ANTIDEPRESSANTS: MAOIs (p.1)

1. Mono-Amine Oxidase Inhibitors (MAOIs)
   - developed in the 1950s
   - are very effective (as effective as the tri-cyclic antidepressants/TCAs)
   - their use is limited by serious (even fatal) side-effects
     - if taken with other catecholamine agonists
       - major concern is **HBP --- cardiovascular accidents** (“strokes”)

2. Current Uses for MAOIs
   - are very effective
   - can be safer than TCAs (esp. re. cardiac arrhythmias)

   - can work in pts. in whom TCAs/SSRIs have failed to work

   - are esp. useful in pts. with “atypical depression”

   - are esp. useful in pts. with **mixed depression & anxiety**

   - are good for tx of **anorexia, bulimia**

   - are good for tx of **bipolar depression & dysthymia**

   - are not good for tx. for depression in **elderly patients**…why?

   - are good for tx. of **panic attacks** and for **phobias**
3. **MAOI Effects on NS/Body**
   there are actually **two MAO enzymes**:
   - MAOA – found in NE and 5HT axon terminals
   - MAOB – found in DA axox terminals, GI tract, liver

   MAOIs block both enzymes --- beneficial main effects & neg. SEs

4. **Non-Selective & Irreversible MAOIs**
   - non-selective = block both MAOA and B enzymes
   - irreversible = the MAOI enzyme is permanently blocked
     - only when new molecules of MAO (A/B) are synthesized can they again metabolize monoamines (NE, 5HT, DA)

   **issues re. switching from one drug to another**
   - e.g. MAOI to an SSRI or TCA

5. **Particular MAOIs** (non-selective, irreversible)
   - phenelzine (Nardil), tranylcypromine (Parnate), isocarboxazid (Marplan)

6. **Pharmacokinetics:**
   - **Parnate** – ½ life = 2 hours, but is irreversible (is actually active metabolite that actually binds to MAO molecule)
     - as the S keeps taking Parnate, over one week about 70% of the MAO is blocked, slowly reaches a “**steady state**” between blocked MAO molecules and newly formed unblocked molecules of MAO

   if S D/Cs the Parnate, it may take several weeks for the MAO levels to recover to normal/baseline levels
   thus, may need **2 to 3 weeks of washout period** before starting a new (monoamine agonistic) antidepressant

   neg. SEs:
ANTIDEPRESSANTS: MAOIs (p.3)

7. **Reversible & Selective MAOIs**
   - are not available in USA yet...but will be
   - are short acting & highly selective, esp. for MAOA
   - have little effect on MAOBs, and thus eating tyramine-rich foods
   - is not a problem
   - because are short acting, multiple doses are necessary
   - no long-term deactivation of MAOA, no effect on MAOB
   - minimal neg. SEs

   e.g. brofaromine
   - toloxatone
   - pirlindole
   - meclobemide (Aurorix)
   - deprenyl, selegilne (Eldepryl)

8. **Miscellaneous**
   - effects on sleep architecture

   “cheese reaction” & how to by-pass same

   Potentiation of other drugs