<table>
<tr><td>Class of Antidepressant</td><td colspan="4">• MAO Inhibitors
• MAO is a mitochondrial enzyme found in nearly all tissues
• Two forms of monoamine oxidase exist:
MAO-A responsible for NE, 5-HT catabolism. It also metabolizes tyramine of ingested food
MAO-B is more selective for dopamine metabolism</td><td>Tricyclic Antidepressants</td></tr>
<tr><td rowspan="3">Pharmacological Actions</td><td colspan="4">1- Inhibit the action of MAO in mitochondria which prevents monoamine breakdown and increases its availability.
2- Blocks mAch receptors (Atropine-like action)
3- Blocks α-adrenoceptors</td><td><u>Blocks:</u>
1- 5HT and NE reuptake
2- α_1-adrenoceptors
3- m_1Ach
4- Histamin H_1 receptors
Elevates mood, improves mental alertness, increases physical activity. (Long duration, no loss of effectiveness, <u>better than MAOI</u>)</td></tr>
<tr><td colspan="2">Selective</td><td colspan="2">Non-Selective</td><td>Tertiary Amines</td><td>Secondary Amines</td></tr>
<tr><td>MAO-A:
NE, Serotonin, and Tyramin metabolism
<u>Moclobemide</u></td><td>MAO-B:
Dopamine metabolism
<u>Selegiline</u></td><td>Reversible:
<u>Tranylcypromine</u>
(persists 7 days after stop)</td><td>Irreversible:
<u>Phenelzine</u>
(persists 2 weeks after stop)</td><td>Not selective to NE (More side effects)
1- <u>Imipramine</u> (Tofranil) → Gives Desipramine (Active metabolite)
2- <u>Amitriptyline</u> (Elavil) → Gives Nortiptyline (Active metabolite)</td><td>More selective to NE (Less side effects)
1- <u>Desipramine</u> (Norpramin)
2- <u>Nortriptyline</u> (Pamelor)</td></tr>
</table>

Indications	1- Atypical depression 2- Resistance to other therapy 3- Social Anxiety(agoraphobia)	Not used in depression.	Seldom used (low benefit/risk ration) ➔**ADR, Food & Drug Interactions** ➔ **Low antidepressant efficacy** **= Low benefit/risk ratio;**	**1- Depression:** - + Lithium in Depressed phase of Bipolar depression - + Antipsychotics in Depressed Psychotic patients - Resistance to other therapy - **In resistant depression if other therapy fail** **2- Other Psychiatric Disorder:** - OCD ***(OCD; ↓ DA & NE in the brain's prefrontal cortex)*** - Generalized Anxiety Disorders - Panic Disorders - Anorexia Nervosa **3- Other Disorders:** - Control Bed-wetting in children (Imipramine/**Desmopressin**): ↑ Contraction of internal sphincter of the bladder, it's gradually withdrawn and should not be given for more than 3 months. (has to bed wetting from depression like jealousy from new brother but if not he will be depressed) - Neuropathic pain: **Tertiary amines** are better because they modulate endorphins (given in smaller doses than those with deprssion. - Prophylaxis of Migrane.

Adverse Effects	1- Atropine-like action causes Antimuscarinic effects (dry mouth,glaucoma) 2- α- adrenoceptors blockage causes Postural hypotension 3- Effects on 5HT2A receptor causes: -Sexual dysfunction (especially in Phenelzine) -Sedation -Weight gain	1- Anticholinergic: (Dry mouth, blurred vision, constipation and urine retention, aggravation of glaucoma) 2- Antihistaminic: (Sedation, confusion, stop sedatives 1-2 weeks before use) 3- Antiadrenergic (α): (Postural hypotension, arrhythmias, conduction defects such as prolonged Q-T intervals and heart block) 4- Weight gain, sexual dysfunction, and impotence 5- Lower seizure threshold → Contraindicated in Seizure disorder. 6- Aggravation of psychosis (schizophrenia) **EARLY IN USE ➔ During 1st month ➔ aggravate suicidal thoughts specially in young aged. Can happen less upon change of dose. So we must observe the patient, also if u change the drug suicide could occur)** **DURING USE ➔ narrow therapeutic index ➔ toxicity can develop** **Excitement, delirium , convulsions, respiratory depression , coma, atropine like- effects, cardiac arrhythmias, sudden death.** DIALYSIS (it doesn't work with dialysis) **STOPAGE OF USE ➔ Withdrawal Symptoms; characterized by cholinergic rebound, flu-like symptoms.**

Food Interactions	**1- Tyramin (in aged cheese, liver, sausages, some meats, and yeast extracts)** **2- Levodopa (in broad and FAVA beans)** **Those compounds are normally degraded by MAO. MAOI inhibits the process of degrading Tyramin which results in Tyramin being absorbed and taken up by adrenergic neurons and converted into false transmitter that replaces NE in the vesicles.** **Net result: HYPERTENSIVE CRISIS.** **Tyramine is a precursor of catecholamines so if it's not degraded by MAO,NE increase and ↑ SNS >> Hypertension**	1- Enhanced toxicity by: - Hepatic microsomal enzymes inhibitors because it is metabolized by liver enzymes. → Contraindicated in liver disease. - Plasma-bound drugs such as **Asprin** and **Phenylbutazone** because TCA is strongly bound to plasma proteins and other plasma-bound drugs decrease it binding and enhance its toxicity. 2- Hypertensive Crisis: with **SSRI**, **MAOI**, and any **Sympathomimetics**. → Contraindicated in heart disease and pheyochromocytoma. 3- Respiratory Depression: with **Sedatives** or **CNS depressants**. → Contraindicated in Chronic bronchitis. 4- Increased Anticholinergic effects: with **Antipsychotics** and **Antiparkinsonisms**. → Contraindicated in Glaucoma and prostate hypertrophy ***Contraindications:** • **Glaucoma** • **Heart disease** • **Liver disease** • **Seizure disorder** • **Thyroid disease (in hyperthyroidism increase in catecholamine activity)** • **Prostate hypertrophy** • **Pheochromocytoma** • **Chronic bronchitis**
Drug Interactions	1- Drugs degraded by MAO: cause sever hypertension → hypertensive crisis. (**Indirect sympathomimetics**, **flu medication**, **local anesthetics**) 2- Drugs that increase Serotonin: cause Fatal Serotonin Syndrome → Hyperthermia, muscle rigidity, cardiovascular collapse (**SSRI**; must keep at least 6 weeks between giving MAOI and SSRI) it causes serotonin syndrome 3- **Pethidine**: MAOI inhibit its metabolism which results in the increase of its levels → ↑ action (Hyperpyrexia, irritability, hypotension, and coma).	