Treatment of Depression in Late Life

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Pre-Lecture Exam Question 1

1. **Which of the following statements is true?**

A. The superiority of the SSRI's in the treatment of late life depression is well-established.

B. The superiority of TCA's in the treatment of late life depression is well-established.

C. Start high, go fast is the standard for antidepressant treatment in late life depression.

D. Infrequent monitoring of treatment response and side effects is recommended.

E. For a specific patient, the choice of antidepressant depends in part on individualized preferences, side effect profile, and the presence of concurrently prescribed medications.

Question 2

2. Which of the following factors does not affect antidepressant dosage decisions in late life depression patients?

A. Reduced GI, renal, hepatic function in older patients

B. Lower albumin levels in older patients

C. Increased muscle to fat ratio in older patients

D. Concurrently prescribed medications

E. Increased receptor-site sensitivity for some neurotransmitters and drugs in older patients

Question 3

3. Combinations of psychiatric medications are sometimes used to treat late life depression for which of the following reasons?

A. Comorbid psychiatric disorders may be present, requiring the additional medication.

B. One medication may offset adverse effects of a concurrently prescribed medication.

C. Psychotic depression is more effectively treated with the addition of an antipsychotic medication to an antidepressant.

D. An augmenter such as lithium carbonate may boost the effectiveness of an antidepressant in some partially-responding patients.

Question 4

4. Which of the following is true of the use of anxiolytics in late life depression?

A. Long-acting benzodiazepines are preferred.

B. Benzodiazepines never worsen depressive mood or other symptoms.

C. Tapering and discontinuation of benzodiazepines can be done abruptly.

D. The minimum effective dose should be used when benzodiazepines are prescribed to elderly patients.

E. All of the above.

Question 5

5. Which of the following is not true of ECT in late life depression?

A. It is often safe, effective, and well-tolerated.

B. It can reduce depression-associated cognitive impairment in some patients.

C. Recent MI or stroke, severe hypertension, or intracerebral mass are absolute contraindications for administering ECT.

D. ECT's effects on memory can be intolerable for some demented, depressed patients.

E. All of the above.

Choosing Antidepressants

- Clinical trials indicate generally similar efficacy among antidepressants
- Controversy remains whether heterocyclics are better for melancholia
- Choose drugs according to side effect profile
  - e.g., sedating drug for agitated depression
  - Consider possible drug-drug interactions, P450 isoenzymes

Strategies for Drug Treatment

- Start low and go slow
- Choose medications according to side effect profiles
- Monitor side effects carefully
- Avoid non-essential polypharmacy
- Adjust one medication at a time

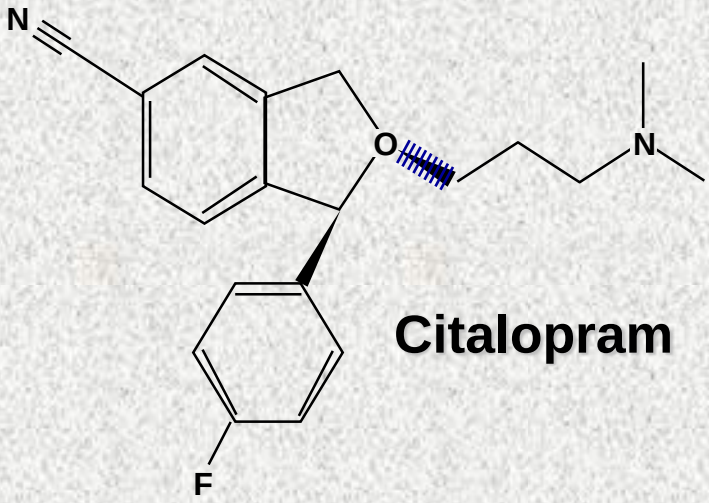
Marketed Antidepressants Used for Geriatric Depression

- **Tricyclics**
  - Amitriptyline (Elavil)
  - Imipramine (Tofranil)
  - Doxepin (Sinequan)
  - Desipramine (Norpramin)
  - Nortriptyline (Pamelor)
- **MAO Inhibitors**
  - Phenelzine (Nardil)
  - Tranylcypromine (Parnate)
- **SSRIs**
  - Fluoxetine (Prozac)
  - Sertraline (Zoloft)
  - Paroxetine (Paxil)
  - Fluvoxamine (Luvox)
  - Citalopram (Celexa)
- **Others**
  - Trazodone (Desyrel)
  - Bupropion (Wellbutrin)
  - Venlafaxine (Effexor)
  - Nefazodone (Serzone)
  - Mirtazapine (Remeron)

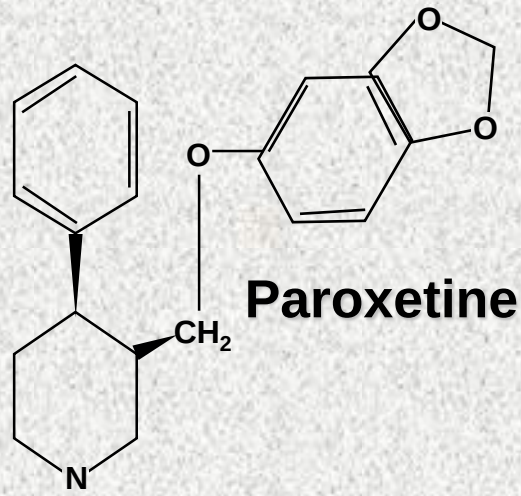
Age-Related Changes Affecting Drug Dosage

- Reduced GI, renal and liver function
- Lower albumin levels
- Increased fat/muscle ratio
- Increased receptor-site sensitivity for many drugs (decreased β-adrenergic)
- Polypharmacy leading to drug-drug and drug-disease interactions

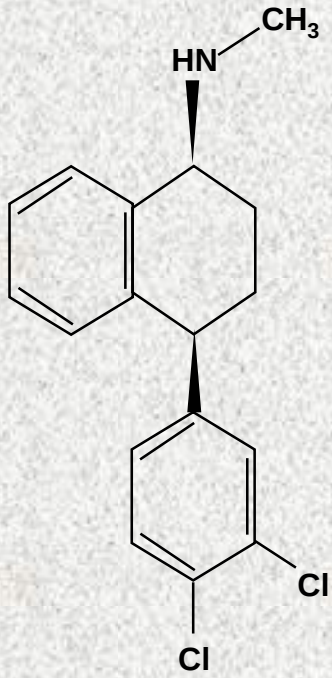
SSRI Structures



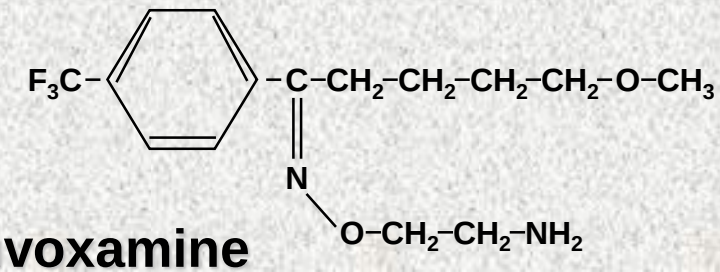
Citalopram



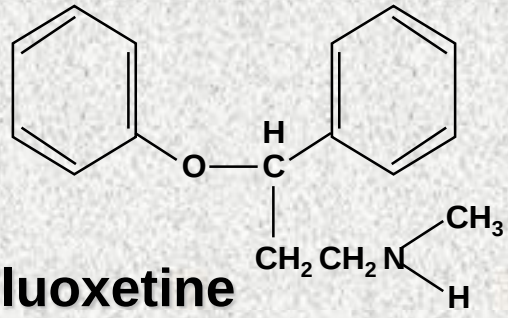
Paroxetine



Sertraline



Fluvoxamine



Fluoxetine

Psychotherapeutic Drug Interactions Are Important in Older Patients

- Elderly patients usually take more than one medication because of multiple illnesses
- Combination therapy is often used:
  - To treat comorbid psychiatric disorders
  - To mitigate adverse reactions associated with some medications
  - To augment efficacy (eg, lithium augmentation of TCA)

In general, the potential for drug-drug interactions in older patients is very high

Drug Interactions Can Take Place on Five Levels

- Gastrointestinal absorption
- Protein binding
- Hepatic metabolism
- Renal excretion
- Receptor site competition

CYP2D6 Inhibition by SSRIs

(Sproule et al, 1997)

Compound	K_i* (μM)
Citalopram	5.1
Paroxetine	0.15
Fluoxetine	0.60
Norfluoxetine	0.43
Sertraline	0.70

* Lower K_i indicates more potent inhibition of CYP2D6.

Polypharmacy and Drug Interactions (1 of 2)

- Hepatic cytochrome P-450 isoenzymes metabolize all antidepressants (except lithium), especially 2D6, 1A2, 2C, and 3A/4
- Age-related physiological changes in enzyme efficiency may increase variability in elderly
- Newer agents, especially SSRIs and nefazodone are potent inhibitors -- when combined with TCA, TCA blood levels elevated