



MOOD STABILIZERS

MOOD DISORDERS

**excessive sadness
(depression)**



**excessive excitement
(mania)**

MOOD STABILIZERS

1. Mood stabilizers are used to treat acute mania (acute treatment) & to help prevent relapses of manic episodes (maintenance treatment) in bipolar disorder & schizoaffective disorder .

2. Less commonly, they may be used for:

- Augmentation of antidepressants in patients with major depression refractory to monotherapy
- Potentiation of antipsychotics in patients with schizophrenia or schizoaffective disorder
- Treatment of aggression and impulsivity (e.g., neurocognitive disorders, intellectual disability, personality disorders, other medical conditions)
- Enhancement of abstinence in treatment of alcoholism

Acute mania

Atypical antipsychotics: Olanzapine, risperidone, quetiapine, ziprasidone, aripiprazole.

Typical: haldol, chlopromazine

Mood stabilizers:
Lithium, valproate, carbamazepine

haldol :

*oral (5-30)mg

*IM (2-10)mg

chlopromazine :

*oral (200-800)mg

*IM (25-50)mg

olanzapine : 5-20 mg

risperidone : 1-6 mg

ziprasidone : 80-160 mg

quetiapine :

*for mania (400-800)

*for depression (300-600)

aripiprazole : 15-30 mg

MAINTAINANCE TREATMENT

LITHIUM (GOLD STANDARD), VALPROATE, CARBAMAZEPINE

LAMOTRIGINE

Mood Stabilizers include :

1. Lithium

the first-line mood stabilizer .

**narrow therapeutic index
(warning for toxicity)
bad S.Es**

2. Anticonvulsants

most commonly
•valproic acid,
•lamotrigine,
and carbamazepine

3. Antipsychotics

olanzapine
risperidone
ziprasidone
quetiapine
aripiprazole

Lithium

- drug of choice in acute mania
- Antimanic agent
- Inhibition of norepinephrine and dopamine release in the brain
- Increase of serotonin production in the brain
- Alteration of Na⁺ / K⁺ ion transport (brain, muscle cells)
- metabolized by the kidney
- Onset of action takes 5–7 days.

**lithium reduces risk of
suicide .**

LITHIUM

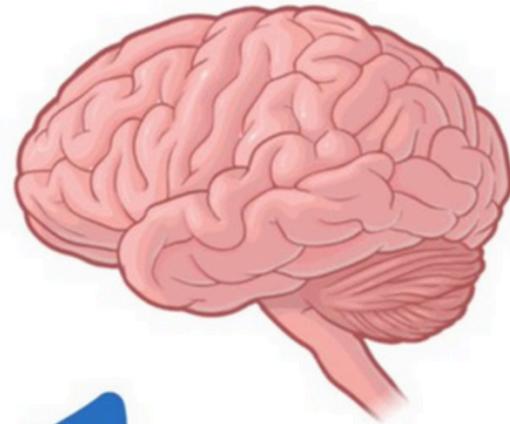
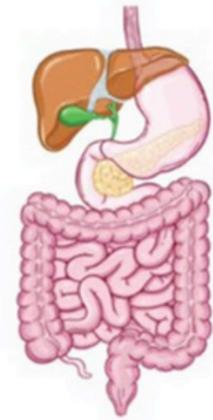
TAKEN ORALLY



RAPIDLY ABSORBED
by GI TRACT



TRAVELS to BRAIN

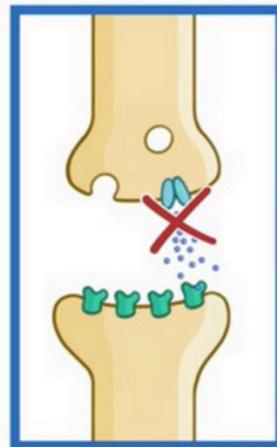


* REGULATES RELEASE
of NEUROTRANSMITTERS

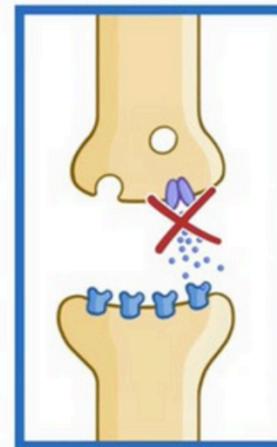
LITHIUM

* INHIBIT RELEASE

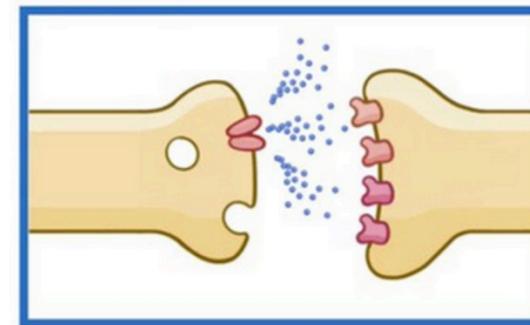
NOREPINEPHRINE



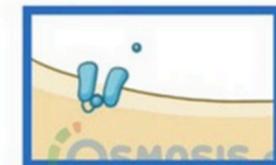
DOPAMINE



* ↑↑ PRODUCTION
SEROTONIN



* ALTERS Na^+ - K^+ ION TRANSPORT
NEURONS
MUSCLE CELLS



Indications

- in acute mania
- and as prophylaxis for both manic and depressive episodes in bipolar and schizoaffective disorders.
- It is also used in cyclothymic disorder and unipolar depression

Contraindications

- Pregnancy (teratogenic in 1st trimester) “Ebstein's anomaly”, breastfeeding
- Children < 12 years
- Cardiac / renal / hepatic impairment
- brain trauma, brain organ syndrome
- NSAIDs, ACE inhibitors, diuretics (decrease secretion)
- Dehydration, hyponatremia
- Thyroid disease

SIDE EFFECTS

•NARROW THERAPEUTIC INDEX

Early:

- Nausea, vomiting, diarrhea, weight gain, metallic taste**
- Polyurea, polydypsia (nephrogenic diabetes insipidus)**
- Fine Tremor, muscle weakness, edema**
- Worsening of psoriasis**
- Acne**
- Hair loss**

•

Late:

- Hypothyroidism, Goitre**
- Memory impairment**
- Nephro toxicity**
- ECG changes : T wave flattening**
- Arrhythmia**
- Lithium can cause Ebstein's anomaly (20 times)**

Most common lithium SEFs are GI distress including reduced appetite, nausea/vomiting, diarrhea

MOST IMPORTANT SIDE EFFECTS

* THIRST



* LETHARGY



* SLURRED SPEECH

* MUSCLE WEAKNESS

* GASTROINTESTINAL SIDE EFFECTS

└ NAUSEA

└ VOMITING

└ DIARRHEA



* SEIZURES

* HYPERREFLEXIA

* ATAXIA

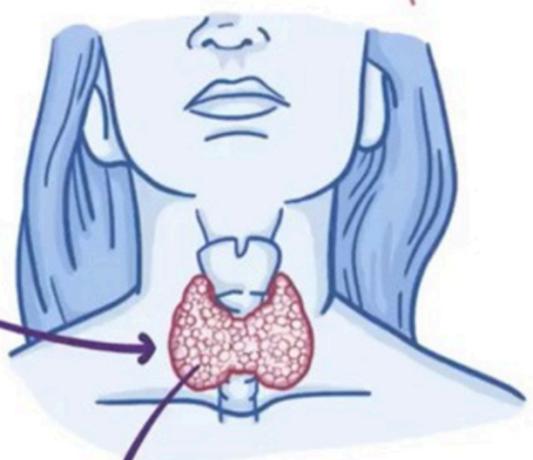


SIDE EFFECTS

LEUKOCYTOSIS
~ ↑ WBC COUNT

LITHIUM

~~TSH~~



~~THYROID HORMONES~~

HYPOTHYROIDISM

- ~ WEIGHT GAIN
- ~ COLD SENSITIVITY
- ~ SLOWER HEART RATE
- ~ MENTAL SLOWNESS
- ~ CONSTIPATION
- ↳ REACTIVE HYPERTROPHY & HYPERPLASIA



GOITER
2022 Edition

* NOT SAFE for PREGNANCY

↳ ↑ RISK of CONGENITAL HEART DEFECTS



EBSTEIN'S ANOMALY

* if LEVELS ↑ to TOXIC LEVELS

↳ ACUTE RENAL FAILURE

↳ SEVERE NEUROLOGICAL SYMPTOMS

- ~ ATAXIA
- ~ CONFUSION
- ~ DYSARTHRIA
- ~ COMA
- ~ DEATH

SIDE EFFECTS

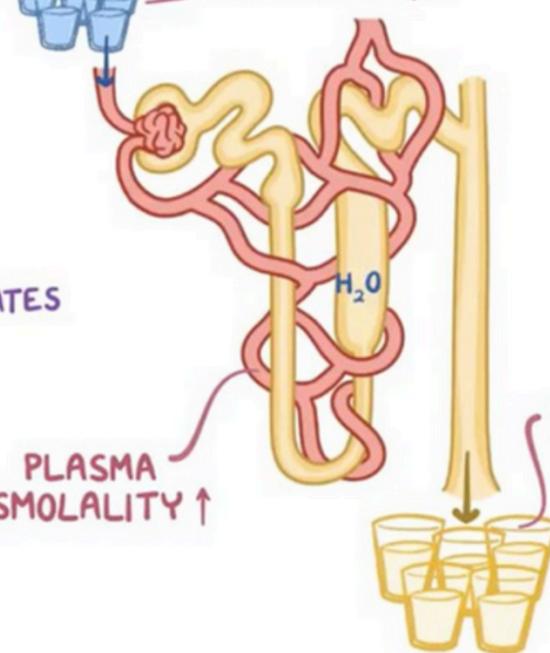
LITHIUM

~~ADH~~

↳ CONCENTRATES URINE

POLYDIPSIA

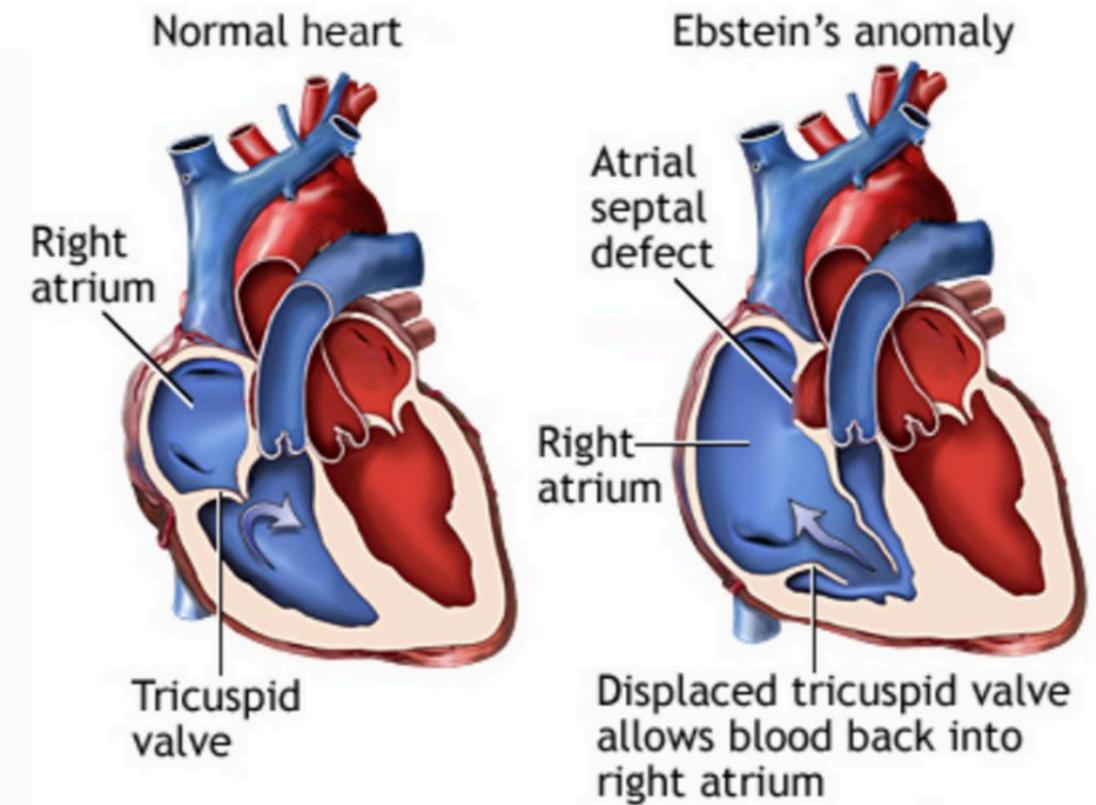
PLASMA OSMOLALITY ↑



POLYURIA

NEPHROGENIC DIABETES INSIPIDUS

- **L**- leucocytes
 - **I** – Increased
 - **T** – Tremors
 - **H**- Hypothyroidism
 - **I**- Increased
 - **U**- Urine
 - **M**- should be avoided in expectant **MOTHER** as it causes Ebstein's anomaly
- Diabetes Insipidus



Serotonin syndrome

LIFE-THREATENING EFFECT of LITHIUM

↳ COMBINED w/ CERTAIN ANTIDEPRESSANT MEDICATIONS

SEROTONIN SYNDROME

↳ ↑↑ SEROTONIN in BRAIN

- * SKIN FLUSHING
- * HYPERTHERMIA
- * AGITATION
- * MUSCLE RIGIDITY
- * SEIZURES
- * ALTERED MENTAL STATUS
- * COMA



Mild Toxicity

<1.5 mEq/L

Fine tremor of limbs

Cog-wheel rigidity

Gastrointestinal disturbances

Polyuria

Polydipsia

Agitation

Confusion

Delirium

Moderate Toxicity

1.5–2.5 mEq/L

Coarse tremors of limbs

Muscle weakness

Muscle twitching

Hyperreflexia

Slurred speech

Blurred vision and nystagmus

Ataxia

Sedation

Lethargy

Hyperthermia

Severe Toxicity

>2.5 mEq/L

Coarse tremors of limbs

Delirium

Stupor

Clonus

Seizures

QTc interval prolongation

Renal failure

Respiratory-complications

Coma

Death

**0.6–1.2 NORMAL BLOOD
CONCENTRATION**
■ **TOXIC: >1.5**
■ **POTENTIALLY LETHAL:
>2.0**

Tremor is the most common
symptoms
of lithium toxicity
ttt : propranolol.

Management to lithium toxicity

–stop Lithium
Hydration

Lithium level, serum electrolytes, renal function, ECG should be obtained as soon as possible

–Lithium level >4 Immediate dialysis

Lithium Drug Monitoring

Blood samples taken 12 hours post dose

Sample should be taken after 5–7 days of treatment initiation

Therapeutic window :of 0.6 – 1.2

Aim for 0.8 – 1.0 during manic phase;
0.4 – 0.8 during maintenance phase

Factors that increase Li+ levels: NSAIDs

**Aspirin (+/-)/ Thiazide diuretics/ Dehydration
Salt deprivation /Sweating (salt loss)/ Impaired renal function**

Prior to initiating, patients should have :

- an ECG,
- basic chemistries,
- thyroid function tests,
- a complete blood count (CBC),
- and a pregnancy test.

A 26 year old male with a past medical history of an unknown mood disorder presents with some medical problem. On review of his labs, you note the following:

White Blood Cells	<i>11.0</i>
Hemoglobin	<i>14.0</i>
Platelets	<i>334</i>
Creatinine	<i>1.9</i>



Which of the following medications is responsible for this adverse drug reaction?

- (A)** Lithium
- (B)** Valproic Acid
- (C)** Lamotrigine
- (D)** Carbamazepine
- (E)** Oxcarbazepine

anticonvulsants

Enhance GABA inhibition

Block excitatory transmitters

Block neuronal Na channel

Block t-type ca channel

Mixed or unknown

A) VALPORIC ACID

mechanisms of actions:

- blocks sodium channels
- and increases GABA concentrations in the brain

Therapeutic uses:

- acute mania, mania with mixed features, and rapid cycling.
- All seizures types

Adverse effects :

- CNS : NDA (nystagmus , diplopia , ataxia)
- Liver : Microsomal enzymeinhibition
- Blood : neutropenia
- Teratogenic : craniofacial anomalies and neural tube deficit
 - Alopecia
 - Pancreatitis
- Fulminant hepatic toxicity weight gain

Valproic acid better tolerated than Lithium

Hemorrhagic Pancreatitis

Gross pathology of acute hemorrhagic pancreatitis. Hemorrhagic fat necrosis and a pseudocyst filled with blood are seen on cross section.



Formulation of Sodium Valproate...

B.CARBAMAZEPINE

Mechanism:

- Acts by blocking sodium channels and inhibiting action potentials.

Therapeutic uses :

- mania with mixed features and rapid cycling
- bipolar disorder

Adverse effects :

1. CNS : NDA (nystagmus , diplopia , ataxia)
- 1.Liver : Microsomal enzyme induction
- 2.Blood : Leukopenia, aplastic anemia, thrombocytopenia, and Agranulocytosis
- 3.Teratogenic : craniofacial anomalies (cleft palate) and neural tube deficit
- 4.Increase ADH secretion >> hyponatremia and edema
- 5.Significant drug interactions with many medications metabolized by the cytochrome P450 pathway
- 6.Toxicity: Confusion, stupor, motor restlessness, tremor, twitching, and vomiting.

C. LAMOTRIGINE

Mechanism:

- work on sodium channels that modulate glutamate and aspartate.

Therapeutic uses:

- Efficacy for bipolar depression,
- little efficacy for acute mania or prevention of mania.

- dizziness, sedation, headaches, and ataxia.
- Most serious side effect is Stevens Johnsons syndrome (life-threatening
- rash involving skin and mucous membranes) in 0.1%. This is most likely in the first 2 to 8 weeks, but is minimized by starting with low doses and increasing slowly.
- Valproate will ↑ lamotrigine levels
- and lamotrigine will ↓ valproate levels.

STEVENS– JOHNSON SYNDROME

(life-threatening rash involving skin and mucous membranes) in 0.1%. This is most likely in the first 2–8 weeks, but is minimized by starting with low doses and increasing slowly.



OTHER ANTICONVULSANTS

(1) Oxcarbazepine (Trileptal)

- As effective in mood disorders as carbamazepine, but better tolerated
- Less risk of rash and hepatic toxicity
- Monitor sodium levels for hyponatremia

2-Gabapentin (Neurontin)

- Often used adjunctively to help with anxiety, sleep, neuropathic pain
- Little efficacy in bipolar disorder

3-Pregabalin (Lyrica)

- Used in GAD (second-line) and fibromyalgia
- Little efficacy in bipolar disorder

4-Tiagabine (Gabitril): Questionable benefit in treating anxiety

5-Topiramate (Topamax)

- May be helpful with impulse control disorders

- Beneficial side effect is weight loss

- Can cause hypochloremic, metabolic acidosis, as well as kidney stones

- The most limiting side effect is cognitive slowing

SIDE EFFECTS

- GI symptoms
- Weight gain
- Sedation
- Alopecia
- Pancreatitis
- Hepatotoxicity or benign aminotransferase elevations
- ↑ ammonia
- Thrombocytopenia
- Teratogenic effects during pregnancy (neural tube defects)

AEDS AND PREGNANCY

■ Around 1-2 % of newborns born to non - epileptic mothers have congenital defects .

This rises to 3-4 % if the mother takes antiepileptic medication .

■ The risks of uncontrolled epilepsy during pregnancy generally outweigh the risks of medication to the fetus , so her drug should be continued .

■ Pregnant should be advised to take folic acid 5 mg / day well before pregnancy to minimize the risk of neural tube defects .

■ Best drugs in pregnancy : lamotrigine - levetiracetam

■ Breast feeding is acceptable with nearly ALL anti - epileptic drugs

ELECTROCONVULSIVE THERAPY (ECT)

ECT is the most effective treatment for major depressive disorder

- A generalized tonic-clonic seizure is then induced using unilateral or bilateral electrodes
- It is often used in patients who cannot tolerate medications or who have failed other treatments
- premedicated with atropine, and then given general anesthesia and muscle relaxants.
- typically a course of 8–12 sessions given three times weekly.
- Monthly maintenance ECT is often used to prevent relapse of symptoms.
- The most common side effects are muscle soreness, headaches, amnesia, seizure and confusion. And heart problems in long term but its rare .
- Contraindicated if there is space occupying intracranial lesion (increase icp)

A 26 year old male with a past medical history of an unknown mood disorder presents with some medical problems . On review of his labs you note the following :

WBCs : 2.2

hemoglobin : 14

platelets : 334

creatinine 0.3

Which of the following medications is responsible for this adverse drug reaction :

- lithium**
- valproic acid**
- lamotrigine**
- carbamazepine**
- oxcarbazepine**

TABLE 3. PSYCHIATRIC USES OF ANTIPILEPTIC DRUGS

Carbamazepine	Agitation, bipolar disorder, impulsivity
Clonazepam	Anxiety
Diazepam	Alcohol withdrawal, anxiety
Gabapentin	Anxiety
Lamotrigine	Bipolar disorder, refractory depression
Lorazepam	Agitation, alcohol withdrawal, anxiety
Oxcarbazepine	Aggression, bipolar disorder, impulsivity
Pregabalin	Anxiety
Topiramate	Alcohol withdrawal, binge eating
Valproic acid	Bipolar disorder

Mood stabilizer	Lithium	Valproic acid	Carbamazepine
Main use	First medical therapy for bipolar disorders	as Lithium in mania prophylaxis	1 st line for acute mania & mania prophylaxis
Note	Only medication to reduce suicide rate	not as lithium effective in depression prophylaxis	Indicated for rapid cyclers and mixed patients
SEFs	Tremor, Confusion, Seizure , Nausea, vomiting , diarrhea, Hypothyroidism Hyperparathyroidism hypercalcemia Polyuria & polydipsia bradycardia Mild leukocytosis	Thrombocytopenia Nausea, vomiting, weight gain, Transaminitis, Sedation, tremor, hair loss and Increased risk of neural tube defect	Rash, Nausea, vomiting, diarrhea, transaminitis ,Sedation, dizziness, ataxia, confusion ,AV conduction delays ,Aplastic anemia ,agranulocytosis Water retention
Before use it	baseline creatinine, TSH, CBC and pregnancy test	LFTs, CBC and pregnancy test	LFTs, CBC and EKG
Steady state achieved after	5 days	4-5 days	5 days
Target	blood level between 0.6-1.2	between 50-125	4-12mcg/ml

THANK
YOU