In the name of ALLAH

Personality disorder's pharmacotherapy

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Personality Disorders

- **Personality** consists of **enduring patterns of perceiving, relating to, and thinking about the environment and oneself** that are exhibited across numerous social and personal contexts.

- **A personality disorder** is diagnosed when personality traits are so inflexible and maladaptive across a wide range of situations that they cause significant distress and impairment of social, occupational, and role functioning
- Symptoms must deviate markedly from the expectations of the individual's culture in order to qualify as a personality disorder.

Epidemiology

The estimated mean international prevalence of personality disorders in the community is 11 percent

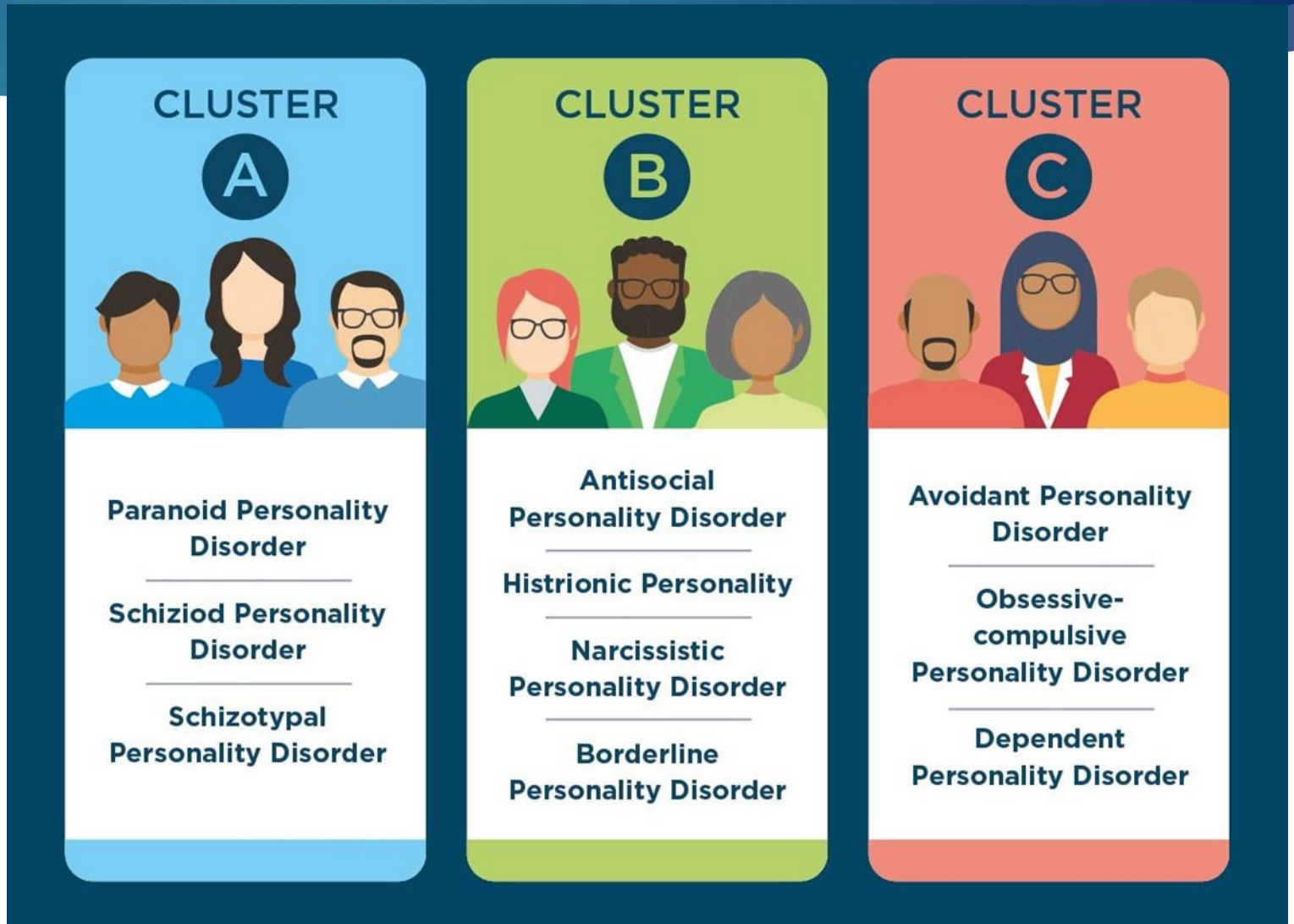
Personality disorders may be slightly more common in males and the young, and are common among the **poorly educated** and unemployed

Obsessive-compulsive personality disorder is associated with higher education and income

Point prevalence rates of personality disorders in international samples from community and clinical populations

Personality disorder	Community samples (mean, percent)	Clinical samples (mean, percent)
Antisocial	1.8	5.9
Avoidant	2.7	24.6
Borderline	1.6	28.5
Dependent	1.0	15.0
Histrionic	1.2	9.7
Narcissistic	0.8	10.1
Obsessive-compulsive	2.5	10.5
Paranoid	1.7	9.6
Schizoid	1.3	1.9
Schizotypal	1.3	5.7
Any personality disorder	11.0	64.4

Types of personality disorders



Principles of pharmacotherapy

- **1.First line : psychotherapy**
- Developing a comprehensive treatment plan addressing biological, psychological, and social needs of the individual.

- **2.Using pharmacotherapy** as an adjunctive treatment to first-line treatment of psychotherapy.

- **Avoiding polypharmacy or frequent medication changes**. Symptoms in patients with personality disorders often wax and wane in relationship to life circumstances
- **The decision to treat an individual** with personality disorder with medication should be based on the individual's risk-benefit profile (including drug efficacy and adverse effects) and their degree of impairment .

- **Assess patient adherence and avoid poly pharmacy**

Principles of pharmacotherapy

- **Pharmacotherapy targeting specific symptom** domains that are common across personality disorders may reduce symptoms more effectively than targeting specific disorders.
- **1.Cognitive-perceptual symptoms (eg, hallucinations, paranoid ideation)** :
- For individuals with cognitive-perceptual disturbances associated with personality disorders, we suggest low-dose antipsychotic medication rather than antidepressants or mood stabilizers .
- These medications may be more effective for disruptive, stress-related cognitive-perceptual experiences than antidepressants or mood stabilizers.
- **2.Impulsive-behavioral dyscontrol (eg, self-injury, theft, interpersonal conflict)** – For individuals with impulsive-behavioral dyscontrol associated with personality disorders, we suggest mood stabilizers rather than antidepressants or antipsychotic medications .
- Mood stabilizers are more effective for impulsivity and behavioral dyscontrol than antidepressants or antipsychotics.
- **3.Affective dysregulation (eg, depressed mood, mood lability, anxiety, anger)** :For individuals with affective dysregulation associated with personality disorders, we suggest mood stabilizers or low-dose antipsychotic agents rather than antidepressants
- Mood stabilizers and low-dose antipsychotic drugs are more effective for affective dysregulation than antidepressants.

Principles of pharmacotherapy

- **Multiple symptom domains —** For patients presenting with personality pathology involving multiple domains (eg, affective dysregulation and perceptual disturbance), share with the patient to assess which symptoms contribute to the overall functional impairment to the greatest degree. The selected domain would suggest a particular class of medication, its use to be weighed based on its risk-benefit profile

- **Multiple psychiatric disorders :** Patients diagnosed with a personality disorder should be assessed for co-occurring psychiatric disorders which, if present, should be treated .
- Such as bipolar disorder, schizophrenia, or moderate to severe major depressive disorder, it is reasonable to assess whether the medication prescribed for these disorders will reasonably address the component of the personality pathology.

- **Suicidality** : Suicidality can be seen in patients with any personality disorder. An increased risk of suicidality is particularly associated with borderline personality disorder.

Disorder based pharmacotherapy (Cluster A)

- **Individuals may appear odd and eccentric**
- **1.Schizotypal personality disorder** :
- As an adjunct to long-term psychotherapy, targeted pharmacotherapy is supported by small clinical trials and our clinical experience for cognitive-perceptual symptoms, cognitive deficits, and social anxiety in the disorder.
- **Cognitive-perceptual symptoms**: low dose antipsychotic medications
- **Prominent cognitive deficits**, adjunctive treatment with a stimulant medication (eg, long-acting methylphenidate) rather than other medications
- **Prominent social anxiety**: SSRIs/ Benzodiazepine .

- **Other cluster A disorders :**
- There are no clinical trials of medication for the other cluster A personality disorders.
- **Patients with paranoid personality disorder and schizoid personality** disorder both have tendencies toward cognitive-perceptual symptoms.
- A low-dose antipsychotic can be used, but expectations should be attenuated and risks of medication must outweigh potentially limited benefits of medication treatment.

Disorder based pharmacotherapy (Cluster B)

- **Individuals often appear dramatic, emotional, or erratic**

- **Antisocial personality disorder :** In general, it is suggested that medication not be used to treat patients with antisocial personality disorder.
- There may be a role for medication in treating severe aggressive behavior that can be seen in the disorder.
- **Borderline personality disorder :** Although not adequately tested, pharmacotherapy for personality disorders has been most extensively studied in borderline personality disorder.
- Results have been variable, with low-dose antipsychotic medication, mood stabilizers, and antidepressants leading to reduction in targeted symptoms in some trials. Suicidality in borderline personality disorder and other personality disorders is discussed above.

Disorder based pharmacotherapy (Cluster B)

- **Narcissistic personality disorder :** medication treatment of patients with narcissistic personality disorder is best kept to a minimum (ie, reserved for severe symptoms that pose a risk to safety and for other co-occurring conditions).

- **Other cluster B disorders** — There are no clinical trials of medication for the other cluster B personality disorder, histrionic personality disorder. Affective dysregulation and impulsivity are commonly seen in patients with this disorder.

Disorder based pharmacotherapy (Cluster C)

- **Typical symptoms: Individuals often appear anxious or fearful**

- **Avoidant personality disorder :** Socially avoidant patterns among patients with avoidant personality disorder have been reconceptualized in terms of social anxiety for the purposes of treatment
- **Examples:** SSRI/ SNRI/Propranolol/ benzodiazepine

- **Other cluster C disorders :** Symptoms of affective dysregulation are prominent in dependent personality disorder and **obsessive compulsive personality disorder**.
- Suicidal urges or behavior are of potential concern, especially in the setting of loss of control over their environment

Pharmacologic Therapy
Example for depression

- **First-line treatmen**t for a **moderate to-severe** depressive episode.
- **Co-occuring in personality disorders**
- Antidepressants have *equivalent efficacy* in groups of patients when administered in comparable doses.
- **Factors for drug section :** patient's **history of response**, history of familial antidepressant response, patient's concurrent medical illnesses and medications, presenting symptoms (eg, insomnia vs. hypersomnia), potential for drug–drug interactions, adverse event profile, patient preference, and medication cost

General Principles

- The patient should be informed that **adverse effects** might occur immediately, while symptoms of depression may take 2 to 4 weeks to improve and up to 3 months for full resolution.
- **Adherence** to the treatment plan is essential for a successful outcome, and tools to help increase medication adherence should be discussed with each patient.
- **Novel antidepressants that target GABA and glutamate** systems may have a more rapid and transient effect on symptoms. They are typically used in conjunction with traditional antidepressants for refractory symptoms.

Compelling diseases

- **1.TCA:** neuropathic pain, migraine prophylaxis, IBS, fibromyalgia
- **2.SSRI /SNRI:** most of anxiety such as GAD, Panic attack ,...
- **Venlafaxine:** GAD/ migraine prophylaxis

Drug I

TABLE 88-9 Select Pharmacokinetic Interactions of Antidepressants

Antidepressant	Interacting Medication/Medication Class	Effect
Selective Serotonin Reuptake Inhibitors		
Citalopram and escitalopram	Omeprazole	Increased concentrations of citalopram and escitalopram
Fluoxetine	Alprazolam	Increased concentrations and half-life of alprazolam; increased psychomotor impairment
	Antipsychotics (eg, aripiprazole, haloperidol)	Increased antipsychotic concentrations; increased extrapyramidal symptoms
	β-Adrenergic blockers	Increased metoprolol concentrations; increased bradycardia; possible heart block
	Carbamazepine	Increased concentrations of carbamazepine; symptoms of carbamazepine toxicity
	Phenytoin	Increased concentrations of phenytoin; symptoms of phenytoin toxicity
	Tamoxifen	Decreased conversion of tamoxifen to active metabolites
	TCAs	Markedly increased TCA concentrations; symptoms of TCA toxicity
	Thioridazine	Thioridazine C_{max} increased; prolonged QTc interval
Fluvoxamine	Alosetron	Increased alosetron AUC (sixfold) and half-life (threefold)
	Alprazolam	Increased AUC of alprazolam by 96%, increased alprazolam half-life by 71%; increased psychomotor impairment
	β-Adrenergic blockers	Fivefold increase in propranolol concentration; bradycardia and hypotension
	Carbamazepine	Increased concentrations of carbamazepine; symptoms of carbamazepine toxicity
	Clozapine	Increased clozapine concentrations; increased risk for seizures and orthostatic hypotension
	Diltiazem	Bradycardia
	Methadone	Increased methadone plasma concentrations; symptoms of methadone toxicity
	Ramelteon	Increased AUC (190-fold) and C_{max} (70-fold)
	TCAs	Increased TCA concentration; symptoms of TCA toxicity
	Theophylline and caffeine	Increased concentrations of theophylline or caffeine; symptoms of theophylline or caffeine toxicity
	Thioridazine	Thioridazine C_{max} increased; prolonged QTc interval
	Warfarin	Increased effect of warfarin
Paroxetine	Antipsychotics (eg, aripiprazole, haloperidol)	Increased antipsychotic concentrations; increased CNS and extrapyramidal symptoms
	β-Adrenergic blockers	Increased metoprolol concentrations; increased bradycardia; possible heart block
	Tamoxifen	Decreased conversion of tamoxifen to active metabolites
	TCAs	Markedly increased TCA concentrations; symptoms of TCA toxicity
	Thioridazine	Thioridazine C_{max} increased; prolonged QTc interval
Sertraline	Methadone	Increased methadone levels

Drug Interactions

Serotonin–Norepinephrine Reuptake Inhibitors		
Venlafaxine and desvenlafaxine	CYP3A4 inhibitors	May increase levels of venlafaxine and *O*-desmethylvenlafaxine especially in CYP2D6 poor metabolizers
Duloxetine	Metoprolol	May increase metoprolol levels twofold
	Tamoxifen	Decreased conversion of tamoxifen to active metabolites
	Thioridazine	Thioridazine C_{max} increased; prolonged QTc interval
Levomilnacipran	CYP3A4 inhibitors	Clinically relevant increases in levomilnacipran concentrations may occur
Mixed Serotonergic (Mixed 5-HT)		
Vilazodone	CYP3A4 inhibitors	Maximum vilazodone dose 20 mg with coadministration of potent CYP3A4 inhibitor
Vortioxetine	CYP2D6 inhibitors	May need to reduce vortioxetine dose by half with coadministration of potent CYP2D6 inhibitor
Serotonin and α-2-Adrenergic Antagonist		
Mirtazapine	Carbamazepine	Mirtazapine concentration decreased (60%)
Norepinephrine and Dopamine Reuptake Inhibitor		
Bupropion	Tamoxifen	Decreased conversion of tamoxifen to active metabolites

TABLE 88-10 Select Pharmacodynamic Medication Interactions of Antidepressants

Medication/ Medication Class	Antidepressants/ Antidepressant Class	Effect and Management
NSAIDs Aspirin Anticoagulants Antiplatelet agents	SSRIs, SNRIs, TCAs, trazodone, vilazodone, vortioxetine	• FDA warning for increased risk of bleeding • Number needed to harm with NSAIDs = 82 vs >700 with SSRI alone • Assess for baseline bleeding risk and monitor closely • Educate at risk patients regarding signs of bleeding • Consider histamine-2 (H_2) antagonist in high-risk patients
Triptans	MAOIs, SSRIs, and SNRIs	• FDA warning in labeling • Very low risk • Monitor for signs of serotonin syndrome when frequent high doses are used • Triptan toxicity possible when almotriptan, rizatriptan, sumatriptan, or zolmitriptan are combined with MAO inhibitors
Linezolid	All serotonergic antidepressants	• Linezolid is weak, reversible, nonselective, MAOI • FDA labeling recommends against use with other MAOIs and recommends discontinuing antidepressants if linezolid is started • Actual rate of serotonin syndrome with combination reported at <1% • Abrupt discontinuation of antidepressants can have negative consequences • If linezolid is indicated and patient is already on an antidepressant, monitor for signs of serotonin syndrome upon initiating combination • If patient is on short course of linezolid and in need of treatment for depression, consider postponing antidepressant initiation until course is complete
Tramadol	Bupropion, duloxetine, fluoxetine, paroxetine	• Decreased metabolism results in increased SNRI activity of tramadol • Rare cases of high dose tramadol combined with CYP2D6 inhibitors resulting in serotonin syndrome have been reported • Monitor for increased signs of serotonin syndrome and decreased analgesic response when combination is used

Selective Serotonin Reuptake Inhibitors

- SSRIs are generally chosen as ***first-line antidepressants*** due to their relative safety in overdose and improved tolerability over traditional TCAs and MAOIs.
- First choice for most types of anxiety

- The SSRIs, as the name implies, have **a low affinity** for other receptors including α_1-adrenergic, histaminic (H1), and muscarinic (M1) receptors

- **Differences in drug interaction profile and pharmacokinetic** (PK) parameters (eg, half-life).

Side Effects

- **Dose-dependent :** generally are mild and limited to 1 to 2 weeks after initiation or dose increases, are gastrointestinal (GI) symptoms (eg, nausea, vomiting, and diarrhea), anxiety, and headache.
- **Both somnolence and insomnia** have been reported with all SSRIs (**Paroxetine and fluvoxamine** may cause somnolence).
- **Sexual Disorders**: including(arousal, libido, orgasm) however it is important to note that depression itself may be associated with sexual dysfunction. USE IN PREMATURE EJACULATION
- SIADH, Vivid dreams, tremor, **sweating ,anti platelet effect....**
- **Citalopram** to a dose dependent increase in QT interval. (>40mg/d)
- **Paroxetine** has more anticholinergic and antihistaminergic activity (sedation, dry mouth, anti pruritic ...)

Tricyclic Antidepressants

- **A type of SNRI !!**
- All TCAs potentiate the activity of NE and 5-HT by blocking their reuptake.
- However, the potency and selectivity of TCAs for the inhibition of NE and 5-HT reuptake vary greatly among these agents .
- **Nortriptyline** is most commonly used and may be selected in patients with comorbid **migraine headaches, neuropathic pain, or fibromyalgia and IBS.**

Side effects

- **Anticholinergic effects**
- **Orthostatic hypotension** is a common, dose-related, and potentially problematic adverse effect that has been attributed to the affinity of the TCAs for α_1-adrenergic receptors.
- In patients with history of myocardial infarction, TCAs should be avoided due to **risk of severe arrhythmias** (QTc prolongation, torsades de pointes)

Mood stabilizers

- Pharmacotherapy is **crucial for the acute and maintenance** treatment of bipolar disorder and includes:
- **Mood Stabilizer :**Lithium, valproate, carbamazepine, lamotrigine, f antipsychotics
- Adjunctive agents such as **antidepressants and benzodiazepines**.

- **Combination therapies** (eg, lithium plus valproate or carbamazepine, lithium or valproate plus an sga) can provide better acute response and long-term prevention of relapse and recurrence than monotherapy in some bipolar patients.

Treatment

- **Treatment of bipolar** disorder must be individualized because the clinical presentation, severity, and frequency of episodes vary widely among patients.
- The treatment of bipolar disorder can **vary depending on what type of episode the patient is experiencing**.
- Once diagnosed with bipolar disorder, patients should remain on a **mood stabilizer**
- **Mood stabilizer:**
- lithium, valproate, or a second-generation antipsychotic
- During acute episodes, medications can be **added** and then tapered once the patient is stabilized and euthymic.

Lithium Carbonate: Tab 300 mg, Tab SR 400 mg

- Chronic lithium administration may modulate **gene expression** and have **neuroprotective** effects.
- Lithium is a monovalent cation that is **rapidly absorbed**, and widely distributed with no protein binding. It is also not metabolized, and is excreted unchanged in the urine and in other body fluids.
- **Efficacy:** Lithium is considered a first-line agent for acute mania acute bipolar depression, and maintenance treatment of bipolar I and II disorders and suicidal idea.

- **Slow Onset (1-2 week)**
- **Dose:** initial 600 mg then 900-2,400 mg/day in two to four divided doses, preferably **with meals**
- Renal impairment: lower doses required with frequent serum monitoring

- **TDM:** There is wide variation in the dosage needed to achieve therapeutic response and **trough serum lithium concentration** (ie, 0.6-1.2 mEq/L [mmol/L]

Side effect

- **Early:** Initial gastrointestinal (GI) and central nervous system (CNS) side effects (lowering the dose, taking doses with food, using extended-release products, and trying once-daily dosing at bedtime).
- Fine hand tremor can be evident in many patients while a course hand tremor may be a sign of toxicity. (switch to long-acting preparation, lower dose if possible) or adding a *β*-adrenergic antagonist).
- Polydipsia with polyuria : associated with or without nephrogenic diabetes insipidus (DI) which reversible with discontinuation of lithium .
- Hypothyroidism can occur in patients treated with lithium, occurring more frequently in women than men.
- **Supplemental exogenous thyroid hormone (ie, levothyroxine) can be added to the patients' regimen.**

- **OTHERS:**
  Acne and folliculitis (1%), reversible leukocytosis, and weight gain.
- Reversible cardiac effects, particularly t-wave flattening or inversion
- **Pregnancy and breastfeeding category** :
  XXXX

Side effect

- **Toxicity** Lithium is an extremely toxic medication if accidentally or intentionally taken in overdose.
- Lithium toxicity usually occurs with blood levels greater than **1.5 mEq/L** (mmol/L), but elderly patients may experience toxicity at lower levels.

- **Several key symptoms**: *GI* (eg, vomiting, diarrhea, or incontinence), *coordination* (eg, fine to coarse hand tremor, unstable gait, slurred speech, and muscle twitching), and *cognition* (eg, poor concentration, drowsiness, disorientation, apathy, and coma)

Toxicity

- **If lithium toxicity is suspected**, the person should go to an emergency room to be monitored and lithium should be discontinued.

- **Drug–Drug Interactions:**
- **ELEVATE?!:** Thiazide diuretics (Na excretion and Li reabsorption), nonsteroidal anti inflammatory drugs, cyclooxygenase-2 inhibitors, angiotensin-converting enzyme inhibitors, and salt-restricted diets can elevate lithium levels.

Lithium Drug Interactions of Clinical Significance

Drugs That Increase Lithium Levels

NSAIDs

Many NSAIDs have been reported to increase lithium levels as much as 50%–60%. This probably is owing to an enhanced reabsorption of sodium and lithium secondary to inhibition of prostaglandin synthesis.

Diuretics

All diuretics can contribute to sodium depletion. Sodium depletion can result in an increased proximal tubular reabsorption of sodium and lithium. Thiazide-like diuretics cause the greatest increase in lithium levels, whereas loop diuretics and potassium-sparing diuretics seem to be somewhat safer.

Angiotensin-Converting Enzyme (ACE) inhibitors

ACE inhibitors and lithium both result in volume depletion and a reduction in glomerular filtration rate. This results in reduced lithium excretion.

Angiotensin II Receptor Blockers (ARBs)

ARBs decrease in sodium and reabsorption via AT_1 blockade results in reduced lithium excretion.

Drugs That Decrease Lithium Levels

Theophylline, caffeine

Theophylline and caffeine may increase renal clearance of lithium and result in a decrease in levels in the range of 20%.

Acetazolamide

Acetazolamide may impair proximal tubular reabsorption of lithium ions.

Sodium

High dietary sodium intake promotes the renal clearance of lithium.

Drugs That Increase Lithium Toxicity

Methyldopa

Cases of sedation, dysphoria, and confusion owing to the combined use of lithium and methyldopa have been reported.

Carbamazepine

Cases of neurotoxicity involving the combined use of lithium and carbamazepine have been reported in patients with normal lithium levels.

Calcium-channel antagonists

Cases of neurotoxicity involving the combined use of lithium and the calcium-channel blockers verapamil and diltiazem have been reported. Lithium interferes with calcium transport across cells.

Antipsychotics

Cases of neurotoxicity (encephalopathic syndrome, extrapyramidal effects, cerebellar effect, EEG abnormalities) have been reported owing to the combined use of lithium and various antipsychotics. The interaction may be related to increase in phenothiazine levels, changes in tissue uptake of lithium, or dopamine-blocking effects of lithium. Studies attempting to demonstrate this effect have yielded differing results.

Serotonin-selective reuptake inhibitors

Fluvoxamine and fluoxetine have been reported to result in toxicity when added to lithium. Sertraline has been reported to cause nausea and tremor in lithium recipients.

Valproate

It is considerable mood stabilizer, quicker onset ,Valproate has antimigraine, mood-stabilizing, and anti aggressive effects

- **Other indications:**
- Seizure, Migraine prophylaxis

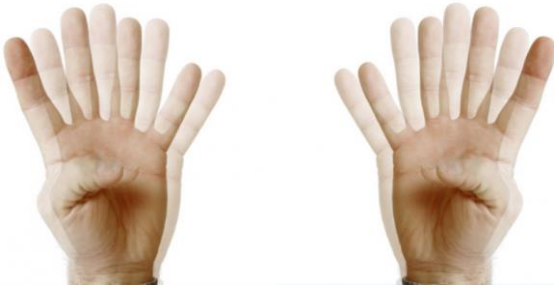
- **Dose:** For outpatients who are hypomanic or euthymic, or for elderly patients, the initial starting dose is generally lower (5-10 mg/kg/day in divided doses . (Max: 60mg/kg/day)
- **TDM: of 50 to 125 mcg/mL** taken 12 hours after the last dose (after 3-4 days)

Adverse Effects

- **The most frequent dose-related** adverse effects with valproate are GI complaints (anorexia, nausea, indigestion, vomiting, mild diarrhea, and flatulence): after meal and EC tab is better tolerated
- **The GI complaints** are usually transient, but giving the medication with food, using lower initial doses with gradual increases in doses, or switching to divalproex sodium extended release tablets can minimize them.
- **Tremor : reduction of the dose or the addition of a β-blocker** can alleviate tremors, and giving the total daily dose at bedtime can minimize daytime sedation.
- **Fine hand tremors, and sedation.**

Adverse Effects

- **Other adverse effects** of valproate include ataxia, lethargy, alopecia, changes in the texture or color of hair, pruritus,
- Transient increases in liver enzymes
- hyperammonemia(NH3)
- **Cosmetic side effects:** increased appetite and weight gain occurs in approximately 50% of patients on long-term valproate therapy.
- **PCOS**



- **L carnitine insufficiency**
- **Thrombocytopenia** can occur at higher doses, and patients should be monitored for bleeding and bruising/ usually benign

Antipsychotic

- **Indications**: Schizophrenia, Agitation, resistant depression, delirium

- **1.Typicals (low potent)**: less EPS/ more sedation

- **Chlorpromazine (Largactil®): Tab 25, 100 mg, Amp 50 mg/2 ml**
- In resistant hiccup
- **Thioridazine: Tab 10, 25, 100 mg (Mellaril®)**
- **Risk of QT prolongation is higher**

Typical (High potent)

- (less sedation, more EPS)

- **Fluphenazine**: Tab 1, 2.5 mg, Amp 25 mg/ml (Modicate,Depixol®)
- **Perphenazine**: Tab 2, 4, 8 mg, Amp 5 mg/ml
- **Trifluoperazine**: Tab 1, 2, 5 mg, Amp 1 mg/ml (Eskasina®)
- **Thiothixene**: Cap 5 mg (Navane®)
- **Haloperidol**: Tab 0.5, 2, 5 mg, Oral Drop 2 mg/ml, Amp 5, 50 mg/ml (Haldol®)
- **Pimozide**: Tab 2, 4 mg (Orap®, Orap Fortt®)
- In Tourette syndrome and **tic disorders**, delusional parasitosis /risk of QT prolongation

- **Flupentixol: Tab 0.5, 1,3 mg and 20mg ampule (fluanxol)**
- Dose: 10-40 mg every 4-10 days

Atypical antipsychotic

- **Less EPS/ less hyperprolactinemia BUT there is the risk of metabolic side effects (obesity, hyperglycemia, Hyper TG ,...)**
- **Mainly first line, select based on other morbidity/ good agent in delirium**

- **They Effect on 5HT3 and Dopamine receptors (negative and positive symptoms)**

- **Clozapine**: Tab 25, 100 mg (Leponex®)
- Most effective (resistant cases)/ specific ADR: agranulocytosis (CBC monitoring)
- **Olanzapine**: Tab 2.5, 5, 10, 15 mg
- Both have highest risk of metabolic ADRs /appetizer , first line in CINV

- **Risk of QT prolongation:**
  - **Thioridazine> haloperidol. Pimozide>olanzapine, quetiapine> risperidone> aripiprazole**
- **Risk of EPS:**
  - **High potent typical> low potent> Atypical**
  - **It seems clozapine and quetiapine have the least risk**
- **Risk of metabolic side effects :**
  - **Clozapine, olanzapine> quetiapine, risperidone> aripiprazole**

Atypical antipsychotic

- **Quetiapine**: Tab 25, 100 mg (Seroquel®)

- **Risperidone**: Tab 1, 2, 3, 4 mg (Risperidal®)
- Good and modest! agent, modest ADRs / risk of hyperprolactinemia>6mg/d

- **Aripiprazole**: Tab 5, 10, 15, 30 mg (Abilify®)
- Less sedation/ **less EPS and metabolic effect**/ may cause irritability
- **Partial D agonist**, may be used in antipsychotic induced hyperprolactinemia

Benzodiazepine (GABA A agonist)

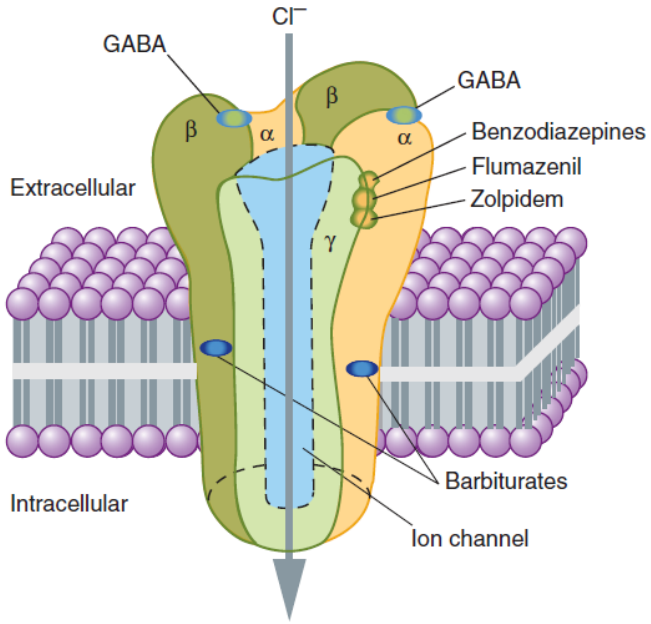


FIGURE 22–1 A model of the $GABA_A$ receptor-chloride ion channel macromolecular complex. A hetero-oligomeric glycopro-

Indications:

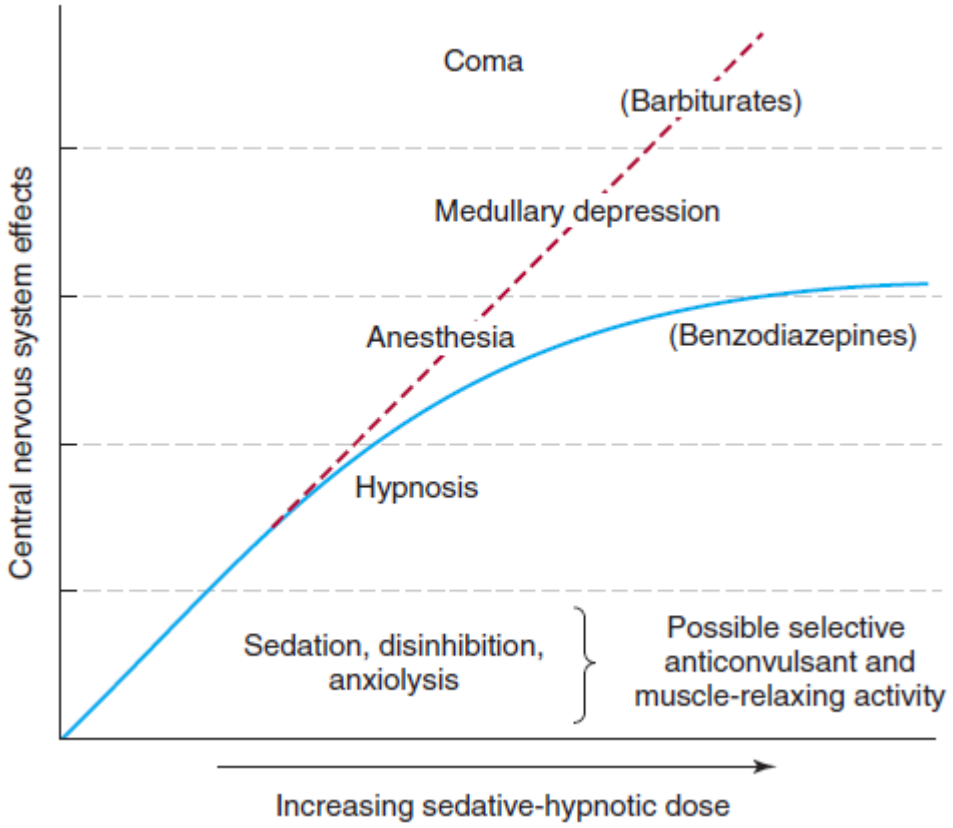
- **Acute stress, panic attack**
- **Insomnia:** including estazolam, flurazepam, and triazolam

- **Muscle relaxant**: diazepam/ clonazepam/ lorazepam
- **Withdrawal state (ethanol): l**onger acting benzodiazepines (eg, chlordiazepoxide, diazepam)
- **No metabolite** (good for elderly ang hepatic impairment): **oxazepam / lorazepam**

- **Clonazepam**: Tab 1, 2 mg (Relative Potency = 0.25)
- Potent/ panic attack /Anti seizure ,muscle relaxant
- **Alprazolam**: Tab 0.5, 1 mg, (Xanax®) (relative potency :0.5 mg)
- **Lorazepam**: Tab 1, 2 mg (Ativan®) (Relative Potency = 1)

Benzodiazepine

- **Diazepam**: Tab 2, 5, 10 mg, Amp 10 mg/2 ml (Valium®), Rectal Tube (Stesolid®) 5, 10 mg
- Muscle relaxent (2-10 mg/d), antisizure
- **Injection forms should not be diluted**
- **Chlordiazepoxide**: Tab 5, 10 mg (Librium®) (Relative Potency =10)
- Longer action/ less risk of abuse
- **Oxazepam**: Tab 10 mg (Oxpam®) potency: 10
- **Flurazepam**: Cap 15 mg potency: 15
- In insomnia (long act/ hang over!)
- **Midazolam**: Amp 5 mg/ml, 15 mg/3 ml
- Fast act,short act
- **In procedure such as endoscopy, agitation. ICU sedation**



- **ADRs**: risk of **abuse** (specially by fast acing : diazepam>alprazolm>lorazepam) anterograde **amnesia**/**tolerance** (not include anxiety)