MOOD STABILIZERS: Anticonvulsants (p.1)

1. **Introduction**
   these medications are more recently being used to tx bipolar disorder
   about 40% of bipolar pts. are not helped by Li or cannot tolerate the
   Li SEs…thus, need an alternative tx
   Li is **not helpful in tx of rapid cyclers** (4+ mood alternations cycles
   per year)

   these meds are also helpful in tx. of rage/explosive behavior
   such behavior may be a variant of the manic state in bipolar pt.
   (rather than a separate personality diagnosis)

2. **carbamazepine/Tegretol**
   this drug particularly is **useful for rapid cyclers**

   carb/Tegretol is **often combined with Li**
   and combination produces better results than either drug used alone

   there is a known **therapeutic window** for carb/Teg, which is the same
   as that used to depress seizures (5 – 10 micrograms/ml blood)

   **pharmacokinetics:**
   **mechanism of action unknown**
   75% protein bound
   is a **liver enzyme inducer** (CYP-3A4 especially)

   **side effects** (milder):
   gastritis, nausea  sedation  ataxia, tremor
   visual disturbances  skin rashes, pimples (incl. allergic reaction)
   impaired cognitive abilities
   dizziness, vertigo  slurred speech  depressed T3/T4 levels

   **more serious SEs:** skin blisters, leucopenia, thrombocytopenia,
   aplastic anemia
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2. **carbamazepine/Tegretol** (cont.)
   - can cause birth defects, so should avoid in pregnancy
     - NTDs (e.g. spina bifida/anencephalia in 1% of fetuses)
     - increased folic acid may help
   
   frequent **drug interactions**…why?
   - see **tolerance** effects when using this drug…why?

   (also used to **treat neuralgic pain**, e.g. trigeminal neuralgia)

3. **valproic acid or valproate/Depakene, Depakote**
   - now the 1st choice for tx of mania (even over Li)
     - actually less effective than Li in treating mania, but does also help
     - decrease depression more effectively than Li
     - effective in 71% of patients

   **mechanism of action:**
   - a **GABA agonist** (enhances synthesis/release of GABA)
   - a **glutamate antagonist** (reduces NMDA-glutamate activity)

   is esp. good for tx. of **acute mania** (alone or w/ antipsychotic meds)
   - for schizo-affective disorder, for **rapid cyclers**, & for very
   - depressed bipolar Ss…does it all!

   this drug also has a **therapeutic window** (50 – 100 micrograms/ml)

   can give a “**loading dose**” (IV “bolus”) vs. regular dosing which will take
   - 3 – 10 days to control acute mania
   - or can add a BZD, sedating antipsychotic (e.g. haloperidol/Haldol)

   **side-effects** (milder):
   - gastritis, nausea
   - sedation, lethargy
   - hand tremor
   - wt. gain (esp.females)
   - alopecia
   - ataxia
   - skin rash
   - changes in liver function
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3. valproate/Depakote (cont.)

serious side effect:  
polycystic ovaries & increased levels of androgens/testosterone  
thrombocytopenia  
potential liver damage (esp. in child)

is a liver enzyme inhibitor (of P450 enzymes)

50% plasma protein bound

(for treatment of bipolar disorder and mania, Li and above two mood stabilizers are the most effective)

3. gabapentine/Neurontin
used also to treat bipolar disorder, anxiety disorders, substance dependency, rage/impulsivity/aggression, and pain…a drug for all reasons!

mechanism of action:  
a GABA analogue (GABA agonist)

not plasma protein bound  
not metabolized (excreted unchanged by kidneys)  
few drug interactions  
elimination ½ life = 5 – 7 hours

may be used in combination with Li, and this combination looks very likely to become a good treatment option for mania/bipolar disorder

side-effects:
sleepiness    dizziness    ataxia    nystagmus
double vision    dry mouth    nausea    flatulence
decreased libido
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4. **lamotrigine/Lamictal**
   also for tx of **borderline personality, PTSD, & schizoaffective disorder**

   absorbed from gut readily, little 1\textsuperscript{st} pass effect
   ½ life = 26 hours

   mechanism of action is unclear...**glutamate antagonist**?
   decreases release of glutamate in hippocampus and cortex

   **side-effects:**
   - dizziness
   - tremor
   - sleepiness
   - headache
   - nausea
   - **skin rash**

5. **topiramate/Topamax**
   another anticonvulsant with possible mood-stabilizing effects

   mechanism of action:
   - Na\textsuperscript{+} channel blocker
   - GABA agonist (increases Cl\textsuperscript{-} influx)
   - glutamate antagonist

   good of rapid cyclers

   effective in 62% of cases (mostly within 3 days)

   **side-effects:**
   - wt. loss
   - impaired cognitive function
   - tingling in fingers, toes
   - irritability, anxiety, depression
MOOD STABILIZERS: Anticonvulsants (p.5)

6. **Atypical Antipsychotics:**
   the very newest recommendations are for these drugs also to be used in the tx of bipolar disorder
   APA (Am. J. Psychiatry, April 2003), just published “The Practice Guideline for the Treatment of Patients with Bipolar Disorder (Revision)” (prior update was 1994)*

**clozapine/Clozaril**
seems to be useful in treatment of mania
use is limited by SE agranulocytosis

**olanzapine/Zyprexa**
**risperidone/Risperdal**

* latest guidelines:
  a. **first-line tx for bipolar disorder**: Li, valproate/Depakote, or olanzapine/Zyprexa
  b. both olanzapine/Zyprexa & risperidone/Risperdal are preferable to clozapine/Clozaril because their SEs are more tolerable
  c. when treating **acute mania** combined drug therapy is first choice: Li + an atypical antipsychotic; valproate/Depakote + antipsychotic if mania is milder, may treat with one drug: Li, valproate, or an antipsychotic
  d. when treating **depression** (in a bipolar pt.), use Li (or may use lamotrigine/Lamictal)
     If one drug does not work enough, use Li + lamotrigine, bupropion/Wellbutrin, or paroxetine/Paxil

Psychosocial therapies should only be used when combined with drug therapy; should not be used instead of drug therapy unless the focus of the therapy is to focus on pt.’s ambivalence about taking medication for their bipolar disorder
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7. In addition to using medications, bipolar pts. (and their families) need psychological treatment related to lowered self-esteem
   - fears of recurrence of Sxs
   - stigmatization
   - interpersonal difficulties
   - academic & occupation problems
   - comorbid drug use (esp. alcohol)

8. Possible Alternate Causes/Contributors to “Mania”
   - antidepressants
   - anabolic steroids
   - caffeine
   - antiParkinson drugs (DA agonists)
   - ephedrine
   - “diet aids”
   - CNS stimulants
   - hyperthyroid
cortisone