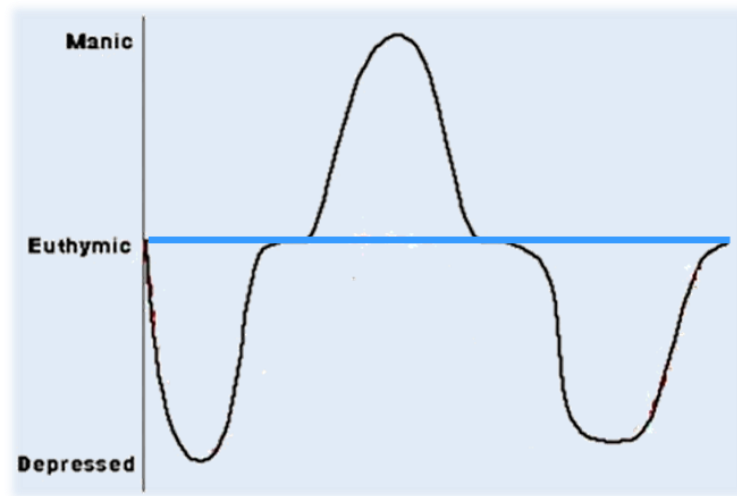


Mood stabilizing drugs

Definition: Is a psychiatric medication used for the treatment of mood disorders characterized by intense and sustained mood shifts typically seen in bipolar depression.



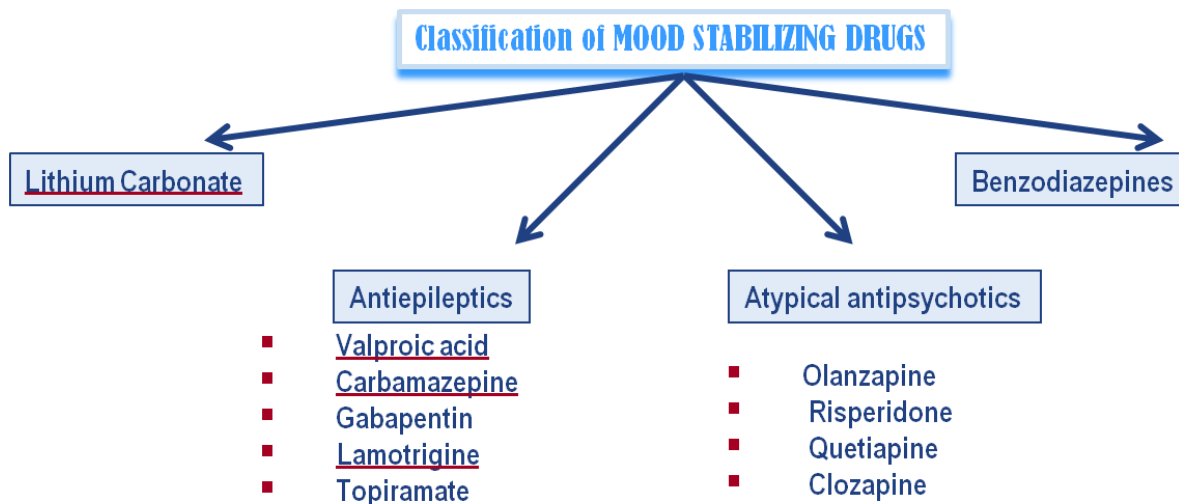
Manic: high energy levels, mood, and cognition. Depression is the opposite. Separated by periods of normal mood

Types of mood cycling:

- Rapid: in the course of a day or multiple times a week
- Slow: stuck in one mood or the other for weeks or months at a time

Actions of mood stabilizer:

- Circadian cycle becomes slower and longer
- Metabolism, hormones, transmitters, sleep-wake patterns become adjusted.



Uses of them:

- Prophylaxis in bipolar disorder with therapeutic effects becoming more predominant, either for prevention of depression or mania
- Mono- or in combination therapy with lithium in acute mania

Lithium

Pharmacokinetics:

Absorption: completely absorbed from the GIT. Peak plasma levels in 30 min—2h

Distribution: distributed in all body fluids. Not bound to plasma proteins. Slow entry into intracellular compartment

Metabolism: none

Excretion: entirely in urine. Lithium clearance is about 20% of creatinine. Less excretion occurs in milk, feces, sweat. Has a narrow therapeutic range. Monitoring of plasma levels is essential. Plasma $t_{1/2}$ 20h

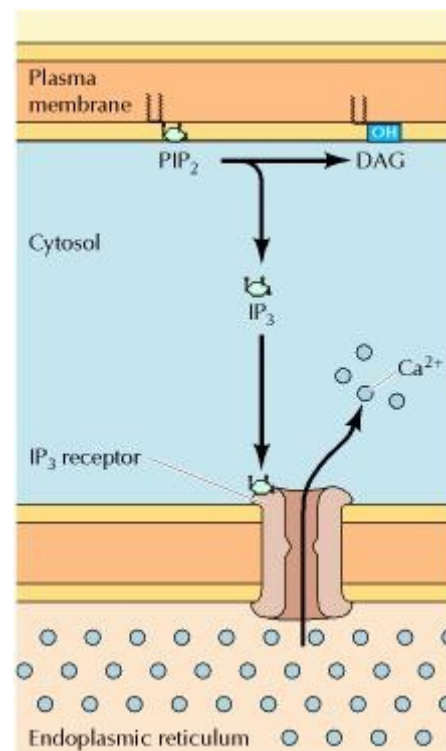
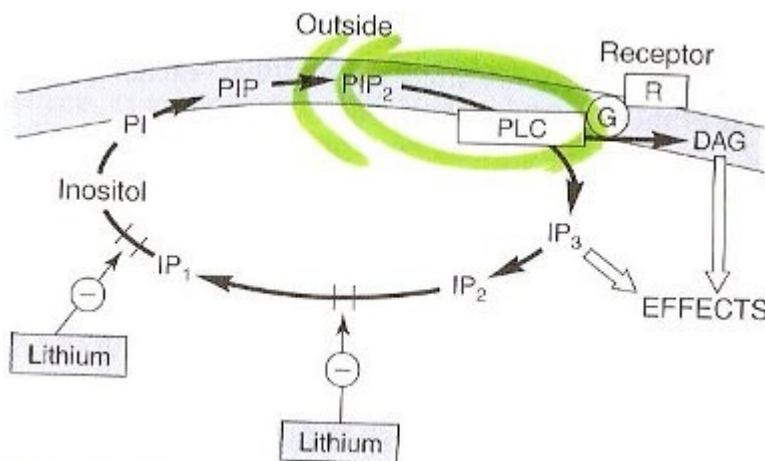
Has a slow onset of action (takes 3-4days to act, so sedative drugs should be given as haloperidol IV)

Mechanism of action:

1. Substituting ions such as Na: alter excitability thresholds, conductivity potentials

Revision of second messenger pathway: from this figure, the ligand will bind to the receptor which lead to production of IP_3 from PIP_2 by the action of phospholipase C. IP_3 when it completes its action will be converted to $IP_2 \rightarrow IP_1 \rightarrow$ inositol $\rightarrow PIP_2$.

2. *Lithium* prevents 2 steps which are $IP_2 \rightarrow IP_1$ and $IP_1 \rightarrow$ inositol. Therefore, the action of adrenaline and Ach is prevented as the second messenger pathway is inhibited.



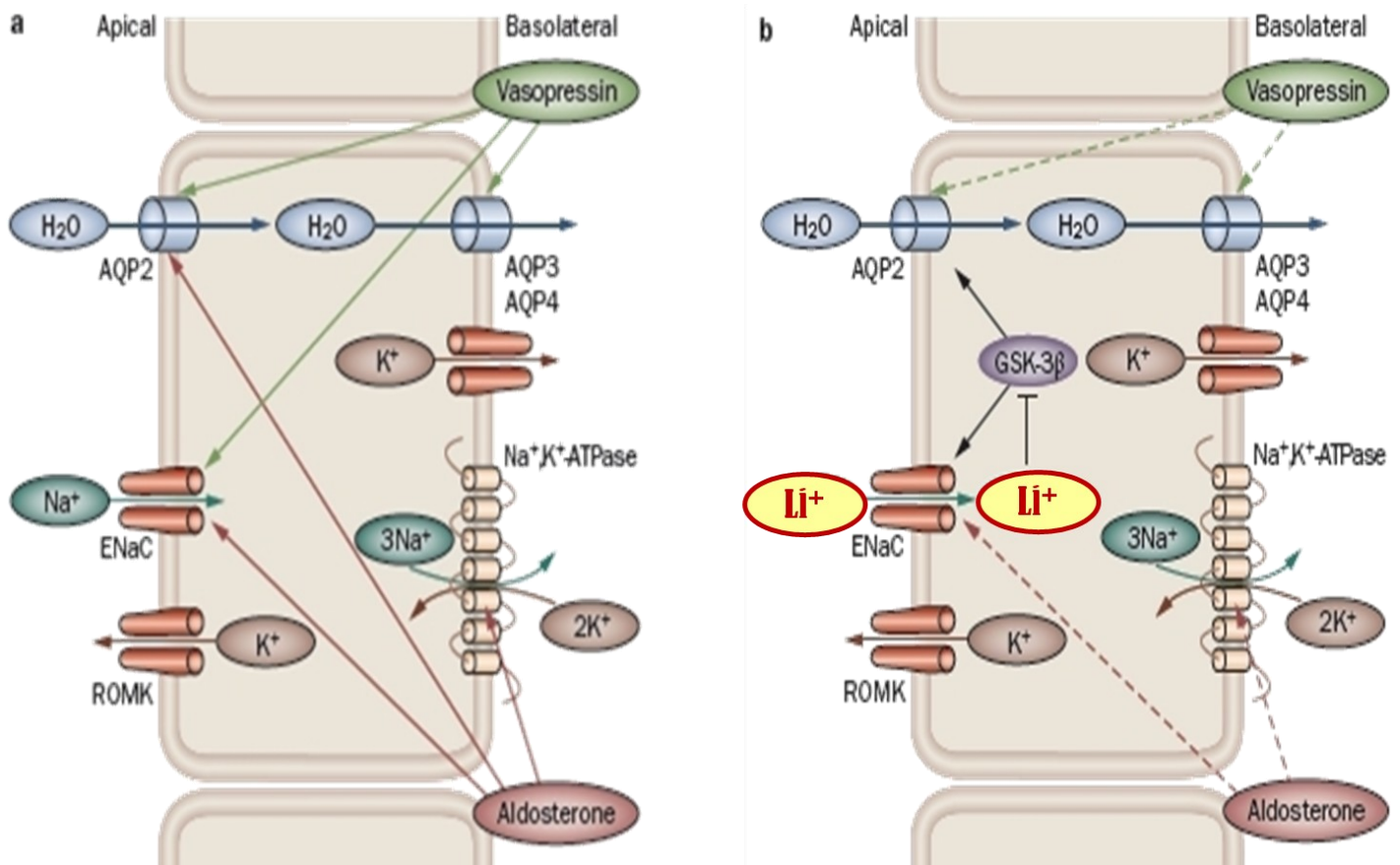
3. Lithium inhibits norepinephrine-sensitive adenylyl cyclase.
4. Reduces myoinositol \rightarrow alteration of protein kinase C \rightarrow alteration of genes responsible for neuroplasticity and neuroprotection.
5. Inhibits glycogen synthase kinase-3 (GSK-3) \rightarrow circadian cycle becomes slower and longer.

Clinical uses:

- Treatment of bipolar affective disorders
- Prophylactic of manic-depressive disorders
- Schizoaffective disorders
- Acute mania
- Aggressive behavior in children
- Premenstrual dysphoria
- Leukopenia; used with other drugs that cause *leukocytosis as an adverse effect*

Adverse effects:

- ⇐ Neurologic effects mainly tremor (alleviated by propranolol or atenolol)
- ⇐ Psychotic effects as mental confusion
- ⇐ Renal effects
 - Polyurea and polydipsia by causing diabetes insipidus*
 - Prolong use may cause chronic interstitial nephritis or nephrotic syndrome
- ⇐ Edema, hypernatremia, increase body weight
- ⇐ Decreased thyroid function: due to uncoupling of TSH receptor from its G proteins
- ⇐ Cardiac effects:
 - Bradycardia-tachycardia (sick sinus syndrome)
 - T wave flattening in ECG
- ⇐ Transient acne eruption and folliculitis
- ⇐ Leucocytosis



**Effects of lithium on vasopressin receptor*

Drug interactions:

- ⇐ Diuretics e.g. thiazides → ↓25% renal clearance of Lithium
- ⇐ NSAIDs decrease renal clearance of lithium
- ⇐ Antipsychotic drugs mainly typical drugs causing severe extrapyramidal adverse effects. (except clozapine and newer antipsychotics)

Pregnancy:

Pregnancy → ↓plasma level of lithium

Post partum → ↑plasma level of lithium suddenly

Newborn:

Breast milk contains a concentration of one-third to one-half that of serum.

Toxicity in newborns is manifested by lethargy, cyanosis, poor suck, Moro reflexes, and hepatomegaly.

Lithium toxicity:

- Therapeutic overdoses are more common than accidental ingestion
- Any value over 2 mEq/L must be considered as indicating likely toxicity
- Toxicity develops when given in the following cases:;
 - ⇐ Renal dysfunction
 - ⇐ Postpartum
 - ⇐ Dehydration or low salt diet
 - ⇐ Use of drugs

Treatment: peritoneal dialysis and hemodialysis

Done.