A MORE DETAILED LOOK AT ANXIETY DISORDERS

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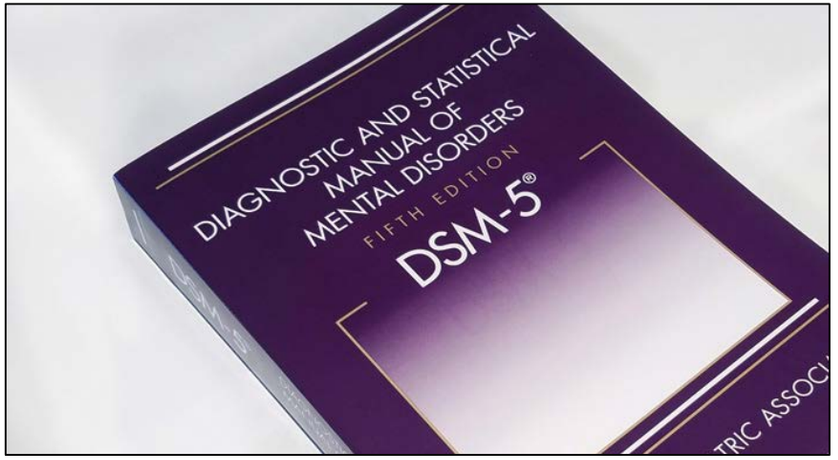
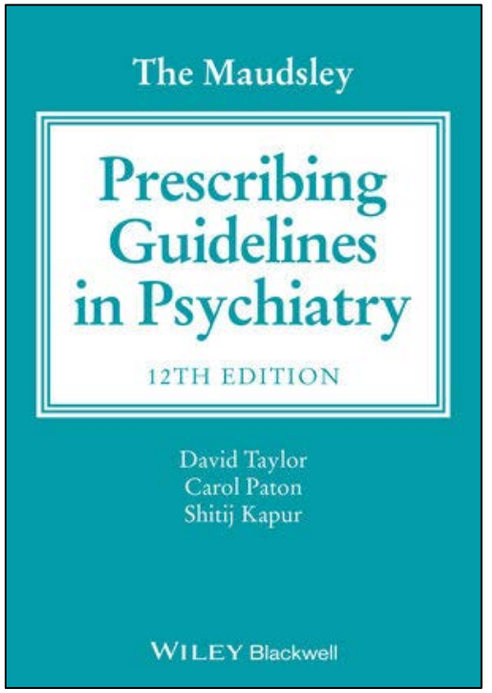
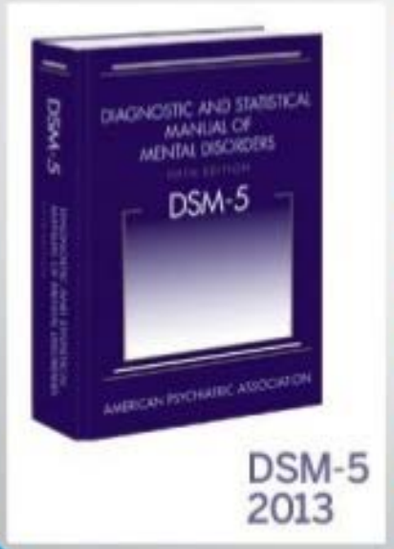
Special Thanks…





BASED ON THE CURRENT DSM-5

9 MENTAL DISORDERS UNDER ANXIETY CATEGORY



1. Separation Anxiety Disorder
2. Selective Mutism
3. Specific Phobia
4. Social Anxiety Disorder
5. Panic Disorder -Panic Attack
6. Agoraphobia
7. Generalized Anxiety Disorder
8. Substance/Medication-Induced Anxiety Disorder
9. Anxiety Disorder Due to Another Medical Condition

Source: https://www.slideshare.net/Lucia_Merino/anxiety-disorders-dsm5-41189388

ANXIETY NOS (NOT OTHERWISE SPECIFIED)

- In real life, patients usually just have “anxiety” that doesn’t fit neatly into any of these specific categories.
- Many patients will have features of many different anxiety disorders, especially when something is wrong with their lives.
- Anxiety disorders are highly comorbid with MDD, substance use disorders, and other anxiety disorders.
- Story of my patient…

AGE OF ONSET

- Separation Anxiety: child diagnosis
- Selective Mutism: child diagnosis

Other DSM anxiety disorders seem to be arranged by age of onset, which is interesting.

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.

WHAT ABOUT **PTSD** AND **OCD**?

- Used to be called anxiety disorders and share many features with anxiety disorders, but moved to different sections of the new DSM because of some of their other features.

- We will touch on these each separately, but very briefly:

  - **PTSD**: Something very bad and life-threatening happens to patient or is witnessed by patient and results in re-experiencing (nightmares/flashbacks), hyper-arrousal, avoidance of triggers, and cognitive/ emotional blunting.

  - **OCD**: Patient has recurrent ego-dystonic intrusive thoughts AND/OR compulsive thoughts or behaviors meant to reduce intensive thoughts.

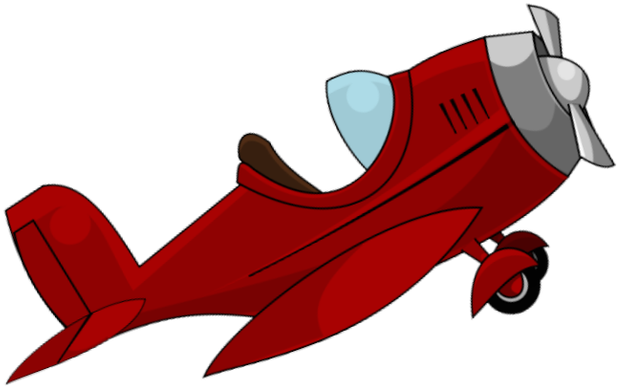
THE CASE OF WILBUR

Wilbur is a 38 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."

THE CASE OF WILBUR

- What is the **diagnosis**?
- How would you **treat** this individual?

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.

BONUS POINT!

WHAT SPECIES OF TARANTULA WAS ON THE LAST SLIDE?

MEXICAN RED KNEE TARANTULA

(MY 11 YEAR OLD SON WANTED TO MAKE SURE THAT YOU KNEW THAT)

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 of 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.

THE CASE OF BRITTANY

- What is the **diagnosis**?
- How would you initially **treat** this individual?

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%)

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.

THE CASE OF SARAH

What do you think?

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 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 (Klonipin)

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)

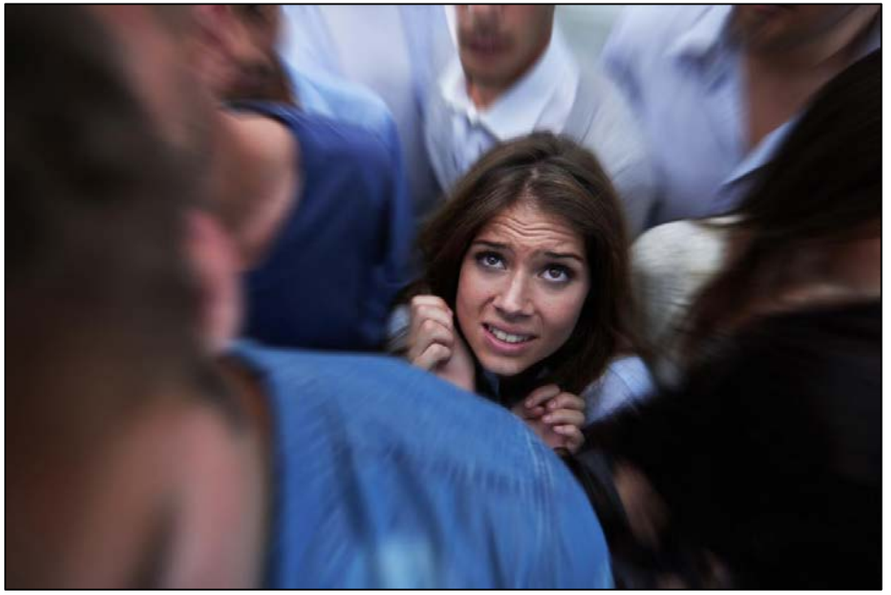
PANIC DISORDER

Non-Pharmacological treatment

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

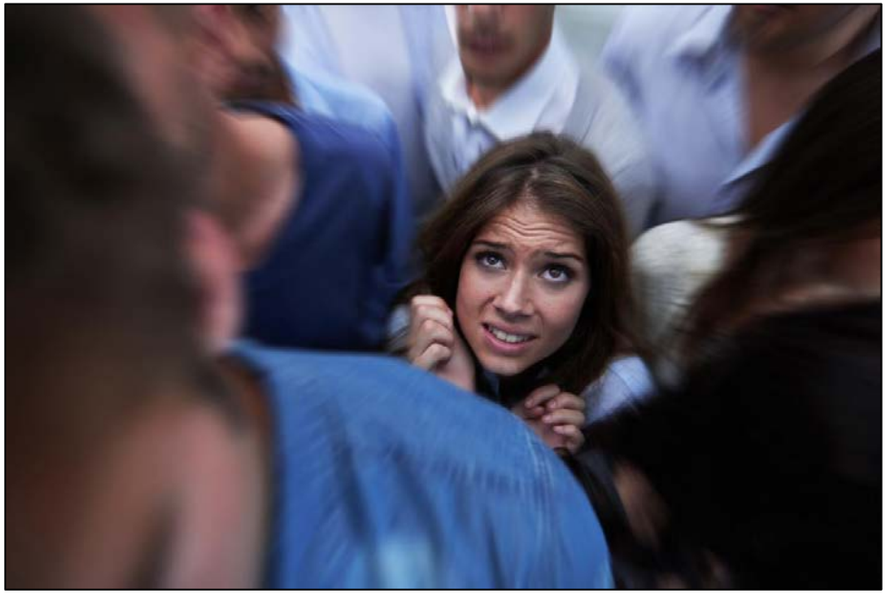
THE CASE OF WINIFRED

25 year old woman who lives in Salt Lake City and works as a paralegal for a law firm about 3 miles from her apartment. She has recently noticed that she dreads taking Traks to work everyday and has instead started to walk. However, she notices that even when walking, if the sidewalk gets too busy she nearly has a panic attack and is afraid that she will not be able to get away or get help in case she starts to look or act "crazy." She has started calling in sick from work and now will get anxious just leaving her apartment. Her sister had to nearly drag her to your office for an evaluation.



THE CASE OF WINIFRED

What do you think?



AGORAPHOBIA

- Fear of at least two of the following:
    - Using public transportation
    - Being in open spaces
    - Being in enclosed places
    - Standing in line or being in a crowd
    - Being outside of home alone
- Patient fears having a panic attack, falling, losing control of bladder function, or some other embarrassing or debilitation symptoms and not being able to get out or get help.
- The agoraphobic situation almost always provokes fear or panic.
- Lasts 6 months or more.
- Fear out of proportion to actual risk (think about someone who really does have fecal incontinence, for example).

AGORAPHOBIA – INTERESTING TIDBITS

- Used to be a subtype of Panic Disorder, and very frequently a patient will have panic attacks first and then develop agoraphobia.
- 1.7 % 12 month prevalence.
- Much more rare in people over 65.
- 2/3 of cases onset before 35, but there is a significant peak after 40.
- Mean age of onset is 17.
    - If proceeded by panic disorder, age of onset is 25-30.
- F>M 2:1

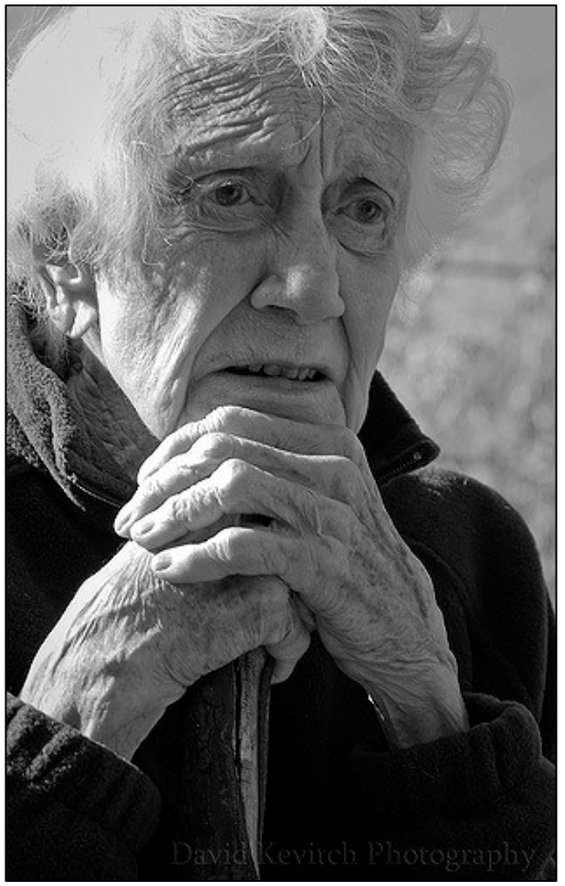
AGORAPHOBIA TREATMENT

Similar to Panic Disorder, as far as I can tell.

Has not been a clinical entity for very long and therefore not a lot of separate dedicated research into this problem specifically.

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…



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!

SEXUAL SIDE EFFECTS

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

1. Mirtazapine (Remeron)

2. Gabapenin 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.)

Benzos: A Short History

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 (Klonipin)	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.