Major Endogenous Depression

Core Symptoms:

• Feeling of misery, apathy and pessimism.
• Withdrawn.
• Low self-esteem, feelings of guilt, inadequacy and ugliness.
• Loss of interest in pleasurable activities.
• Indecisiveness, loss of motivation.
• Retardation of thought and action. Sleep disturbance and significant weight change (without dieting or changes in appetite).
• Psychomotor agitation or retardation.
NEUROTROPHIC HYPOTHESIS

• There is evidence that nerve growth factors e.g. brain-derived neurotrophic factor (BDNF) are important in nerve function.
• The evidence suggest that depression is associated with loss of neurotrophic support.
• BDNF probably affects neuronal survival and growth by activating tyrosine kinase receptor B in neurons and ganglia.
• The hypothesis states that antidepressant therapies increases neurogenesis and synaptic connections in cortical areas e.g. hippocampus.
Tricyclic Antidepressants (TCAs)

3° Amines: Imipramine, Amitriptyline

2° Amines: Desipramine, Nortriptyline

Selectivity

2° Amines -- NE $\geq$ 5-HT

3° Amines -- 5-HT $\geq$ NE
MAOIs

Pharmacokinetics:
- PO – good
- Hepatic metabolism
- Excretion: kidneys
- Irreversible inhibitors - phenelzine, isocarboxazid, selegiline
- Reversible inhibitors – tranylcypromine, moclobemide (reversible inhibitor of MAO type A ie RIMA)
SSRIs

- Fluoxetine
- Sertraline
- Paroxetine
- Fluvoxamine
SELECTIVE SEROTONIN REUPTAKE INHIBITORS

• Their efficacy is comparable to TCA
• They are more tolerable at therapeutic dose and in overdose.
• They have less side effects than the TCA: little or no sedation, no alpha receptor blocking effect, does not cause seizure and no cardiac effects.
• They do not interfere with cognitive and psychomotor function.
• They are the group of first choice in depression.
• Examples are fluoxetine (prototype) and sertraline.