	Amine Reuptake Inhibitors		
	Tricyclic antidepressants (TCAs)	**Selective Serotonin Reuptake inhibitors (SSRIs)**	**Serotonin and Norepinephrine reuptake inhibitors (SNRIs)**
Examples	ami**triptyline**, imi**pramine**, clomi**pramine**	fluo**xetine**, citalopram, and **sertraline**	duloxetine, venlafaxine
MOA	**Block reuptake transporter proteins** of NE & 5HT→ ↓Reuptake of NE & 5HT→ ↑Conc. of 5HT & NE	Selective inhibition of reuptake of 5HT→ ↑ Conc. of 5HT	Block reuptake of 5HT & NE→ ↑ Conc. of 5HT & NE
Pharmacologic effect	TCA antidepressant effect appears **2-4 weeks** after starting drug therapy. ↑ Conc. of synaptic 5HT and NE **down-regulate presynaptic autoreceptors** → ↑ neuronal firing.	↑ Conc. of synaptic 5HT **down-regulate presynaptic autoreceptors** → ↑ neuronal firing.	Opposed to older TCA drugs, SNRIs **do not antagonize** muscarinic, adrenergic, or histamine receptors and produce **few autonomic, sedative, or cardiovascular** side effects.
SE	**1. TCAs produce autonomic side effects:** • Atropine-like action (زغلولة) • Block α1-receptor → orthostatic hypotension **2. Sedation (block of H1 receptors)**→ should be administered at bedtime **3. Weight gain** **4. Overdose is associated with:** • Cardiac arrythmias (treated with **sodium bicarbonate**) • Seizures (treated with **diazepam**	**1.Nervousness, dizziness, and insomnia** (↑Alertness so administered in the morning) → decrease with continued use **2.Male sexual dysfunction (Major cause of discontinuation)** **3. SSRIs + MAOIs**→ Serotonin syndrome	
Uses	1. Depression 2. (OCD) → **clomipramine** 3. Eating disorders 4. Panic disorders 5. Neuropathic pain → **Amitriptyline**. 6. Nocturnal enuresis → **imipramine**	1. Depression **(1st line)** 2. (OCD)→ fluoxetine & **fluvoxamine** 3. Eating disorders→ fluoxetine 4. Panic disorders 5. Premenstrual dysphoric disorders (PMDD)	1. Depression **(Alternative to SSRIs)** 2. Generalized anxiety disorder→ duloxetine 3. Neuropathic pain → duloxetine

TCAs drug interactions:

1. TCAs + MOAIs →↑ in 5HT (serotonin syndrome) → agitation, confusion, **muscle rigidity**, **severe HTN**, **hyperthermia** and **cardiovascular collapse**.

2. Additive adverse effects with:
   - Other sedative drugs
   - Drugs that increase QTc interval → ↑ risk of cardiac arrhythmia

3. TCAs are metabolized by CYP2D6 hepatic enzymes

	Multi action drugs "Atypical Antidepressants"				MAOIs
	Bupropion	**Mirtazapine**	**Trazodone**	**Nefazodone**	
MOA & Examples	-Weak **inhibitor of reuptake of DA & NE** -**Non-competitive** antagonist at nicotinic cholinergic receptors	**blocks α2- receptors** on **noradrenergic** and **serotonergic** nerve terminals → ↑ **NE & 5HT release**	**Inhibit biogenic amine reuptake** **More selective for 5HT** **Block 5HT-2A receptors**	**More selective for NE**	-MAO-A→ Metabolizes 5HT more -MAO-B→ Metabolizes DA more **-1st-generation MAOIs** → **Phenelzine**→ irreversible inhibitors of **both MAO-A and MAO-B.** **-2nd-generation MAOIs** → moclobemide → reversible **inhibitors of MAO-A** **-3rd generation MAOIs** → **Selegiline** → selectively inhibits **MAO-B** → **transdermal patch**. -MAO-A inhibitors → ↑ 5HT levels → downregulation of presynaptic autoreceptors → ↑ firing of serotonergic neurons.
SE	-Agitation & Insomnia -↑Risk of **seizures** -Few anticholinergic side effects -very little sedation, and rarely produces cardiovascular effects or sexual dysfunction	-**Sedation** -**Weight gain** -↑ hepatic enzyme levels -Rare agranulocytosis	**Priapism**	____	**-Serotonin syndrome** (as before): stop TCAs & SSRIs **2 weeks** before switching to it **-Cheese reaction** (tyramine containing food) → Severe HTN **-Tyramine:** Indirect sympathomimetic metabolized by MAO-A in the liver & intestine → Secretes NE
Uses	-Depression -**Quitting of smoking** -It+Naltrexone (opioid antagonist)→ Weight reduction	**Depression**	**Depression** **Insomnia** (low dose causes sedation)	____	**Last option Anti-depressant (In resistant cases)**
Pharmacologic effects	____	____	____	____	-Delayed effect as other drugs -MAOIs have many potentially serious interactions with other drugs and with food