MOOD STABILIZERS: Anticonvulsants (p.1)

l. **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. **<u>carbamazepine/Tegretol</u>** (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. **<u>valproic acid or valproate/Depakene, Depakote</u>**

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:
polycyctic 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. **<u>lamotrigine/Lamictal</u>**
   also for tx of **borderline personality, PTSD, & schizoaffective disorder**

   absorbed from gut readily, little 1st 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. **<u>topiramate/Topamax</u>**
   another anticonvulsant with possible mood-stabilizing effects

   mechanism of action:
      Na+ channel blocker
      GABA agonist (increases Cl- 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	

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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
caffeine
ephedrine
CNS stimulants
cortisone
anabolic steroids
antiParkinson drugs (DA agonists)
"diet aids"
hyperthyroid