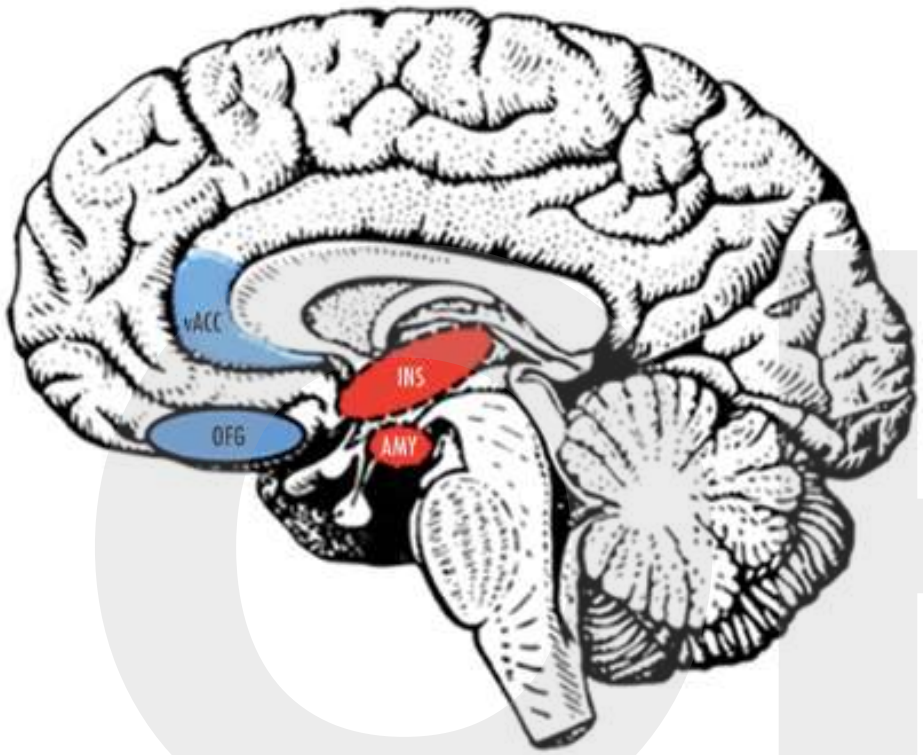
(2) (a) persistent worry
(b) change in behavior

(3) NOT effects of substance (drugs + medication)

(4) NOT another disorder

From Video “Panic Disorder” – by Osmosis – accessed at https://www.youtube.com/watch?v=YxELZyA2bJs

Panic Disorder
Neurobiology



Reduced Volume:
- Orbitofrontal Gyrus (corrects no longer appropriate responses)

Hypofunction
- Ventral Anterior Cingulate Cortex (assesses salience of emotional information)

Hyperactive
- Amygdala (detecting fear)
- Insular Cortex (interoceptive awareness and selecting emotionally relevant context for sensory stimuli)

Overactive fear detection
Overactive awareness of internal physical sx
Overactive selection of emotions to match physical sx

+

Underactive assessment of importance of emotions
Difficulty stopping inappropriate responses

Arciniegas, DB, ed., The American Psychiatric Association Publishing Textbook of Neuropsychiatry and Clinical Neurosciences, 6th Ed, Ch. 26, APPI, Washington DC, 2018

Panic Disorder
Epidemiology/Course

- Median Age of onset: ~20-24 years old
  - But many diagnosed individuals report history of childhood "fearful spells" and childhood belief that symptoms of anxiety are harmful.
- Symptoms wax and wane over lifetime based on stress load, and periods of panic can be separated by years.
- Severity of panic attacks wane in late age due to dampening of autonomic arousal.
- Has overlap with several culture bound syndromes
  - Trung Gio – "hit by the wind" – assoc w Vietnamese culture
  - Khyal – "wind attacks" – assoc w Cambodian culture
  - Ataque de Nervios – "attack of nerves" – Latin American

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2- Gabbard G. O., (Ed) (2014). Gabbard's Treatment of Psychiatric Disorders (5th Ed). Arlington, VA, USA; American Psychiatric Publishing, Inc..

Panic Disorder Treatments

Cognitive Behavioral Therapy

- Psychoeducation
- Cognitive Restructuring
- Exposure
  - Interoceptive Exposure
  - Situational Exposure
- Relapse Prevention

Medications

SSRIs

SNRIs

Benzodiazepines

- Neither CBT, nor medications are significantly more effective than the other
- No SSRI/SNRI/TCA performed better than others
- As persons with Panic Disorder are more sensitive to sx, start very low with medication doses
- Combination CBT+SSRI offer only very marginal increases in long term response
- Combinations of CBT+benzodiazepine may do slightly worse than CBT alone

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Panic Disorder Treatments

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Table 15 Recommendations for pharmacotherapy for panic disorder

First-line	Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, paroxetine CR, sertraline, venlafaxine XR
Second-line	Alprazolam, clomipramine, clonazepam, diazepam, imipramine, lorazepam, mirtazapine, reboxetine
Third-line	Bupropion SR, divalproex, duloxetine, gabapentin, levetiracetam, milnacipran, moclobemide, olanzapine, phenelzine, quetiapine, risperidone, tranylcypromine
Adjunctive therapy	**Second-line**: alprazolam ODT, clonazepam **Third-line**: aripiprazole, divalproex, olanzapine, pindolol, risperidone
Not recommended	Buspirone, propranolol, tiagabine, trazodone

CR = controlled release; ODT = orally disintegrating tablets; SR = sustained release; XR = extended release.

FDA Approved

Case – Pandora – Part 3

Panic Disorder

PCP offers 7 tabs of Clonazepam 0.5mg, and offers referral to CBT. Pandora politely declines the CBT for now due to difficulty carving out time.

14 months later, Pandora requests a refill of another 7 tabs of Clonazepam 0.5mg, as she anticipates possible increase in anxiety, potentially panic attacks, as she enters her clinical rotations. She is still not interested in CBT, again stating her time doesn't allow it.

Test Yourself Again

1) What is the difference between fear and anxiety?

Fear: rapid response to actual threat; Anxiety: preparatory emotion to ready for future possible threat.

2) What is the difference between a Panic Attack and Panic Disorder?

Panic attack: a discrete episode of rapid onset cluster of autonomic arousal sx. Panic Disorder: recurrent and unexpected panic attacks, with at least 1 mo of significant worry about having another panic attack or altered behavior due to panic attacks.

3) For Generalized Anxiety Disorder, which is better, medications or CBT?

They are equivalent.

4) What classes of antidepressants are first line treatments for GAD and Panic Disorder?

SSRIs and SNRIs

Common Presentations in Primary Care:
Anxiety Summary

Generalized Anxiety Disorder

- Inadequately modulated/organized conscientiousness physiology
- Diagnosed by excessive generalized worries + physical sx >6 mo, causing dysfunction
- Treatment: CBT or SSRI/SNRI/Buspirone>Benzodiazepines

Panic Disorder

- Inappropriately activated fear physiology
- Inappropriate sensitivity to internal somatic state/sx.
- Diagnosed by recurrent, unexpected panic attacks, and prompting worry about more or behavioral change in response to panic attacks
- Treatment: CBT or SSRI/SNRI/Benzodiazpines

Questions?






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