MAOIs and Tricyclics...

have side effects, drug interactions, toxicity, delay in onset of therapeutic effects, and aren’t efficacious in all patients, so “second generation” drugs were developed.

Selective Serotonin Reuptake Inhibitors (SSRIs)

fluoxetine (Prozac®)
sertraline (Zoloft®)
paroxetine (Paxil®)
fluvoxamine (Luvox®)
nefazodone (Serzone®)
citalopram (Celexa®)

SSRIs

Are not efficacious in all depressed individuals
Do not have a more rapid onset of therapeutic actions
Have little effect at muscarinic, histaminergic or α-noradrenergic receptors
Have a different spectrum of side effects

SSRIs

Can produce anxiety, insomnia, sleepiness, nausea, sexual dysfunction, withdrawal syndrome
Use with MAOIs can cause serious and potentially fatal reactions (serotonin syndrome)

SSRIs

• major depressive episodes
• obsessive-compulsive disorders
• social anxiety disorder (paroxetine)
• posttraumatic stress disorder (sertraline)
• useful in treating: panic disorders, eating disorders, personality disorders, impulse control disorders, and PMS.

Other Second Generation Antipsychotics

Trazodone (Desyrel®)
Bupropion (Wellbutrin®, Zyban®)
Alprazolam (Xanax®)
Venlafaxan (Effexor®)
The most effective treatment for depression is electroconvulsive therapy (ECT).

- Developed in early 1900’s for treating schizophrenics
- Didn’t help schizophrenics - but did help 80-90% for major depression
- Don’t know why it works - down-regulates β-adrenergic receptors
- Greatest drawback: long-lasting memory deficits

ECT

- Applied to one hemisphere (usually right)
- Ultra-short-acting anesthetic-methohexital
- Muscle relaxant - succinylcholine
- Antimuscarinic - atropine

Bipolar Disorder: suffer mania and depression

Manic episode
- Racing thoughts
- Hyperactivity
- Easily distracted
- Grandiose sense of self
- May hear voices
- Highly energetic

Bipolar Disorder

- 20% of those with major endogenous depression
- Manic phase
  - little sleep
  - talk rapidly and non-stop
  - mania without depression extremely rare
- can precipitate severe mania if given classic antidepressants, so give anti-manic drugs

Bipolar Disorder

- Frequently involves psychotic symptoms.
- Delusions and hallucinations are common.
- These symptoms can occur in 20 to 50% of patients with bipolar disorder.
- The acute phase of bipolar disorder is often indistinguishable from schizophrenia, primarily due to psychotic symptoms.
Lithium

- effective for 60-80% of manic-depressives
- requires several weeks for full effects
- doesn’t affect mood of normals
- manic-depressives are even more likely to commit suicide than endogenous depressives

Lithium has a very low therapeutic index.

- Therefore, it is prescribed by plasma levels.
  - Level of 0.8-1.2 mEq/L
    - therapeutic
  - Level of 1.5-2 mEq/L
    - weakness, diarrhea, ataxia, nausea, vomiting, drowsiness
  - Level of 2-3 mEq/L
    - dizziness, ataxia, blurred vision, tinnitus, vertigo, confusion, blurred speech, myoclonic twitching, hyperreflexia, hypertension, dysarthria
  - Level >3 mEq/L
    - seizures, arrhythmias, hypotension, stupor, spasticity, coma, death

Treatment of Lithium Toxicity

- No good antidote
- Stop the medication
- Increase excretion with mannitol, urea, or aminophylline
- Hemodialysis in levels >3.0 mEq/L
- Avoid sodium depletion (Na⁺ competes for reabsorption in kidney)

Mechanism of Lithium

- Therapeutic mechanism not known
- Lithium blocks the formation of inositol from inositol phosphate
- Lithium attenuates receptor-coupled G-protein function

Lithium

Lithium blocks the effect of ADH on the kidney: nephrogenic diabetes insipidus (polyuria/polydipsia)

Lithium blocks the effect of TSH on the thyroid: hypothyroidism* (one-third need T4)

Anticonvulsants are playing a bigger role in bipolar disease

- Divalproex Sodium (Depakote®)
- Carbamazepine (Tegretol®)
- Gabapentin (Neurontin®)
- Lamotrigine (Lamictal®)
- Topiramate (Topamax®)
**Adjunctive Pharmacotherapy**

- Benzodiazepines
  - sleep and sedation in mania or hypomania
  - insomnia in depression
- Antipsychotics
  - adjunctive treatment for mania with psychosis or psychotic depression
  - olanzapine (Zyprexa) has new FDA approval for mania

**Combination therapy is standard for bipolar disorder**

- Atypical antipsychotics are increasingly used as adjunctive therapy
- Newer anticonvulsants are emerging as efficacious agents for mood stabilization
- Mood stabilizer plus an antipsychotic is more effective than mood stabilizer alone
- Antidepressants may worsen disease course

---

Which of the following is NOT caused by “atypical” antipsychotics?

A. Weight gain  
B. Tardive dyskinesias  
C. Diminution of negative symptoms  
D. Diminution of positive symptoms  
E. Hyperprolactinemia

Which of the following is NOT recommended for the treatment of bipolar disorder?

A. Lithium  
B. Amitriptyline  
C. Carbamazepine  
D. Lamotrigine  
E. Olanzapine

- A. Weight gain
- B. Tardive dyskinesias
- C. Diminution of negative symptoms
- D. Diminution of positive symptoms
- E. Hyperprolactinemia

- A. Lithium
- B. Amitriptyline
- C. Carbamazepine
- D. Lamotrigine
- E. Olanzapine