Drug	MOA	Pharmacokinetics	Adverse effects	Drug Interactions
1) Tricyclics(TCA) -Imipramine -Clomipramine -Desipramine(NE) -Amitriptyline(5-HT) -Doxepin **Clinical Indications:** 1- Treatment of depression; - With lithium in depressed phase of bipolar depression - In resistant depression if other therapy fail -With antipsychotics in depressed psychotic patients. 2-Other psychiatric disorders; ▪ Obsessive-compulsive disorders (OCD) (OCD: decrease of DA & NE in the brain's prefrontal cortex.) ▪ Generalized anxiety disorders ▪ Panic disorders ▪ Anorexia nervosa 3-Other disorders; ▪ Control bed-wetting in children; Imipramine >> contraction of ▪ internal sphincter of bladder . Better desmopressin (antidiuretic) Gradually withdrawn / Treatment period do not exceed 3 months. ▪ Neuropathic pain; better Tertiary amines >>modulate endorphins Give in smaller doses than that prescribed for depression. ▪ Prophylaxis of migraine	Block the Re-Uptake of NE & 5-HT. Selective to NE High Affinty to 5-HT -Block ADR (α1), Histamine (H1) & Ach (M1)receptors.	Lipophilic with High protein binding; basic in nature، metabolized in liver. -Given once daily -Some of them give active metabolites Imipramine >>Desipramine Amitriptyline>>Nortriptyline	Sedation Cardiovascular effects (Tachycardia and hypotension) Anticholinergic effects (dry mouth,constipation, urinary retention -Weight gain. -Seizure -Hypomania So it's contraindicated in Glaucoma ,Heart disease ,Liver disease ,Seizure disorder ,Thyroid disease,Prostate hypertrophy ,Pheochromocytoma, Chronic bronchitis	-Being strongly bound to plasma proteins>>toxicity enhanced by aspirin, phenylbutazone, -Being metabolized by hepatic microsomal enzymes >>toxicity enhanced by enzyme inhibitors. -With MAOIs, SSRIs or any sympathomimetic drugs >>cause hypertensive crisis -Additive to sedatives or other CNS depressants >> decrease respiration -Additive to antipsychotics & anti parkinsonism's>> increase anticholinergic effects.
2-Drugs that Inhibit Mono AminoOxidase (MAOIs) Iproniazide (anti TB) - non-selective Inhibitors: Irreversible Phenelzine.(Hydralazine derivatives) (Reversible)Tranylcpramine.(Non-Hydralazn) -reversible selective (Meclobemide)	-↑Serotonin -↑NE Possess both α Adrenoceptor & mAch blocking effects Selective for MAO-A	All are well absorbed, metabolized & excreted in urine Uses: Only for resistance Depression where phobia and anxiety are the main symptoms.	-Antimuscarinic effects. -Postural hypotension.(antiadrenergic side effect) - Sexual dysfunction mainly with phenelzine. - Sedation , sleep disturbance. -Weight gain mainly with phenelzine. - Hepatotoxicity (with phenelzine) -Weight loss with Tranylcypramine	Drug-drug and food interaction. 1-Food containing tyramine (Old chese, wine, Pickles, smoked fish) 2-Sympathomimetic drugs like (Tricyclics; psedoephedrine.→ hypertensive crisis. 3-SSRIs →serotonergic syndrome. 4- If with pethidine>inhibition of metabolism > ↑ its levels > leads to hyperpyrexia, irritability, hypotension and coma.

New Generation

1) Selective Serotonin Reuptake Inhibitors (SSRI) Fluoxetine Citalopram Paroxetine Sertraline; Fluvoxamine -Fluoxetine differs from others members of this class in : 1. It has a longer $t_{1/2}$ (50hrs). 2. Available → as sustained release preparations →once weekly. 3. Metabolite norfluoxetine = potent as parent drug $t_{1/2}$ 10 days.	Selective uptake of 5-HT in presynaptic cleft. Clinical uses: -First choice for most depression -Fluoxetine is approved in (all ages) -Anxiety and panic disorders -Obsessive-compulsive disorders -Some eating disorders (bulimia) -Pain associated with diabetic neuropathy - Premature ejaculation -Premenstrual syndrome. -Alcohol abuse. -Anorexia nervosa -Genrailized anxiety disorder	T1/2 Too long (3-11 days): Fluoxetine. Rest are 24hrs. They are p450 enzyme inhibitors Primarily excreted through kidney; not paroxetine & sertraline undergo partially fecal excretion. They are enzyme inhibitors -Weak inhibitors < Sertraline, Citalopram →↓ interaction -Strong inhibitors > Fluoxetine, Paroxetine →↓ metabolism of TCA, neuroleptic, some antiarrhythmic, β-blockers. -Primarily excreted through kidney; not paroxetine & sertraline → undergo partially fecal excretion.	Nausea , Vomitting & ↓appetite (5HT3.) -Insomnia & anxiety (Except Paroxetine) -Impotence & sexual dysfunction(5HT2) -Enzyme inhibition (Fluoxetine) -agitation, nervousness > fluoxetine >citalopram -Sedation & lassitude >paroxetine, sertraline -Anorexia & weight loss -Mild CV & minimal antimuscarinc side effects unlike TCAs -Withdrawal manifestation < intensity than TCAs	Drugs interactions due to their -significant inhibitory action at CYP450 (Except Citalopram). - Enzyme inhibitors →↓ metabolism = ↑ toxicity of TCA, neuroleptic, some antiarrhythmic, β-blockers. - serotonergic syndrome: if combined with MAOIs > other ADDs
2) α2 – adrenoceptors antagonists Mirtazepine Mianserin	Increasing the release of 5-HT & NE by blocking α2.	**Advantages with chemotherapy** -Improves appetite -↓nausea & vomiting (5-HT_3 blocking) - ↑ body weight (↑appetite because of 5HT2 Blocking) -Sedation (potent antihistaminic) -Less sexual dysfunction (5-HT_2 blocking) -Has no anti-muscarinic effect .		↑appetite →good for patients taking cancer chemotherapy. Sedation. Constipation. Rarely leads to agranulocytosis (Mianserin).
3. Serotonin and Noradrenaline Reuptake Inhibitors (SNRIs) Venlavaxine(Desvenlafaxine is its metabolite)	Act by blocking 5-HT and NE uptake Has mild antimuscarinic effect (no antiadrenergic and antihistamine effect)	Short $t_{1/2}$ →↑HR & BP	Like SSRIs, Seizure, Constipation,maybe accompanied with withdrawal symptoms	
4. Norepinephrine Dopamine Reuptake Inhibitors (NDRIs) Bupropion	NE and DA reuptake inhibitor, with no direct action on 5HT. Acts as a nAch antagonist	Advantages: No sexual dysfunction given in young No weight gain, No orthostatic hypotension.) Side effects: Seizures; it decreases threshold of neuronal firing		
5. Norepinephrine Reuptake Inhibitors [NRIs] Reboxetine	Block only NET No affinity for 5HT, DA, ADR, H, mAch receptors So, has positive effects on the concentration and motivation in particular		Minimal only related to activation of ADR system as tremor, tachycardia, and urinary hesitancy	Safe to combine with SSRIs
6- Trazodone	-Selective blocker of 5-HT uptake but has significant α- blocking effect; -Blocks 5-HT2 receptors (Priapism)		priapism ,hypotension, Arrythmogenic and sedation	
7-Nefazodone	Structurally related to trazodone but does not has the sedative effect and does not block α- adrenoceptors Hepatotoxic (Cause hepatic failure)			likes most SSRI inhibit P450 3A4 isoenzyme