

Anxiety

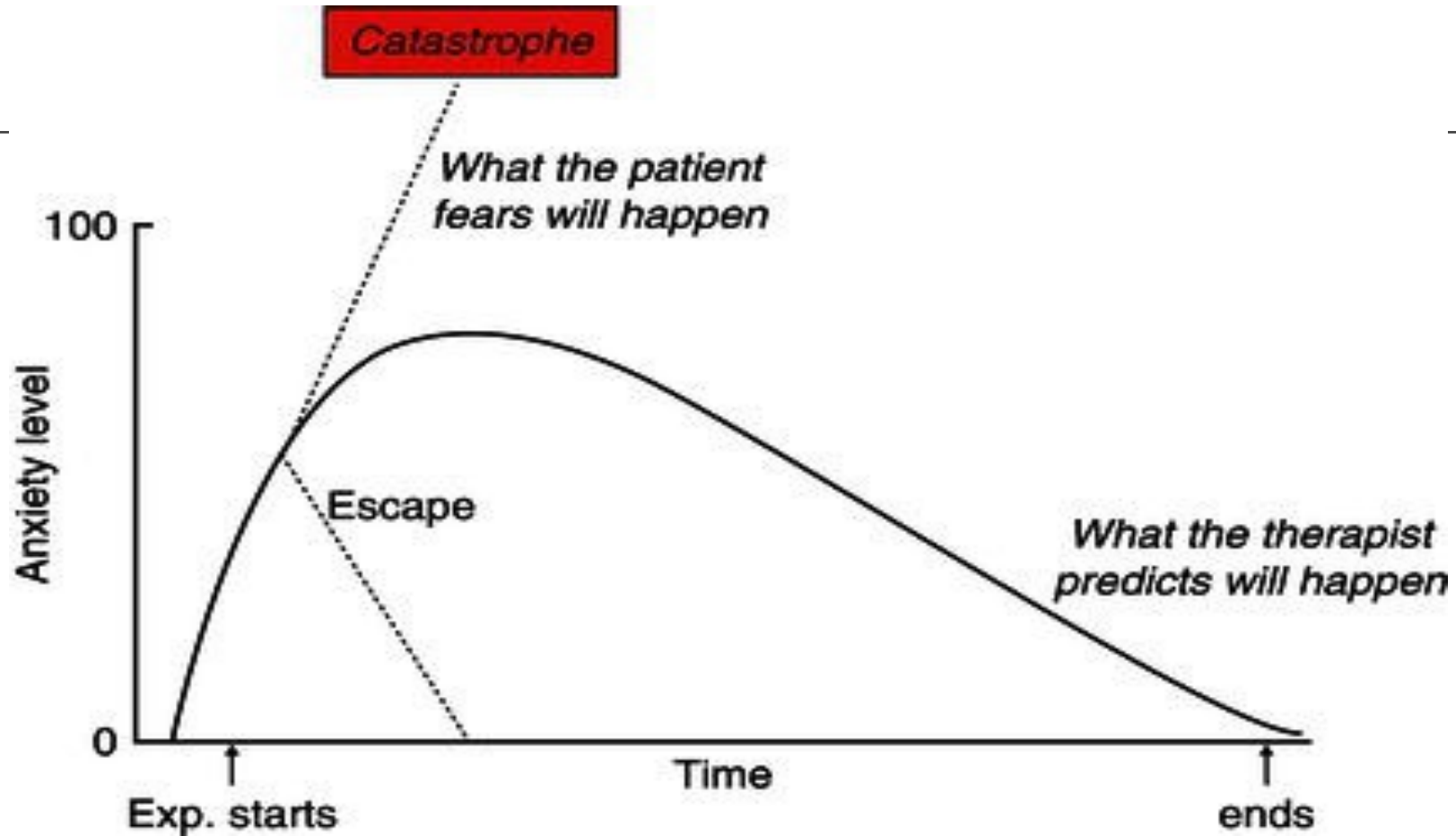
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WILBUR DATTILO MD

ASSISTANT CLINICAL
PROFESSOR OF PSYCHIATRY

UNIVERSITY OF UTAH SCHOOL
OF MEDICINE





AVOIDANCE.

What feeds anxiety?



ONE PHRASE SUMMARIES...

- **Specific Phobia:** Fear of a specific thing (spiders, heights, flying on a plane)
- **Social Anxiety:** Fear of being scrutinized by others
- **Agoraphobia:** Fear of being in crowds/public places
- **Generalized Anxiety Disorder:** Worry about everything all of the time
- **Substance induced:** Think intoxication or withdrawal from almost anything, including medications we prescribe (opioids and benzos)
- **Related to a Medical Condition:** Thyroid, heart, adrenal, respiratory, GI, neurological disorders that cause anxiety.

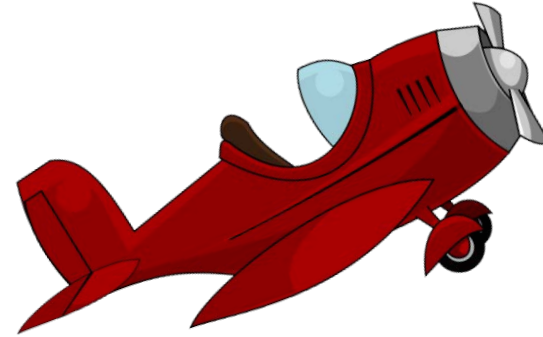
The case of Wilbur

Wilbur is a 39-year-old man who presents at the insistence of his wife. Wilbur's mother lives in a different state and occasionally he wants to visit her, but the most efficient mode of travel is by airplane. Airplanes ALWAYS immediately cause Wilbur intense fear and panic, so he often cancels trips at the last minute. When he doesn't cancel trips he tries to drive, but if he has to take an airplane he experiences extreme distress which almost always threatens his marriage. He brings a note from his wife, which reads, "He needs Xanax."



Specific phobias

1. Phobic object almost ALWAYS produces IMMEDIATE fear or anxiety.
2. Phobic object is actively avoided or endured with extreme distress.
3. Fear or Anxiety is out of proportion to actual risk.
4. The fear causes social, occupational, relationship, or other impairment.
5. Common kinds: Fear of Animals (spiders, dogs, cockroaches) Nature (heights, storms, water), Blood/Injections, Situations (elevators, airplanes, enclosed spaces).
6. 12 month prevalence 7-9% in USA, much lower in under-developed countries (where there are plenty of actual risks to worry about).
7. Most people have more than 1 specific phobia.
8. Age of onset is usually 7-11 years, much less common in older people.
9. F>M 2:1



Specific phobias

1. Very limited role of pharmacology.
2. This may be a disorder where an occasional PRN benzodiazepine makes a lot of sense (i.e. someone is afraid to get on an airplane which they have to do once every 6 months).
3. Main-stay of treatment would be working with a psychologist/ social worker on Exposure/Response Prevention Therapy.



BEHAVIORAL THERAPIES: EXPOSURE RESPONSE PREVENTION

- The “go to” for phobias and OCD.
- Basically consists of formulized exposures to aversive stimuli paired with prevention of phobic behaviors.
- Can do graduated vs. “flooding” exposures.
- *First example:* patient has a phobia of heights and you do a flooding exposure where you take him to the top of Sears Tower in Chicago and have him stand on the glass floor.
- *Second example:* patient has fear of spiders, so you start with pictures of spiders, then a live spider across the room, building up to having patient hold a tarantula.

The case of BRITTANY



Brittany is a 22-year-old woman who presents with chief complaint of anxiety. She would like to make friends at her new job, but she is terrified of new people. She feels that she always says something “weird” when she has to talk to new people and ends up being sure that everyone thinks she is “stupid.” She has had this problem for at least the last 5 years, first noticing it in high school. It has gotten so bad that she has started missing days of work and she might get fired. She admits that when she does go to work, the only way she can make it through is to put a little vodka in her kale smoothie.

SOCIAL ANXIETY DISORDER (SOCIAL PHOBIA)

- Extreme fear of social situations
- Fear of humiliation or embarrassment
- Avoidant behaviors
- Anxious anticipation of social situations
- A subtype for people who are only anxious when they talk in front of others

- 12 month incidence 7% in the USA (only 2.3% in Europe)
- F>M 1.5-2.2X
- 75% of people have onset between 8 and 15 years of age.
- Lowest spontaneous remission rates of any anxiety disorder (35%)

What may be going on in Social Anxiety: Physiology/ Cognitive/ Behavior

Physiologically: Thought to be related to dysregulation of Amygdala responses to novelty and/ or hypersensitivity to faces/ judgement originating in the amygdala. Thalamic bypass of cortical structures with diminished soothing through ACG of PFC wisdom. Activation of SNS is final common pathway

Cognitions about others rejecting. EXPECTATION of being humiliated or embarrassed (usually by sympathetic response).

Behaviors: Avoiding social interactions

SOCIAL PHOBIAS AND SUBSTANCE USE

- Benzodiazepines are good emergent management for PRN usage.
- People with social phobia will often find that alcohol helps, therefore comorbid Alcohol Use Disorder is highest in this group.



“Don’t ask me for stimulants and benzos. Just use alcohol and caffeine like the rest of us”

– Bill

Meyer

SOCIAL PHOBIA

- First line treatments
 - SSRIS
- Other treatments
 - Pregabalin
 - Gabapentin
 - Benzodiazepines augmentation of SSRIs (especially clonazepam)
 - Buspar has evidence ONLY for augmentation of SSRI treatment
 - Propranolol (only for performance anxiety)
 - MAOIs
 - Antipsychotics: Olanzapine and Quetiapine have evidence, but also side-effects
 - Venlafaxine
 - Valproic Acid (Depakote)

SSRIS IN SOCIAL ANXIETY DISORDER AND OTHER AD

- In studies on SAD, SSRIs have worked with a NNT of between 3 and 7. Need to treat 3-7 people to have one person benefit who would not have benefitted from placebo.
- SSRIs have side effects, commonly: flushing, nausea, and diarrhea (which usually go away when a person gets used to the dose) and sexual side effects (anything from arousal to orgasm) which usually do not go away until the person discontinues the drug.
 - Studies indicate that people with social anxiety disorder are more prone to the sexual side effects, probably because they already have so much going against having a fulfilling sexual experience from the get-go.
- SSRIs + anti-inflammatory drugs increase the risk of GI bleeding by 9X (PPIs reduce this risk)

SSRIS IN SOCIAL ANXIETY DISORDER AND OTHER AD

- Paroxetine is most likely to cause weight gain (25% chance of 7% increase compared to <5% chance for other SSRIS).
 - It is category D in pregnancy, known to increase risk of septal defects. It is also the most anti-cholinergic (dry-ness).
 - Why use it?
- A lot of people with SAD who were switched from SSRI to placebo stayed well. May consider first use of SSRI as a trial and see how a patient does off of it in a couple of months.
- Citalopram increases QTc quite a bit in a dose dependent fashion (this is unfortunate because there is a lot of evidence that higher doses work better in treatment resistant people).
- Lexapro doesn't seem to increase QTc nearly as much in dose ranges with similar efficacy.

SOCIAL PHOBIA

- Non Pharmacological Strategies:
 - CBT
 - Exposure therapy
 - Drugs + Therapy probably best

COGNITIVE THERAPIES: AS EXPLAINED BY MARC PORRITT

- Can be used for all anxiety disorders.
- Have patient track anxiety-related and anxiety-producing thoughts.
- Help patient to challenge these thoughts and explore possible alternatives/worse case scenarios.
- May include behavioral exposure scenarios; this is why it is usually called CBT (cognitive behavioral therapy)
- *Example: As patient has social anxiety, she imagines that people at the restaurant are looking at her/judging her. Therapist works to challenge these ideas and explore other possibilities (i.e. “What else might they be looking at?”)*
 - This therapy might include a trip to the restaurant for practice with therapist.

The case of Sarah

Sarah is a 28-year-old woman. She started having episodes of extreme fear and panic for no clear reason. During these episodes she reports palpitation, sweating, trembling, shortness of breath (feels like she is suffocating), nausea, dizziness, chills, and feelings of numbness and weakness. During these episodes she feels like the world is “not real” and/or that she is going crazy or about to die. She is terrified that she will have a panic attack in public and has stopped going out unless absolutely necessary.



PANIC DISORDER

- Sudden unpredictable episodes of severe anxiety typically lasting 30-45 minutes
- Shortness of breath
- Fear of suffocation/dying
- Urgent desire to flee
- **Limited activities because of fear of having another attack**

- 12 month prevalence 2-3%
- Native Americans have highest rates
- F>M 2:1
- Usual age of onset 20-24 years; very rare in childhood

PANIC ATTACK SPECIFIER

- DSM 5 recognizes that panic attacks can be part of any anxiety disorder or of other mental illnesses, or of regular life.
- Panic attacks can be precipitated or un-precipitated.
- Let me tell you about my most recent panic attack...reminds me that anxiety is the body's alarm system. Sometimes something is wrong!

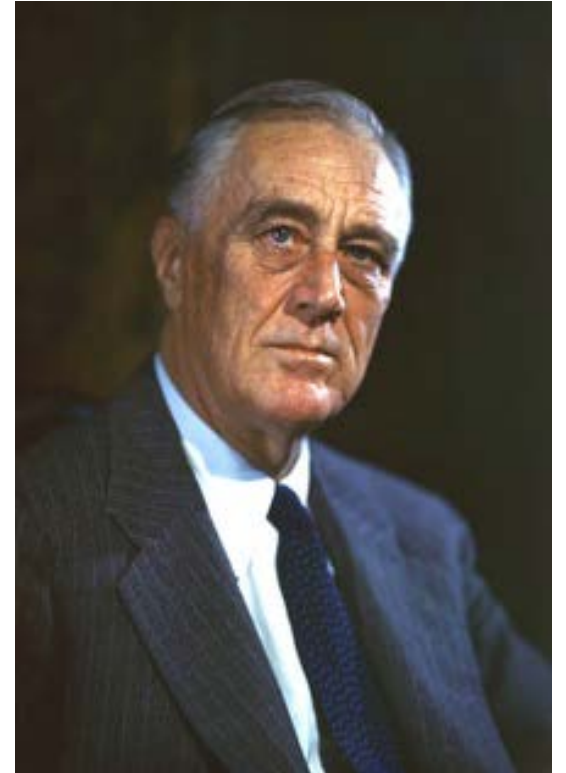


Panic neuroanatomy, cognitions, behaviors in mindless fear

Neuroanatomy: Hyperactive amygdala or Basal Ganglia set of cascade from hypothalamus, sometimes for no reason. This leads to increased NE and sympathetic nervous system response.

Cognitions: Unattached anxiety is terrifying. Mind tries to attach un-moored anxiety to something. “I am going to die”. “I am going crazy”. “I am losing control”

Behaviors: mental avoidance (don’t think of anything that can cause panic), avoiding activities, and avoiding the feeling of fear (until there is nothing to fear but fear itself).



PANIC DISORDER

Emergency Management

- Benzodiazepines work quickly, but panic usually returns when Benzos are withdrawn.
- Some guidelines recommend *against* using in Panic Disorder because of addiction potential and because patients don't get better over time.
- Panic disorder patients will have a hard time getting off of Benzos...
 - 75% will not be willing to come off of Alprazolam (Xanax), 25% could not get off of Clonazepam (Klonopin)

PANIC DISORDER

First Line treatment

- **Selective Serotonin Reuptake Inhibitors**
 - Action is usually delayed and they can initially worsen symptoms.
 - May consider starting at ½ the normal starting dose (suggested by some)
- **Other treatments**
 - Mirtazapine (Remeron)
 - TCA's
 - Valproic Acid (Depakote)
 - Venlafaxine (Effexor)
 - Gabapentin
- **More Experimental**
 - Inositol
 - Pindolol (Beta Blockers)

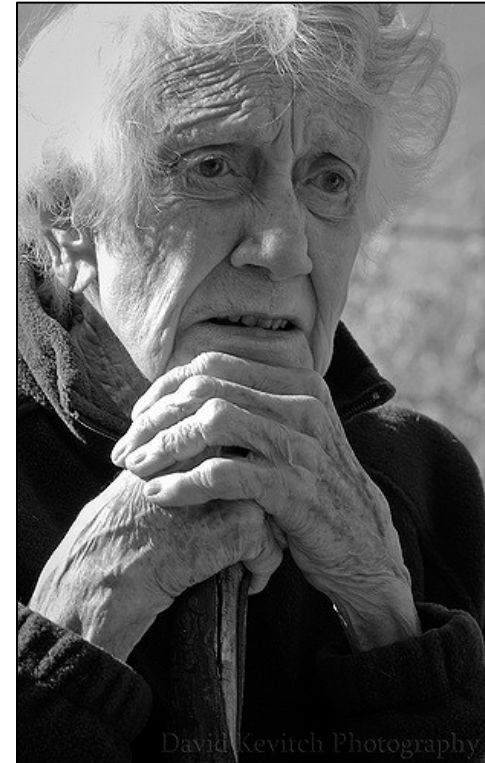
PANIC DISORDER

Non-Pharmacological treatment

- CBT
- Relaxation training
- Evidence is that therapy + meds is NOT better than either alone

The case of Agnes

Poor Agnes has always been anxious. She worries about everything, all of the time. She reports feeling restless and always “on edge.” She is frequently tired. She complains of her mind going blank and difficulty concentrating. She finds herself feeling irritable and snapping at grandchildren. She has a hard time sleeping. She also feels depressed...



Screening tools that are used

The Hamilton **Anxiety** Rating **Scale** (HAM-A)

GAD7

Beck Anxiety Inventory

GENERALIZED ANXIETY DISORDER

- Irrational worries
- Muscle tension
- Somatic symptoms (tachycardia, hyperventilation, diarrhea)
- Often co-morbid with MDD and OCD
- 12 month prevalence 1.7% - 3.4%
- F>M 2:1

- More common in people of European descent
- Developed countries > non-developed countries
- Median age of onset is 30, but wide range.
- Earlier onset = more comorbidity
- Remission rates are low

GENERALIZED ANXIETY DISORDER

Emergency Treatment: anxious distress, insomnia, suicidal ideation/risk

- Benzos for 2-4 weeks max (again, some benzos easier to get people off of than others)
- May consider antipsychotics

GENERALIZED ANXIETY DISORDER

- SSRIs: Note in GAD, SSRIs can sometimes initially make symptoms worse and patients should be started on HALF of the normal dose.
 - Think “how is a person who worries about everything going to deal with a medication that causes strange sensations in his/her body?”
 - Fluoxetine and Sertraline have the best evidence.
- This is a place where Hydroxyzine may be a really good choice for augmentation (rather than getting patient on Benzos; European studies are promising...)
- Others meds with evidence: SNRIS (Venlafaxine and Duloxetine), Mirtazapine, Pregabalin (approved in Europe)
- You could also try:
 - Buspar (takes a while to work)
 - Beta blockers for somatic symptoms (tachycardia)
 - Quetiapine
 - TCA's

GENERALIZED ANXIETY DISORDER

Non-Pharmacological treatment:

- Reassurance
- Pastoral counseling/supportive therapy
- CBT (cognitive behavioral therapy)
- Relaxation
- Exposure therapies
- EXERCISE!

Acceptance and Commitment Therapy

Interventions intended to change the way an individual **relates** to their thoughts and experience, instead of extinguishing behaviors (behavioral therapy) or changing thoughts (cognitive therapies).

A patient does not try to “get rid” of anxiety, but instead tries to live a life in alignment with their values “in spite” of the anxiety.

Reinforcing value-based behaviors and not illness related behaviors.

For example, A patient with Panic Disorder stays in the house out of fear that he will have a panic attack. A therapist would teach the patient to become mindful of anxiety symptoms and leave the house in spite of having those feelings **ACCEPTING** that he may have a panic attack but still **COMMITTING** to living a life that he values.

Psychodynamic therapy

This therapy postulates that people are largely driven by unconscious needs and conflicts.

Understanding what is going on at a sub-conscious level (bringing it to consciousness) helps people to have INSIGHT into these issues and allows them to be “more rational actors in the drama of their lives.”

For example, a patient with GAD worries about everything. He works with therapist for 1-2 years and explores his childhood/ relationship with parents and realizes that his current insecurities are related to attachment with mother/ father. He learns to accept and forgive himself for things mistakes he has made and realizes that he “tried his best.”

List of Disorders with Brief Descriptors

Obsessive Compulsive Disorder (OCD): Obsessions (recurrent and persistent thoughts, urges, or images that are experienced as intrusive and unwanted) AND/OR Compulsions (Repetitive behaviors or mental acts that an individual feels driven to perform in response to obsession or according to rules that are applied rigidly).

Body Dysmorphic Disorder: Preoccupation with perceived body flaw (which others don't perceive)

Hoarding: Cant get rid of things, and clutter ensues.

Trichotillomania: Compulsively removing hair from head, eyelashes, eyebrows.

Excoriation (Skin Picking) Disorder: Compulsively picking at one's skin.

Obsessive Compulsive Disorder

Obsessions, Compulsions, or Both

- Obsessions:
 - Recurrent persistent thoughts, urges or images that are experienced as unwanted/ intrusive and usually cause distress.
 - The individual attempts stop ignore/ suppress thoughts/ urges/ images OR attempts to neutralize them with some other thought or action (Compulsion)
- Compulsions
 - Repetitive Behaviors that an individual feels driven to perform in response to obsessions
 - The Behaviors are aimed at preventing or reducing Anxiety or distress, or preventing some dreaded event or situation, BUT the acts are not connected with what they are meant to prevent in any realistic way
- Significant distress, disability, or time spent on obsessions or compulsions.

Specifiers

With good or fair insight: Individual recognizes that obsessive-compulsive disorder beliefs are definitely or probably not true

With poor insight: Patient thinks that they are probably true

With absent insight/ delusional beliefs: Person is absolutely convinced that they are true.

Tic related: Patient has current or past history of Tic Disorder

- Tics happen in 30% of persons with OCD, more common in males with childhood onset.

Usual OCD obsessions/ compulsions

Cleanliness/ Germs/ Contamination

Symmetry (repeating, counting, arranging)

Forbidden or taboo thoughts (aggressive, sexual, religious)

Harm (fear of harming self, others, and need to check things)

Some Factoids

12 month prevalence 1.2%. Females affected slightly more often than males. Males more likely to have onset in childhood.

Mean age of onset is 19.5, 25% of cases by the age 14.

Onset after 35 is rare, but not unheard of.

25% of males have onset before age 10.

Usual onset is gradual, but acute onset is noted.

Usual course is waxing and waning.

Remission rates in adults low (~20%)

Childhood onset remits by adulthood in 40% of cases.

50% contemplate suicide, 25% attempt.

Increased risk amongst physically, sexually abused in childhood, or other stressful/ traumatic events.

Comorbidity

76% have another anxiety disorder

63% have another mood disorder (41% have major depressive disorder)

23-32% have obsessive compulsive personality disorder

Not the same as OCPD!

Most people who say that they have OCD actually mean that they have OCPD (obsessive compulsive PERSONALITY disorder).

This personality disorder applies to people who are overly structured, rigid ,and perfectionistic in a way that is damaging to their relationships. They have a hard time being “flexible.”

Many people with OCD also have OCPD, but the treatments are different.

Screening Questions for OCD

Do you wash or clean a lot?

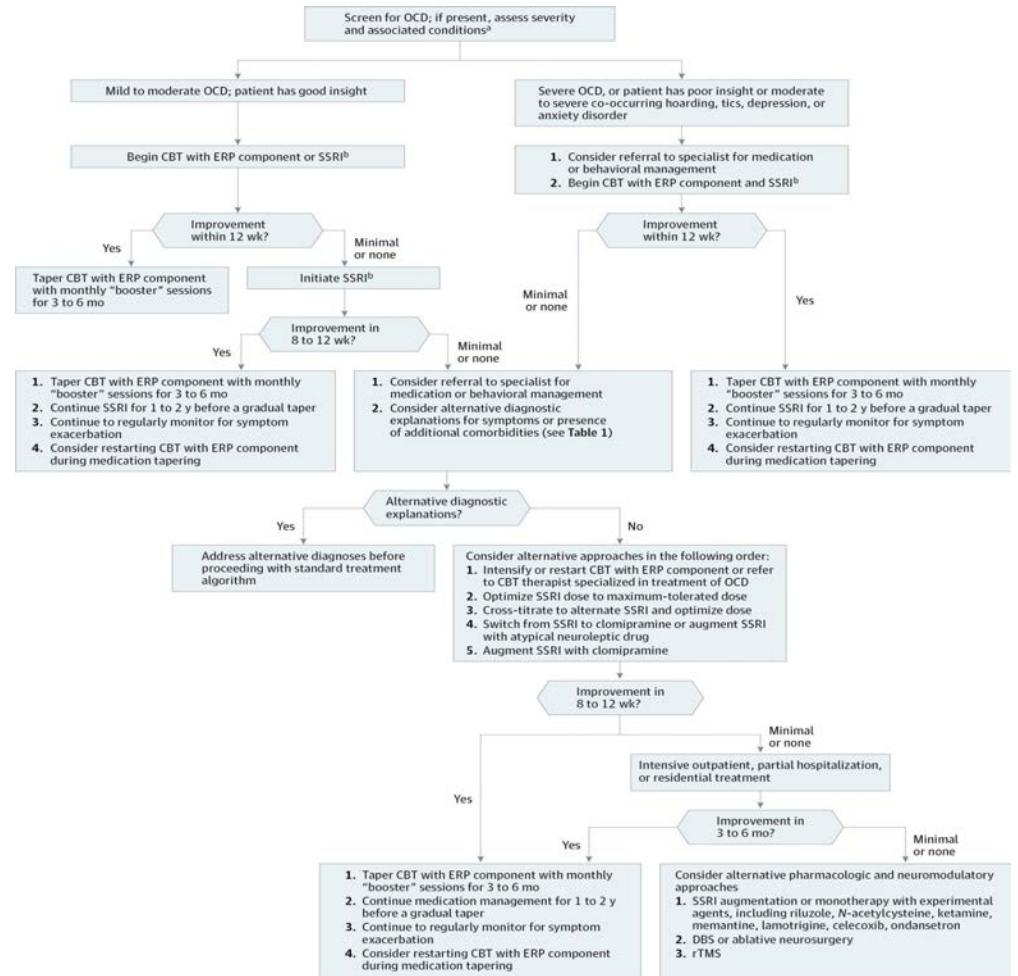
Do you check things a lot?

Is there any thought that keeps bothering you that you would like to get rid of but cannot?

Do your daily activities take a long time to finish?

Are you concerned about putting things in a special order, or are you very upset by mess?

If patient screens +, consider having them look at the Yale Brown Obsessive Compulsive Inventory which is widely available for free on the internet. (Best, if you have time, review it with them).



From: **Obsessive-Compulsive Disorder Advances in Diagnosis and Treatment**

JAMA. 2017;317(13):1358-1367. doi:10.1001/jama.2017.2200

That last slide, main points.

For mild/ moderate cases you can choose between starting ERP therapy OR an SSRI. For more severe cases, both an SSRI and ERP therapy should be pursued concurrently.

SSRI doses should be pushed as high as tolerated as long as patient is still not well. Experts will often push past maximum FDA recommended doses and monitor the patient carefully.

The TCA clomipramine is very serotonergic and could be may after a failed trial of high dose of an SSRI. SE limit use.

Augmentation with an atypical antipsychotic is the next step in the treatment algorithm especially if the patient has TICS or very poor insight.

Remember that comorbidities are common. Consider ECT if depression is severe. Last resort for many patients is a deep brain stimulator or ablative neurosurgery.

Behavioral therapies: Exposure Response Prevention

Go to for phobias and OCD.

Basically, consists of formulized exposures to adverse stimuli paired with prevention of phobic behaviors.

As an example: someone has OCD with lots of obsessions and compulsions around cleanliness. Have patient list all things that make him anxious and pick things at about 4-6/10 level of distress to start working on: don't wash your hands for the session after you shake mine.

First line medications for OCD from AFP

<i>DOSAGE (MG PER DAY)</i>				
<i>SSRI</i>	<i>STARTING</i>	<i>TARGET</i>	<i>MAXIMAL</i>	<i>COST*</i>
Citalopram (Celexa)	20	40†	40†	\$4 (\$200)
Escitalopram (Lexapro)	10	20	40	\$13 (\$240)
Fluoxetine (Prozac)‡	20	40 to 60	80	\$4 (\$305)
Fluvoxamine‡	50	200	300	\$17 (not available)
Paroxetine (Paxil)‡	20	40 to 60	60	\$4 (\$160)
Sertraline (Zoloft)‡	50	200	200	\$10 (\$215)

This might be a good time to talk about antipsychotics in the setting of anxiety disorders.

OCD is the only “anxiety” disorder in which antipsychotics are routinely recommended for severe cases.

Risperidone has the best evidence because it is the atypical antipsychotic which has been around the longest.

You can use others. Here are the most commonly used:

Drug/ usual doses.	Pro	Con
Risperidone (Risperdal®) 1-6mg	Cheap. Has the most evidence. Side effects are reasonable especially at low doses.	Of “atypicals” most likely to cause EPS and Prolactin Elevation (galactorrhea and breast development in men).
Olanzapine (Zyprexa®) 5-30mg	Now generic. Besides Clozapine, widely considered the most effective antipsychotic. Cause sedation (if that is needed). Little EPS. Effective for a wide range of psychiatric problems.	Very significant weight gain and metabolic side effects. And sedation which makes it intolerable for many.
Quetiapine (Seroquel®) 12.5-800mg	Very sedating even in low doses. Can help if sleep is a major issue. One of the few antipsychotics that has a small street value (people like it).	Sedation can be intolerable, especially as you edge towards effective antipsychotic doses.
Aripiprazole (Abilify®) 2-20mg	Not usually sedating People can still go to work/ school on this medicine easily Has been shown to be a good augmentation agent for MDD	Can cause extreme restlessness (akathisia) Still quite expensive (best place to get it is Costco)
Ziprasidone (Geodon®)	Much better metabolic profile compared to others. Good for people with comorbidities/ excessive weight gain on others	Sedating, needs to be taken with meals, need to watch QTc interval closely. Likely somewhat less effective for severe illness.
Lurasidone (Latuda®)	Very good metabolic profile. One of the few drugs approved for bipolar depression. No QT prolongation.	Sedating, needs to be taken with food. Very expensive. Not cheaper than \$110 anywhere. Likely less effective for severe illness.

DISORDER	DIAGNOSTIC CRITERIA	CLINICAL FEATURES	PREFERRED TREATMENT
Body dysmorphic disorder	Preoccupation with perceived defects or flaws in physical appearance that leads to repetitive behaviors or mental acts in response to the apparent concerns	Poor insight Seeks care from dermatologists and cosmetic surgeons to address perceived defects Symptom onset during adolescence Waxing and waning course	Cognitive behavior therapy (exposure and response prevention) Some evidence for SSRIs
Excoriation (skin-picking) disorder	Recurrent skin picking resulting in skin lesions Repeated attempts to decrease or stop skin picking	More common in females Symptom onset at the beginning of puberty	Habit reversal therapy Limited studies evaluating response to pharmacotherapy
Hoarding disorder	Persistent difficulty discarding or parting with possessions because of strong urges to save items and/or distress with discarding items Accumulation of possessions to a degree that the space where possessions accumulate cannot be used as intended	75% of patients with hoarding disorder have comorbid mood or anxiety disorders The hoarding causes significant distress or impairment in function Symptom onset between 11 and 15 years of age Symptoms or hoarding behaviors progressively worsen	Behavior therapy targeted toward removal of hoarded items and reduction in

Reference stuff that we probably wont
have time to discuss....

SEXUAL SIDE EFFECTS

If a patient has sexual side effects in the setting of an anxiety disorder, consider:

1. Mirtazapine (Remeron)
2. Gabapentin or Pregabalin (Lyrica)
3. Nefazodone
 - Risk of fatal/transplant necessary liver failure is 1/300,000 which is enough to have it frowned upon and withdrawn from many global markets. (Compare this to the risk of dying in a motor vehicle accident in a year which is ~ 1/10,000.)

Chlordiazepoxide (Librium) first synthesized in 1955 by accident.

Started being marketed in 1960 with Valium being a huge hit for Hoffmann La Roche in the Wild West days of direct-to-consumer advertising.

Valium was aggressively marketed (especially to housewives) as a safe, non-addictive way to manage the stresses of life.

Valium and other benzos do have the advantage of being relatively safe compared to their barbiturate ancestors. Think of Marilyn Monroe's overdose...in comparison it is hard to kill yourself with benzos alone.



MOST POPULAR BENZOS (2011)

Alprazolam (Xanax): 49 million prescriptions

Lorazepam (Ativan): 27.6 million prescriptions

Clonazepam (Klonopin): 26.9 million prescriptions

Diazepam (Valium): 15 million prescriptions

Temazepam (Restoril): 8.5 million prescriptions

MOST POPULAR BENZOS (2011)

	How much = 1 mg of Lorazepam?	Time to peak Plasma concentrations (hrs)	Half Life (hrs)	How fun are they to use as rated by addicts (0-100)
Lorazepam (Ativan)	1 mg	0.5 – 1	8 – 24	75
Diazepam (Valium)	5 mg	1 – 2	100	80
Alprazolam (Xanax)	0.5 mg	1 – 2	12 (rapid on/ off)	70
Chlordiazepoxide (Librium)	25 mg	1 – 4	100	32
Clonazepam (Klonopin)	0.25 mg	1 – 4	30	Unknown

PHARMACOLOGICAL THINGS OF INTEREST

Both diazepam (Valium) and chlordiazepoxide (Librium) are changed to Desethyl Diazepam (active metabolite) and then to Oxazepam in the liver.

Clonazepam is nitro-reduced in the liver.

Lorazepam, Oxazepam, and Temazepam are only glucuronidated in the liver, which takes a lot less liver to do (safer in people with liver disease).

A shout out to Tricyclic Antidepressants!

These are oldies but goodies. Imipramine was the first antidepressant, very closely related to early antipsychotics.

First the **bad news**: They are deadly in overdose (mess with cardiac sodium channels), are very likely to cause histaminergic effects (sleepy and hungry), anti-cholinergic effects (dryness, urinary retention, delirium), and orthostatic hypotension.

The **good news**: These have been shown to be some of the most effective antidepressants, especially as people get older (almost no efficacy in kids, work great in old people except for side effects). They are cheap. You can usually add them, in low doses, to other antidepressant therapy.

If you have a patient who has chronic pain, insomnia, or headaches in addition to depression or anxiety, try a low dose amitriptyline or nortriptyline at night. They might love you for it.

Other notable tricyclics...

Chlomipramine: very, very serotonergic; gold standard for treatment of OCD.

Doxepin: recently rebranded as a sleep aid Silenor® but you can very cheaply give generic 10mg Doxepin for sleep as it is not addictive and most patients don't yet know that it doesn't work for them (if they only want benzos/Ambien).

A Shout Out to Mirtazapine

It boosts transmission of serotonin and norepinephrine and also dopamine in the frontal cortex, but is not a reuptake inhibitor, does not increase serotonin, and has no potential to cause serotonin syndrome.

For this reason, it does NOT cause sexual dysfunction.

It is very anti-histaminergic, but not anticholinergic.

Main side effects are sedation and weight gain. Sedation is often desirable in anxious populations.

It is very good for sleep, anxiety, nausea, and actually a quite good antidepressant.

Use it.

Substance-Use Related Anxiety Disorder

- Intoxication with : alcohol, caffeine, PCP, hallucinogens, inhalants, stimulants
- Withdrawal from: alcohol, opioids, sedative, hypnotics, anxiolytics, and even stimulants.
- Medications: bronchodilators, anticholinergics, insulin, thyroid medications, oral contraceptives, antihistamines, antiparkinsonian meds, corticosteroids, antihypertensive, anticonvulsants (Keppra), antipsychotics (akathisia) and almost anything else
- Environmental: Heavy metals, insecticides, carbon monoxide, gasoline.

Substance Use Related..Continued

- Many people who struggle with addiction and who are in recovery have a very difficult time recognizing and tolerating painful emotions such as anxiety.
- This comes for at least these reasons:
 - Drug abuse has powerful emotionally stunting abilities (Emotional age is usually = to age when patient started using)
 - People who are drawn to drug abuse may have been less able, at baseline to deal with emotions than peers who were not drawn to substances
 - Substance use and withdrawal can increase anxiety tremendously
 - The go-to coping strategy for people with substance use problems is to take something that makes them feel better.
- If you are working with someone who is recovering from a substance use disorder will end up treating a lot of ANXIETY and INSOMNIA.

Insomnia

Insomnia is so prevalent amongst people with anxiety disorders that it is worth talking about for a moment.

- Insomnia is usually not the primary problem: it is usually a symptom of another kind of problem. Many times it is related to an anxiety problem, depression, bipolar illness, psychotic illness, substance abuse, or a medical problem
- Insomnia can take on a life of its own as a person worries about whether or not they can get to sleep and in that sense it becomes its own anxiety disorder.
- As discussed earlier, not sleeping is a significant risk factor for suicide, so it is worth treating.
- Some people with TBI and other rare medical conditions have primary insomnia that is difficult to treat and is beyond the scope of this discussion

CBT-I: Cognitive Behavioral therapy for Insomnia

Over the long run, most people would benefit most from CBT-I.

- CBT-I is widely available in digital (app) formats, workbooks, and there are a lot of free handouts on the internet
- CBT-I has Cognitive Components including setting realistic expectations (a 70 year old woman is not supposed to sleep like a 13 year old girl) and de-catastrophizing (getting poor sleep for one night is okay)
- CBT-I has behavioral component which are broadly SLEEP HYGEINE, RELAXATION TRAINING, and SLEEP RESTRICTION.

IF YOU HAVE TO USE MEDICATIONS, HERE ARE SOME THOUGHTS.

AGENT	HOW IT WORKS	PROS	CONS	OTHER
BELSOMRA [®] SUVOREXANT	OREXIN RECEPTOR ANTAGONIST	LESS ADICTIVE THAN OTHERS. REDUCES TIME TO SLEEP BY 6 MINUTES, INCREASES DURATION OF SLEEP BY 16 MINUTES.	NEXT DAY DROWSINESS, TEMPORARY PARALYSIS. EXPENSIVE . SCHEDULE IV, SOME RISK OF DEPENDENCE.	AS FAR AS I AM AWARE, NO HEAD-HEAD STUDIES WITH OTHERS. Will set you back at least \$350/ month
ROZEREM [®] RAMELTEON	MELATONIN RECEPTOR AGONIST	FOUND TO PREVENT DELIRIUM COMPARED TO PLACEBO. LIMITED ABUSE POTENTIAL. IT IS NOT SEDATING.	EXPENSIVE, AND ON- AVERAGE, PATIENT'S AVERAGE EXPERIENCE IS MEDIocre. CAN INCREASE DEPRESSION/ CAUSE SUICIDAL THOUGHTS.	At least \$390 dollars a month. SOMEONE STILL NEEDS TO EXPLAIN TO ME WHY I WOULD TAKE THIS INSTEAD OF MELATONIN.
MELATONIN	TELLS YOUR BRAIN THAT IT IS TIME TO GO TO SLEEP.	CHEAP, QUITE SAFE	LIMITED EFFICACY. IS NOT SEDATING.	AVAILABLE OTC. WHY NOT TRY IT FIRST?
AMBIEN [®] ZOLPIDEM	BINDS TO GABA A RECEPTORS. SHORT HALD LIFE 2-3 HOURS.	PEOPLE LIKE IT A LOT. SAFER WITH LESS ABUSE POTENTIAL COMPARED TO BENZOS. \$10/ MONTH	COGNITIVE EFFECTS, INCREASED RISK OF FALLS/ FRACTURES. RARE SLEEP BEHAVIOR DISTURBANCES. REBOUND INSOMNIA	WOMEN SHOULD TAKE 5MG, MEN 10. AS WITH ALL SLEEP MEDS, PEOPLE WILL EVENTUALLY HABITUATE TO IT.
LUNESTA [®] ES-ZOPICLONE	BINDS TO GABA RECEPTORS.	PEAKS IN .45 TO 1.3 HOURS, HALF-LIFE 6 HOURS.	SAME AS ABOVE, BUT WITH LESS REPORTS OF SLEEP BEHAVIORAL ISSUES.	\$25/ MONTH
SONATA [®] ZALEPLON	BINDS TO GABA RECEPTORS	VERY SHORT HALF-LIFE (LESS THAN AN HOUR) MAKES IT LESS LIKELY TO AFFECT YOU THE NEXT DAY. CAN REPEAT DOSE	SAME AS ABOVE	\$17/ MONTH

CLASS: Drugs	PROS	CONS
1ST generation antihistamines: Doxylamine (Unisom®) or Diphenhydramine (Benadryl) Or Hydroxyzine	Cheap. OTC, antihistamine that crosses blood brain barrier, reduces histamine mediated inflammation, (allergic reactions).	Antihistamines cause increased hunger and weight gain. These medications are extremely anticholinergic (dryness, mental slowing, and delirium). Hang-over effect the next day.
Trazodone <i>Desyrel</i>	Cheap. Relatively safe. Not habit forming. Use 25-100mg a night. I use it all of the time. Unlikely to hurt anyone.	Orthostatic hypotension. Has not been shown to be super effective. Priapism is a very rare side effect, but one you want to warn males about. Not really an antidepressant at these doses.
Mirtazapine <i>Remeron</i>	Pretty cheap. Not habit forming. Good antidepressant at higher doses, better for sleep at lower doses. Less likely to cause sexual dysfunction compared to other antidepressants.	Has not been shown to work for outside of the setting of depression. Anticholinergic (dry mouth, constipation). Weight gain.
Tricyclics (amitriptyline <i>Elavil</i>)	Very cheap. Not habit forming. Very effective especially for older patients with severe depression (paradox is that these patients are most likely to be harmed by side effects). Work well for pain (migraines).	Orthostatic hypotension, weight gain, and quite anticholinergic (therefore dryness and delirium-potentiating). Cardiac toxicity in overdose.
Doxepin <i>Silanor</i>	A very very anti-histaminergic tricyclic antidepressant. Not habit forming. Used at very low doses it promotes sleep. It has been FDA approved for insomnia (Silanor \$300+/ month) or you can give generic Doxepin 10mg for \$11/ month)	Cardiac toxicity is an issue, but when prescribing this low of a dose, even if patient takes whole bottle they are only getting ~ 2 doses of an effective antidepressant dose.

OTHER THINGS THAT ARE USED FOR INSOMNIA

CLASS: Drugs	PROS	CONS
Benzodiazepines (Tenazepam <i>Restoril</i> / Lorazepam <i>Ativan</i> Diazepam <i>Valium</i>)	Anxiolytic, sedative, myorelaxant, amnesic properties. Much safer than barbiturates in overdose (will not themselves cause respiratory depression).	Habit forming. Tolerance and potentially fatal withdrawal syndrome (similar to alcohol), increase risk of falls in elderly, increased risk of dementia in those who take them regularly. AVOID in people with history of substance abuse.
Antipsychotics (Seroquel, Risperdal, olanzapine)	Not habit forming. Patients don't like to take. Are meant to be used in people who are psychotic. Can be used for very psychiatrically ill patients with a variety of problems and have evidence in augmentation of antidepressants, bipolar depression, severe OCD, severe anxiety, and any disorder where psychotic or nearly psychotic-RUMINATIONS are part of the picture.	Some are expensive. Very extensive metabolic and extra-pyramidal side effects. Not to be used
Anticonvulsants (Gabapentin)	Can be good for everything. Pain, anxiety, insomnia. Good for substance abusers. Almost no problems caused by intentional or unintentional overdose.	Not that great for sleep, but help anxiety which can worsen sleep.