

- 1. Ref. 2.c.1. stimulants--the dual nature of some stimulants may need to be addressed; i.e., after a period of caffeine abstinence, caffeine may sedate rather than arouse in one who uses caffeine habitually. L-phenylalanine should be considered in this group.
- 2. Ref. 2.c.2. depressants-consider L-tryptophan, antihistamines, tri-cyclic antidepressants.
- 3. Ref. 2. b. interference is misspelled.
- 4. ref. 2. c. 2. Do you really want to include benzodiazepines under depressants? A consistent theme through many sections of the document is the difference between enhancing a particular behavioral state beyond its normal levels, and countering the degraders of a particular behavioral state. To that extent, one could conceptualize the benzodiazepines as counters to the "sleep-degrader" of anxiety. Classic depressants could be seen as enhancing or producing the state of sleep even in the normal organism; they would, of course, be useful in countering sleep degradation factors, but could also be used in the "non-degraded" organism, to produce prophylactic sleep for example. If you wish to address this distinction, you may then wish to include the various applications of prophylactic sleep, non-benzodiazepine anxiolytics, and potential sleep degradation factors with potential pharmacologic counters.
- 5. Ref. 2. d., Problems: Note that the compounds you are discussing are those which have a very high potential for misuse. Note the set of problems which becomes apparent following prolonged use, including ineffectiveness/tolerance.
- 6. Ref. 2. a. Relative to the other "pills" in the document, one could argue that we know the most about brain mechanisms involved in sleep/arousal.
- 7. Consider the possible uses of depressant and stimulants used in coordination with each other. Will you address the problem of sleep inertia and pharmacologic counters? Throtropin-releasing hormone is a possible candidate for these areas of concern.