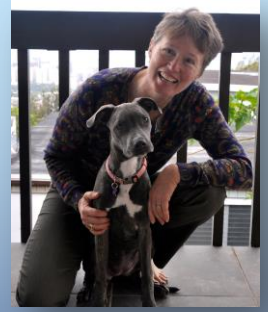


Antidepressants & Antipsychotics



"For years now, we've been led to believe that if we're falling behind in the joy department, we need only take a pill to feel calm and content. Yet, as many people are aware, antidepressants have been linked to significant side effects, including decreased sexual desire, weight gain, even an increased risk of suicide. Adding insult to injury, the drugs may not work as well as advertised; a 2008 study found that some can be no more effective than sugar pills. And according to a report in The New England Journal of Medicine, many negative antidepressant study results have never been published. All in all, the prescription route to happiness may be less safe or effective than even doctors realize."

Dr. Mehmet Oz, on [Oprah](#), talking about antidepressants.

Of the top 200 drugs, by \$'s, for 2011, about 8% are antidepressants or antipsychotics.

- Abilify
- Seroquel
- Zyprexa
- Geodon
- Seroquel XR
- Venlafaxine
- Pristiq
- Risperdal Consta
- Lexapro
- Invega
- Invega Sustenna
- Effexor XR
- Bupropion
- Cymbalta

15% By total prescriptions

- Lexapro
- Trazodone
- Cymbalta
- Sertraline x2
- Seroquel
- Fluoxetine x2
- Citalopram x2
- Venlafaxine
- Lyrica
- Abilify
- Paroxetine
- Risperidone

<http://www.pharmacytimes.com/publications/issue/2012/July2012/Top-200-Drugs-of-2011>

These medications carry serious risks. All of the antidepressants increase the risk of suicide. All of the antipsychotics increase the risk of death in patients with dementia. They all have discontinuation syndromes as well.

Background on Antidepressants

Before the 1950's, opioids were used since they often cause euphoria. **Buprenorphine (Buprenex)** is still used, off label.

Likewise, amphetamines can cause euphoria, but are just as likely to cause anxiety, psychosis, insomnia, delirium, sexual dysfunction and withdrawal if used routinely. Before the 1960's, though, amphetamines were used as antidepressants.

In 1951 the Tricyclic Antidepressants (TCA's) were developed from chlorpromazine, which itself was first synthesized by Rhone-Poulenc in 1950 based on phenothiazines from the German dye industry that had been found in the 1800's to have strong sedating and antipsychotic properties. Imipramine was the 1st TCA, discovered accidentally as researchers looked for improved antipsychotics.

Also in the 1950's, Iproniazid, a drug 1st discovered as part of a doctoral thesis in 1912, was found to have monoamine oxidase blocking activity.

By 1957, Iproniazid was recognized as an antidepressant (and an antiTB drug!).

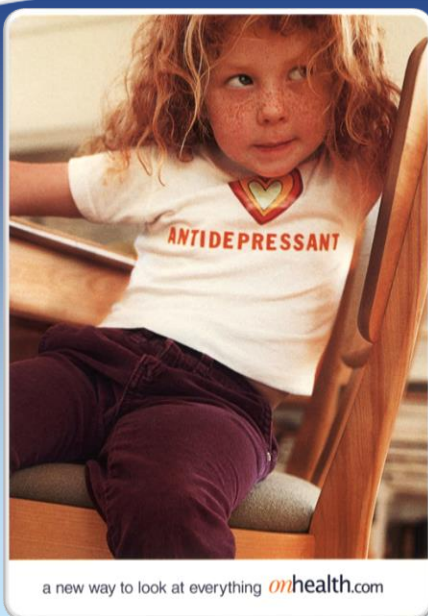
In the 1970's, several companies tinkered with the chemistry of antihistamines to arrive at the top 5 SSRIs separately, but almost simultaneously. FDA approval took many years, so Fluoxetine was approved in 1987, Sertraline in 1991, Paroxetine in 1997, Citalopram in 1998, and Escitalopram in 2002. One side effect of the SSRIs is delayed ejaculation, so they are now used to treat PREMATURE ejaculation....

In the 1980's, Trazodone and Bupropion came on the market. In the 1990's Bupropion began to be used in smoking cessation programs, separate from its use as an antidepressant.

The 1990's also saw the approval of Venlafaxine in 1993 and Mirtazapine in 1996. Mirtazapine is notable for being an excellent antiemetic and causing less sexual dysfunction than other antidepressants.

Duloxetine was approved in 2004 and is now used for fibromyalgia and neuropathic pain as well as depression. In 2012, it acquired a new indication for chronic musculoskeletal pain related to osteoarthritis or lower back pain.

Vilazodone (Viibryd) is a SSRI and 5-HT_{1a} agonist approved in 2011. It causes less sexual dysfunction and less weight gain than most antidepressants, but does cause insomnia, vomiting and diarrhea.



SSRI Discontinuation Syndrome: FINISH

F = Flu-like symptoms

I = Insomnia

N = Nausea

I = Imbalance

S= Sensory disturbances

H = Hyper arousal

Not much of an issue with fluoxetine (Prozac) due to its very long half-life & active metabolites.

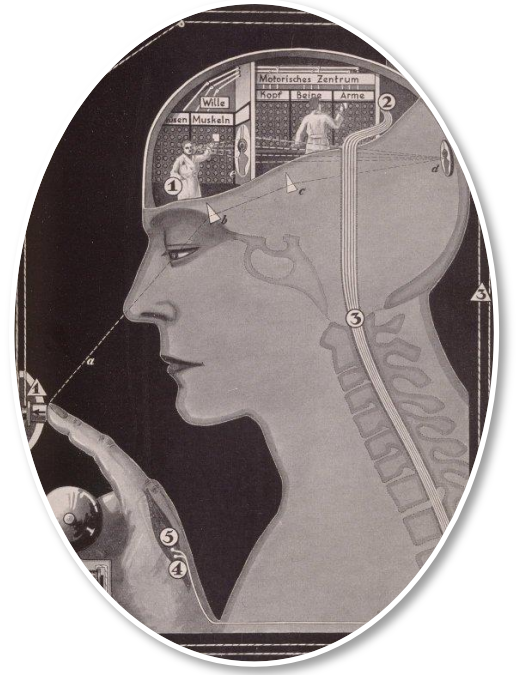
Antidepressants

Antidepressants may unmask previously undiagnosed bipolar disorder.

Before giving any antidepressant, screen for bipolar risk:

- Get a detailed psychiatric history of the family
 - Suicide
 - Bipolar disorder
 - Major depressive disorder
 - Other psychiatric illness

To read about each of the antidepressants covered in lecture, Click the link.



SSRIs

[Sertraline](#) (Zoloft)

[Paroxetine](#) (Paxil)

[Fluoxetine](#) (Prozac)

[Citalopram](#) (Celexa)

[Escitalopram](#) (Lexapro)

MAOI

[Selegiline](#) (Eldepryl, [Emsam](#))

TeCA

[Mirtazapine](#) (Remeron)

TCA's

[Imipramine](#) (Tofranil)

[Amitriptyline](#) (Elavil)

[Nortriptyline](#) (Pamelor)

[Doxepin](#) (Sinequan, [Zonalon](#), Silenor)

http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022036lbl.pdf

Other

[Trazodone](#) (Desyrel, Oleptro)

[Bupropion](#) (Alplenzin, Wellbutrin, [Zyban](#))

NEW in 2011!!! (1st new one in years)

Vilazodone ([Viibryd](#))

Antipsychotics

Like the antidepressants, the antipsychotics typically have a latency between initiation of therapy and onset of beneficial effects.

The 1st generation, or "Typical," antipsychotics are also known as major tranquilizers. Because of the tendency of these drugs to cause so much sedation, along with a plethora of other effects, including EPS, the 2nd generation, or "Atypical," antipsychotics were developed. In actuality, the "atypical" nature of the 2nd generation drugs was that they had less affinity for the D2 receptors in the brain and more for various adrenergic, histaminic, cholinergic and serotonergic receptors.

Side effects common to all antipsychotics include:

- Increased risk of death in elderly patients with dementia
- Increased risk of EPS in neonates born to mothers taking antipsychotics during the 3rd trimester of pregnancy
- Sedation and/or insomnia
- Dizziness
- Agitation and/or EPS
- Hyperglycemia
- Hyperlipidemia
- Hyperprolactinemia (more in 1st generations) leading to sexual dysfunction
- Increased appetite and weight gain
- Dry mouth, constipation, GI upset
- Hypotension, hypertension and tachycardia
- Pain – usually an altered response to pain
- Vision abnormalities or changes



New warning for antipsychotics

In February 2011, the FDA required changes to the label warnings for all antipsychotics. The pregnancy section was updated to contain information about the potential risk for extrapyramidal signs (EPS) and withdrawal symptoms in newborns whose mothers were treated with an antipsychotic during the 3rd trimester of pregnancy.

Symptoms in these babies may include:

- Agitation
- Altered muscle tone
- Tremor
- Sleepiness,
- Severe difficulty breathing
- Difficulty feeding

The FDA announcement, which contains a list of medications affected, may be viewed by clicking [HERE](#):

(continued)

[Chlorpromazine](#) (Thorazine) is considered the 1st antipsychotic, getting FDA approval in 1957. [Thiothixene](#) (Navane) and [Haloperidol](#) (Haldol) were approved a decade later in 1967. It wasn't until 1989 that [Clozapine](#) (Clozaril) came on the market, followed by [Risperidone](#) (Risperdal) in 1993, Olanzapine ([Zyprexa](#)) in 1996 and Quetiapine ([Seroquel](#)) in 1997.

Chlorpromazine is derived from phenothiazine dyes. It is strongly sedating and antiemetic. We also cover Promethazine ([Phenergan](#)) and Prochlorperazine ([Compazine](#)), both are phenothiazines used as anxiolytic antiemetics.

In fact, several antipsychotics are excellent antiemetics. The butyrophenones, including [haloperidol](#), have been used for decades to prevent post-op nausea and vomiting. Olanzapine ([Zyprexa](#)) and the antidepressant Mirtazapine ([Remeron](#)) are as good as the setrons (e.g., Ondansetron or [Zofran](#)) at preventing emesis due most causes, except motion sickness and pregnancy.

Because of the effects on appetite, weight gain, blood lipids and blood glucose, all patients on antipsychotics should be periodically monitored and a treatment plan developed that tracks these parameters.

Antipsychotics may also cause an inability

to properly regulate body temperature, usually this is related to an inability to sweat (an anticholinergic effect). Patients should be instructed that they may become easily overheated.

Clozapine ([Clozaril](#)) is considered to be the 1st of the 2nd generation, or atypical, antipsychotics. It has a number of things that set it apart. It causes:

- Almost NO EPS, none.
- Severe blood dyscrasias which require ongoing monitoring
- Severe hypotension and damage to the myocardium
- Seizures
- It also LOWERS the risk of suicide and is used to "prevent" suicide in at risk patients.

Because clozapine is associated with severe blood dyscrasias, particularly agranulocytosis and more specifically a loss of neutrophils, all the antipsychotics come with a warning about the risk.

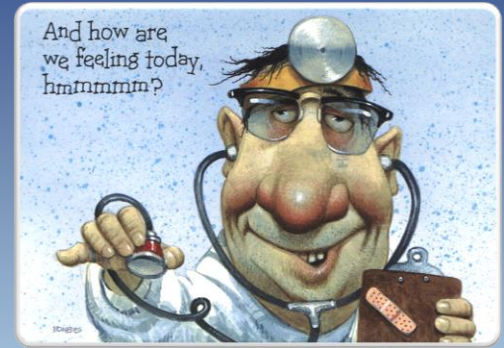
The other atypicals we cover include Olanzapine, Quetiapine and Risperidone.

Quetiapine ([Seroquel](#)) is rarely associated with cataracts, an unusual side effect for the antipsychotics, but which requires monitoring.

All the antipsychotics now have a warning regarding fetotoxicity.

Drug-induced EPS: Extrapyramidal Symptoms

Many antipsychotics block D2 receptors located in a part of the brain responsible for modulating voluntary movement called the substantia nigra. This area is outside (extra) the so-called pyramidal tracts that run from the motor cortex to the spinal cord. The pyramidal tracts are concerned with skilled motor movements. The extrapyramidal motor pathways provide muscle tone, posture, and fine motor integration. The pyramidal tracts are voluntary; the extrapyramidal tracts are largely involuntary. Parkinson's disease occurs when the substantia nigra neurons die, EPS occurs when the D2 receptors are blocked. Some EPS is reversible, some treatable, but tardive dyskinesia is a permanent form of drug-induced EPS.



Treating drug-induced EPS

Benzotropine (Cogentin)
Diphenhydramine (Benadryl)
Amantadine (Symmetrel)
Trihexyphenidyl (Artane)

Homework and Exercises

1. Read the "START HERE" announcement in Laulima for updates and instructions.
2. Read about Antidepressants and Antipsychotic drugs in Chapter 23 & 24, **Pharmacology of Mood Disorders & Pharmacology of Psychoses**. Adams & Urban, PHARMACOLOGY Connections to Nursing Practice.
3. Review the Powerpoints and listen to the audio from the face-to-face lecture. You may opt to watch the appropriate videos for this lecture. Review any handouts available for this lecture in the Course Index.
4. Complete the SLO practice set for Antidepressants and Antipsychotics in Tasks, Tests and Surveys.
5. Use "Chat," "Discussions and Private Messages" or the lecture "Forum" to ask questions and find answers or to seek assistance.
6. Complete the online quiz in Laulima, Tasks, Tests and Surveys.

If you have any questions, email me at abeale@hawaii.edu