ANTIDEPRESSANTS: “2ND Generation” Drugs (p. 1)

1. **Introduction**

These drugs are neither the traditional TCAs (tricyclic antidepressants), nor are they SSRIs or “dual-action” selective reuptake inhibitors.

These drugs show **comparable effectiveness to TCAs, MAOIs**

These drugs were developed in the **1970s and 1980s** to improve on the TCAs.

Like the SSRIs that were developed later, show **fewer, less problematic SEs**: less antiACh effects, less cardiovascular toxicity, less toxic in OD. Thus, are good for elderly pts. or pts. with cardiovascular risk.

Most have almost **no risk of orthostatic hypotension**

Have different chemical structures vs. the TCAs, are heterocyclics (4 & 5 rings), are structurally similar to the BZDs, are structurally similar to the **neuroleptics**

Some of these drugs **decrease NE reuptake** (NE transporter protein blockers): e.g. maprotiline (Ludiomil), nomifensine (Merital), amoxapine (Asendin)

Some of these drugs also **block post-synaptic RS for DA**…and thus are useful in treating a pt. with both depression & psychosis. E.g. Asendin
ANTIDEPRESSANTS: 2\textsuperscript{nd} Generation Drugs (p.2)

2. **maprotiline/Ludiomil**
   - is a SNRI
   - as efficacious as imipramine/Tofranil
   - has a long ½ life
   - can cause seizures (although rare)
   - **does not impair cognitive functions**
   - usually not a first choice drug

3. **amoxapine/Asendin**
   - primarily a SNRI
   - as efficacious as imipramine/Tofranil in treating depression
   - slightly more efficacious than imipramine in treating anxiety & agitation
   - also blocks post-synaptic DA RSs…similar to neuroleptics/antipsychotics
   - can have Parkinson-like SEs (EPSEs)
   - good for treating pts. with both depression and psychotic Sxs
   - very toxic in OD (can cause seizures --- death)
   - has the highest antiACh effects of all the 2\textsuperscript{nd} generation antidepressants
   - orthostatic hypotension, sedation

4. **trazodone/Desyrel**
   - not an SNRI, not an SSRI
   - does block the 5HT2 RSs, and --- down regulation of postsynaptic 5HT RSs
   - relatively long onset of Sx relief, 2 to 5 weeks
   - SEs: drowsiness, sedation (20% of pts.)
   - priapism (rare, but can have serious consequences)
   - less antiACh effects
   - small/moderate impairment of cognitive function
   - less toxic in OD

5. **bupropion/Wellbutrin**
   - blocks the reuptake of DA & of 5HT (no effects on NE), **SDRI**
   - is a weak DA & 5HT agonist
   - may also directly stimulate the postsynaptic DA RS
ANTIDEPRESSANTS: 2\textsuperscript{nd} Generation Drugs (p.3)

5. bupropion/Wellbutrin (cont.)
   can cause + psychotic Sxs at high doses…why?
   no orthostatic hypotension
   low risk of lethal effects in OD
   note: however, decreases the threshold for seizures
   no impotency SEs, in fact may even facilitate sexual behavior
   good for tx of anxiety
   SEs: anxiety, insomnia, even PAs in susceptible Ss
   dizziness, nausea
   headache
   also good for tx. of bipolar mood disorder
   is also used to block (formerly abused) drug cravings (e.g. in former smoker)
   is called “Zyban” when used for that purpose (marketed separately from “Wellbutrin”)
   why would this drug be helpful in this context?...

(6. alprazolam/Xanax)
   is a GABA agonist (no effects on NE, 5HT, or DA)
   high abuse potential
   but does have some antidepressant effects…
   usually used as an anxiolytic, but might be useful as an augmenting drug in a pt. with both depression and anxiety