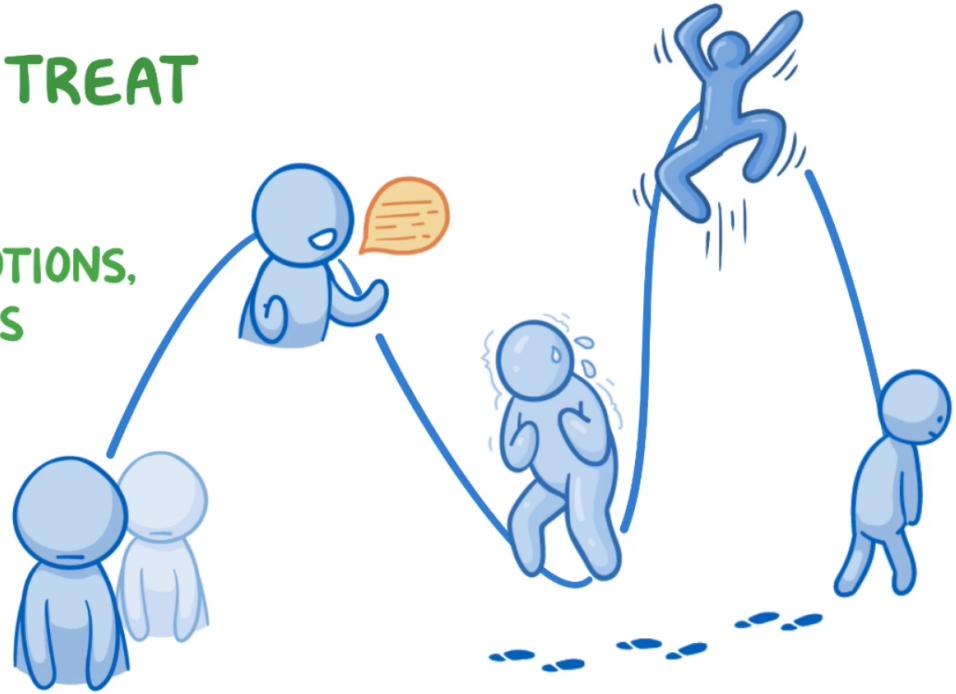
MOOD STABILIZERS

* MEDICATIONS used to TREAT **BIPOLAR DISORDER**

  ↳ DRAMATIC SHIFTS in EMOTIONS, MOOD, & ENERGY LEVELS



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

Acute mania

- Atypical antipsychotics:

Olanzapine, risperidone, quetiapine, ziprasidone , aripiprazole.

- Typical: haldol,chlopromazine
- Mood stabilizers: Lithium ,valproate, carbmazipine

Maintenance

- Lithium (gold stnadard)
- Valproate
- Carbamazipine
- Lamotrigene

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)

FIRST-LINE:

* LITHIUM

OTHER MEDICATIONS:

ANTIEPILEPTICS

* CARBAMAZEPINE
* VALPROIC ACID
* LAMOTRIGINE

ANTIPSYCHOTICS

* OLANZAPINE

LITHIUM

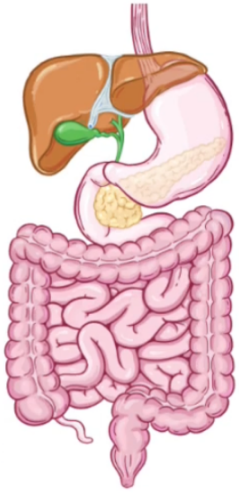
TAKEN ORALLY

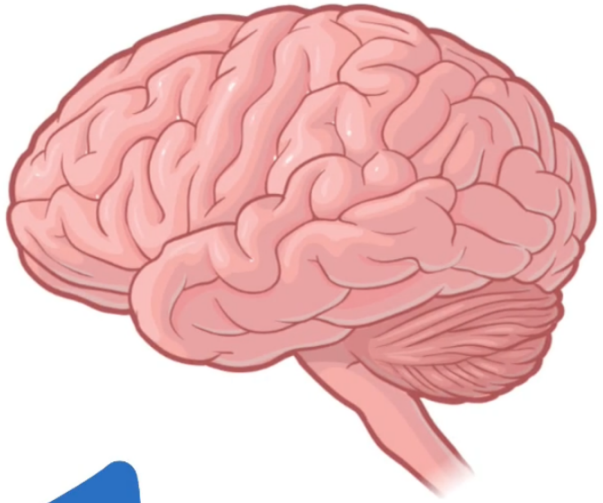
↓

RAPIDLY ABSORBED by GI TRACT

↓

TRAVELS to BRAIN



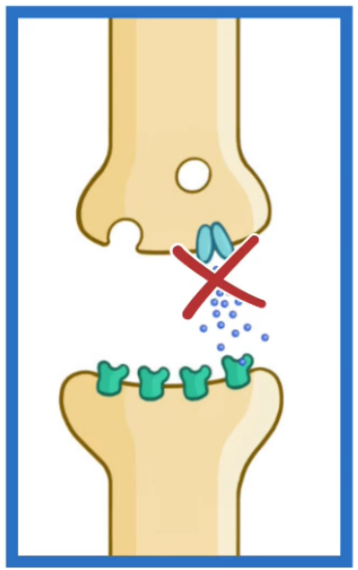


* REGULATES RELEASE of NEUROTRANSMITTERS

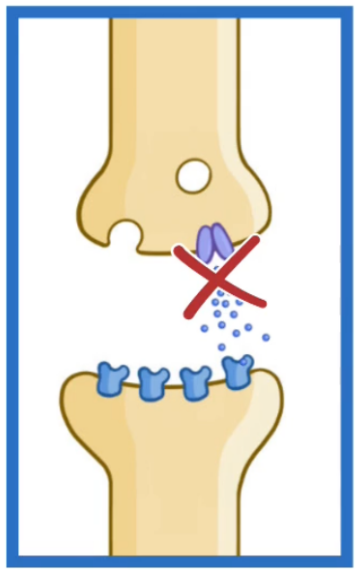
LITHIUM

* INHIBIT RELEASE

NOREPINEPHRINE

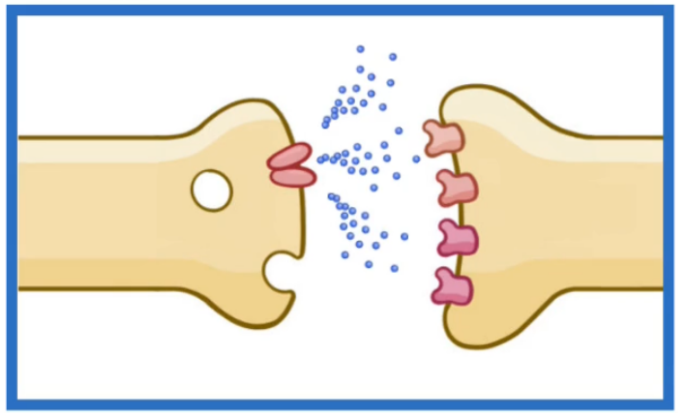


DOPAMINE



* ↑↑ PRODUCTION

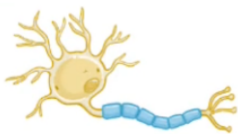
SEROTONIN

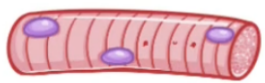


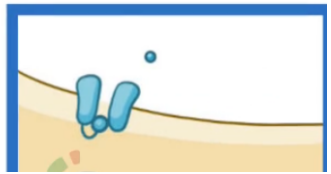
* ALTERS Na^+–K^+ ION TRANSPORT

NEURONS

MUSCLE CELLS







Indications

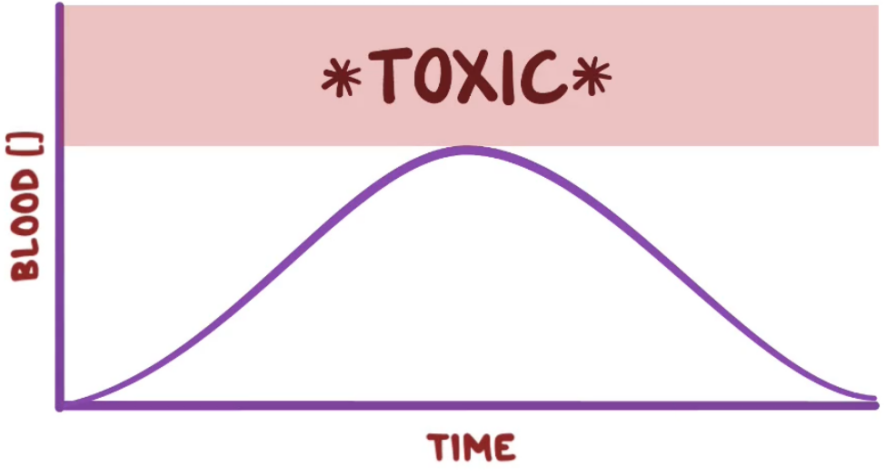
- in acute mania

- and as prophylaxis for both manic and depressive episodes in bipolar and schizoaffective disorders.

- It is also used in cyclothymic disorder and unipolar depression.

SIDE EFFECTS

* BOXED WARNING for TOXICITY
  - NARROW THERAPEUTIC INDEX
    - SMALL VARIATIONS in BLOOD CONCENTRATIONS can result in SERIOUS SIDE EFFECTS & TOXICITY



Side effects :

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 :

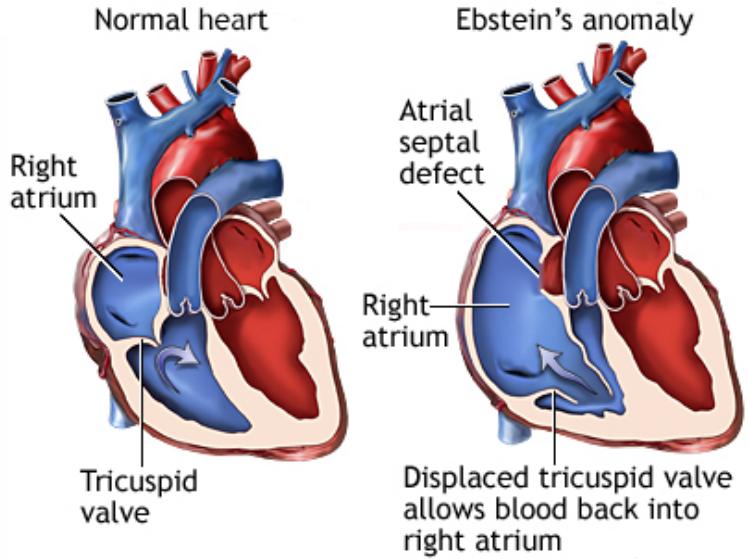
- **Hyothyroidismp, Goiter**
- **Memory impairment**
- **Nephro toxicity**
- **ECG changes : T wave flattening**
- **Arrhythmia**

Just to remember

- L- leucocytes
- I – Increased
- T – Tremors
- H- Hypothyroidism
- I- Increased
- U- Urine

Diabetes Insipidus

- M- should be avoided in expectant MOTHER as it causes Ebstein's anomaly



Toxicity

mild	plasma levels 1.5-2 mEq/L	1. anorexia 2. vomiting 3. diarrhoea 4. coarse tremor 5. ataxia 6. Dysarthria تلعثم 7. confusion 8. Sleepiness
moderate	2-2.5 CNS	1. impaired consciousness 2. neurological signs: 3. nystagmus 4. muscle twitching 5. hyperreflexia 6. convulsions
Severe overdosage	>2.5	1. toxic psychosis 2. convulsions 3. syncope 4. oliguria 5. circulatory failure 6. coma and death

Management of 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

Prior to initiating, patients should have :

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

Mood stabilizers include :

1. lithium

- the first-line mood stabilizer .

2. anticonvulsants

most commonly
- valproic acid,
- lamotrigine,
- and carbamazepine.

3. antisychotics

- olanzapine

Anticonvulsants

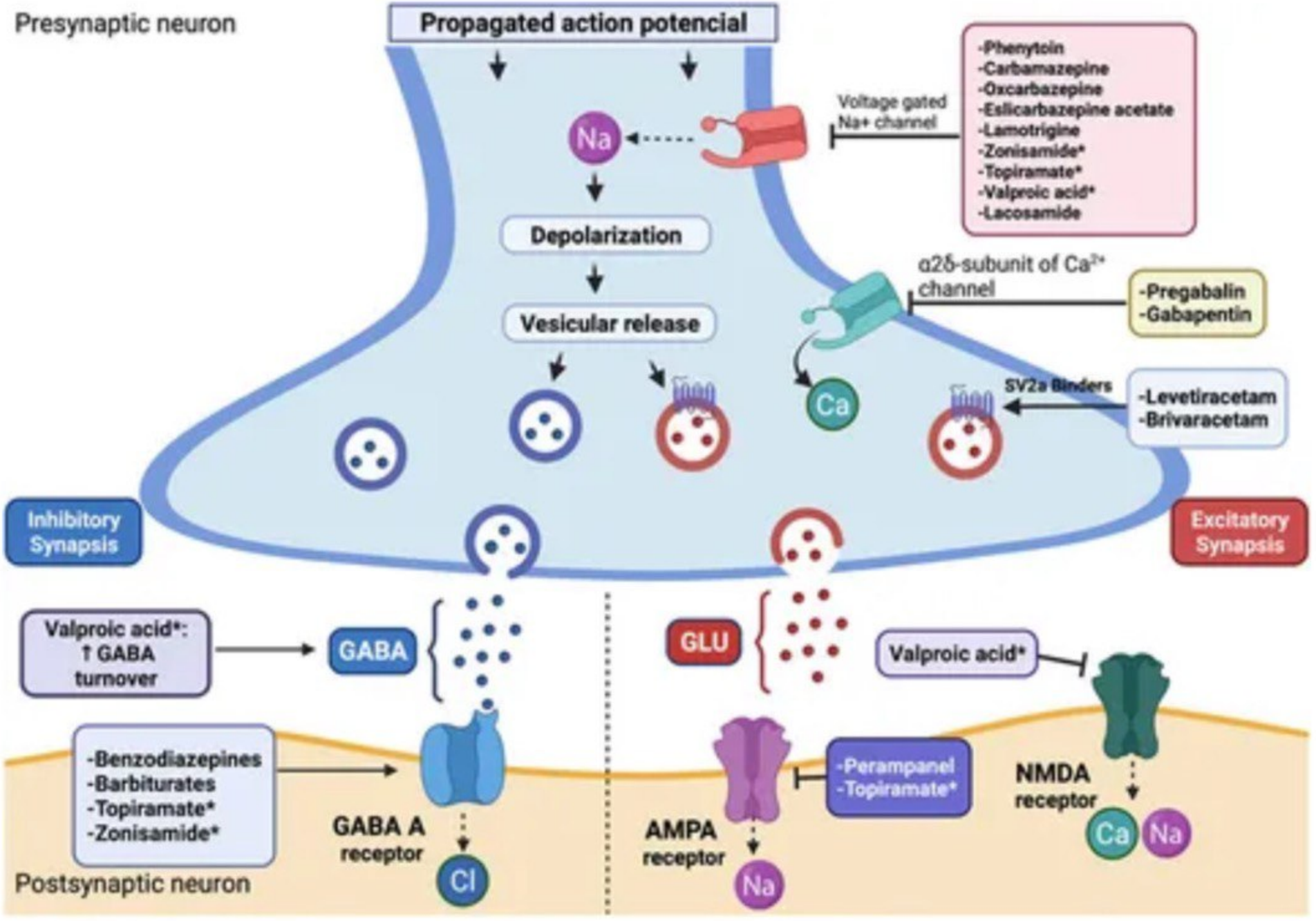
Enhance GABA inhibition

Block excitatory transmitters

Block neuronal Na channel

Block t-type ca channel

Mixed or unknown


Presynaptic neuron
Propagated action potencial
Na
Depolarization
Vesicular release
Voltage gated Na+ channel
-Phenytoin
-Carbamazepine
-Oxcarbazepine
-Eslicarbazepine acetate
-Lamotrigine
-Zonisamide*
-Topiramate*
-Valproic acid*
-Lacosamide
α2δ-subunit of Ca2+ channel
-Pregabalin
-Gabapentin
Ca
SV2a Binders
-Levetiracetam
-Brivaracetam
Inhibitory Synapsis
Excitatory Synapsis
Valproic acid*: ↑ GABA turnover
GABA
GLU
Valproic acid*
-Benzodiazepines
-Barbiturates
-Topiramate*
-Zonisamide*
GABA A receptor
Cl
AMPA receptor
Na
-Perampanel
-Topiramate*
NMDA receptor
Ca
Na
Postsynaptic neuron

Valporic Acid

Mechanism

Multiple mechanisms of action:

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

Theraputic uses

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

Addverse effect

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

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...

Carbamazepine

Mechanism

- Acts by blocking sodium channels and inhibiting action potentials.

Theraputic uses

- mania with *mixed features* and *rapid-cycling*
- bipolar disorder

Addverse effect

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

lamotrigine

Mechanism

work on sodium channels that modulate glutamate and aspartate.

Theraputic uses

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

Addverse effect

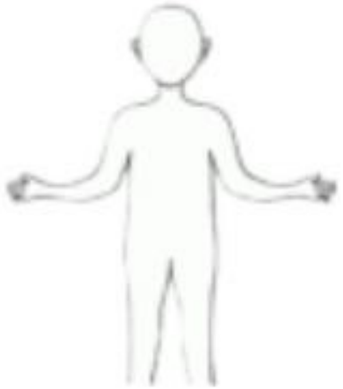
- dizziness, sedation, headaches and ataxia.
- **Stevens-Johnson syndrome**
- Valproate will ↑ lamotrigine levels, and lamotrigine will ↓ valproate levels
- Insomnia

Stevens–Johnson Syndrome

< 10% — Body surface area — > 30%

SJS | Toxic epidermal necrolysis

Lesions start on face & thorax



Etiology

Drugs
- Sulfonamides
- Phenobarbital, carbamazepine, lamotrigine
- Allopurinol
- NSAIDs

Infection
- *Mycoplasma pneumoniae*

Clinical
- Prodrome (influenza-like)
- Cutaneous lesions (coalescing erythematous macules with purpuric centers)
- Mucosal lesions (can precede or follow skin eruptions)
- Urethritis

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)

TABLE 3. PSYCHIATRIC USES OF ANTIEPILEPTIC DRUGS	
Carbamazepine	Agitation, biopolar 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

Lab Tests for Mood Stabilizers

Lithium

- Serum level: target 0.6 - 1.2 mmol/L
- Electrolytes (sodium, potassium)
- Kidney function (creatinine, GFR)

Valproic acid

- Serum level: target 50-100 mcg/L (American) or 350-700 mmol/L (SI units)
- Liver enzymes

Carbamazepine

- Serum level: target 4-12 mcg/L (American units) or 20-50 mmol/L (SI units)
- Complete blood cell count (CBC)

A Quick Guide to Common Lab Tests

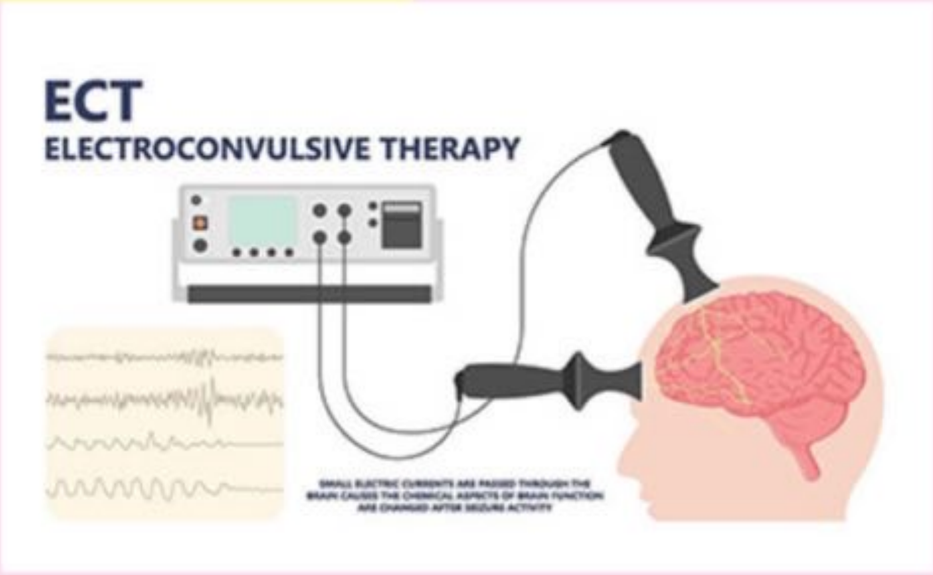
AEDS and pregnancy

- ■ 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

ECT

ELECTROCONVULSIVE THERAPY

- 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 .

Any Questions?

Thank you for listening.