# DRUGS USED IN MOOD DISORDERS

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# LEARNING OUTCOMES

By the end of the lecture, students will be able to describe the following with regard to mood stabilizers

- Mechanisms of action
- Pharmacokinetics
- Adverse and toxic effects

# OUTLINE....

A. Definition-Bipolar Affective Disorder

B. Classification of Mood Stabilizers

C. Pharmacological Profile of Lithium

D. Toxicity of Lithium

# BIPOLAR AFFECTIVE DISORDER

- Recurrent episodes of elevated mood and depression, together with changes in activity levels

# MANIC SYMPTOMS

- Elevated  or irritable mood
- Increased activity or psychomotor agitation
- Reduced need for sleep
- Inflated self esteem or grandiosity
- Increased or pressure of speech
- Flight of ideas

# TREATMENT OF BPD

- Acute treatment of episodes of illness aims to resolve symptoms and reduce immediate risk to self or others

- Long term treatment aims to prevent future episodes of illness and help regain a premorbid level of functioning and reduce longer term suicide risk

# MOOD STABILISERS

A. **Lithium**
B. **Anticonvulsants**
    i. Sodium valproate
    ii. Carbamazepine
    iii. Lamotrigine
C. **Antipsychotics**
    i. Quetiapine

# LITHIUM

- Lithium carbonate and lithium citrate used therapeutically
- Mechanism of action – poorly understood
- Several hypotheses:
  I. impact on monoamines
  II. affect secondary messengers

# PHARMACOKINETICS

- Absorbed readily and almost completely from the GI tract; peak concentrations in 1-2 hrs
- Distributes to a volume of distribution ~TBW
- Elimination
  - 95%- in urine
  - 4-5% - in sweat
  - 1% - in faeces

# RENAL ELIMINATION

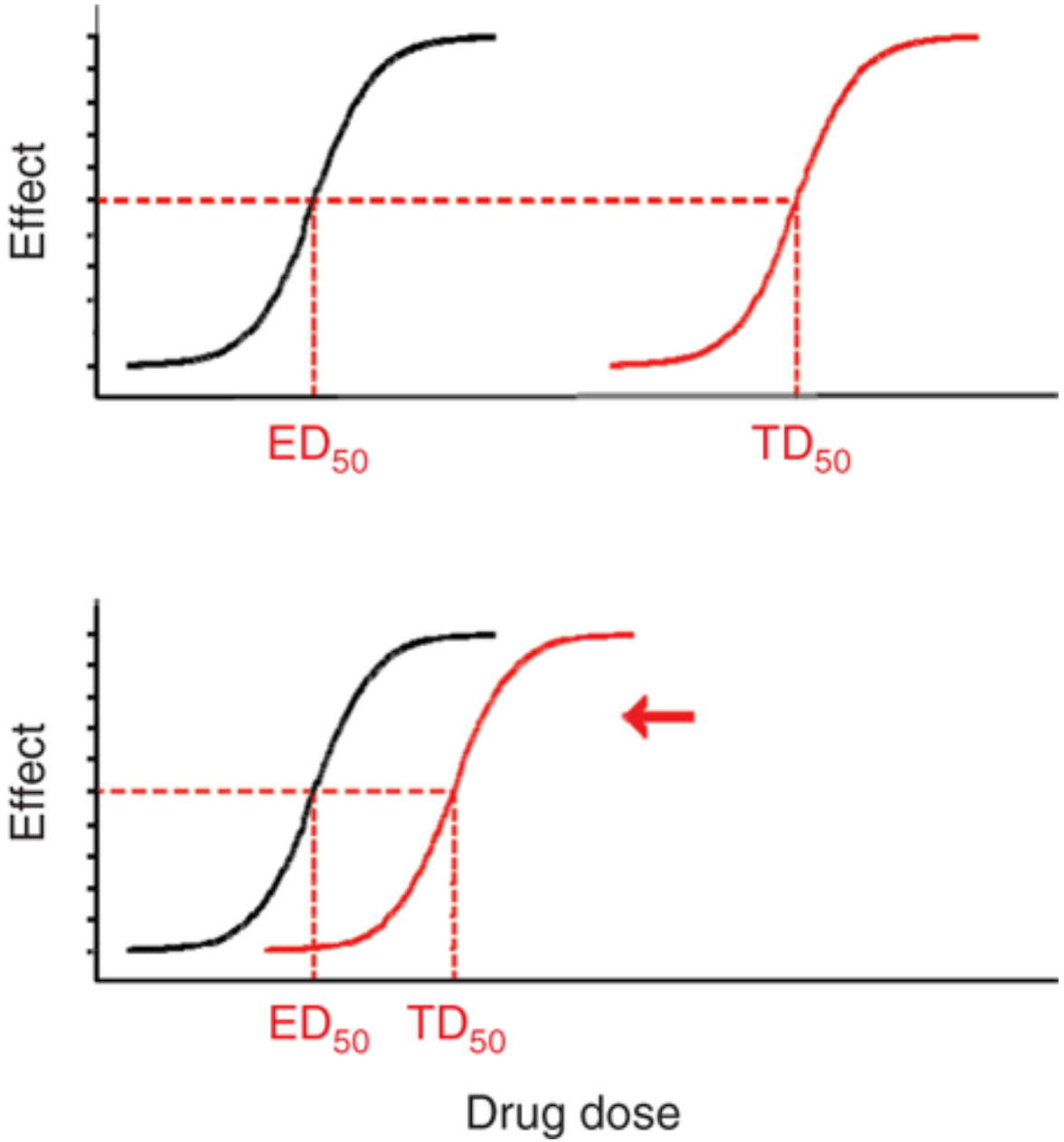
- Two phases:
  - initial phase – first 6-12 hrs
  - slow phase- over the next 10-14 days
- Elimination $t_{1/2}$ ~ 20-24 hours

- Completely filtered, and 80% is reabsorbed in the proximal tubules
- $Li^+$ competes with $Na^+$ for reabsorption, and $Li^+$ retention increased by $Na^+$ loss

  e.g. Diarrhoea, thiazide diuretics

# SERUM LEVEL MONITORING

- Serum concentrations of $Li^+$ follow a clear dose-effect relationship between 0.4 and 1.0 mEq/L
- But with a corresponding dose-dependent rise in polyuria and tremor as well i.e. Narrow therapeutic index
- $\therefore$ Serum level monitoring crucial
- Therapeutic Li concentration : 0.6 - 1.0 mmol/L


Effect
ED50
TD50
Effect
ED50
TD50
Drug dose

# ADVERSE DRUG REACTIONS

- GI Effects:
  - Anorexia
  - Nausea, vomiting
  - Abdominal pain
  - Diarrhoea

# ADVERSE DRUG REACTIONS

- CNS Effects
  - Fine hand tremor
  - Incoordination, ataxia, or slurred speech
  - Seizures
  - Weight gain
- Renal Effects
  - Nephrogenic diabetes insipidus - polyuria and compensatory polydipsia

# ADVERSE DRUG REACTIONS

- Endocrine Effects
  - Goitre and hypothyroidism commonly

    (Due to competition for the iodide transport within the thyroid and inhibition of synthesis and release of thyroid hormones)

  - Rarely thyrotoxicosis

    (Due to direct toxic effect of lithium on the thyroid gland)

# ADVERSE DRUG REACTIONS

- Cardiac Effects:
  - ECG changes(common) - T-wave flattening/inversion and appearance of U waves
  - Very rare – tachy/brady arrhythmias
    e.g. AV conduction block
    Torsade de pointes

# ADVERSE DRUG REACTIONS

- Skin Effects:
  - Allergic reactions -dermatitis, folliculitis, and vasculitis
  - Acne- worsening and new onset
  - Psoriasis – worsening as well as new
  - Alopecia

# Li and Pregnancy

- 1st Trimester:Cardiovascular anomalies of the newborn, especially Ebstein's malformation

- 3rd Trimester: Neonatal goiter, CNS depression, hypotonia ("floppy baby" syndrome)

# DRUG INTERACTIONS

- Diuretics(esp. thiazides)
- NSAIDs
- ACEIs, ARBs

} Li Retention

- Xanthines (theophylline,caffeine)

reduce Li concentration

# Li TOXICITY

- Levels > 1.5 mEq/L are toxic

**MILD**
Nausea
Diarrhoea
Blurred vision,
Polyuria
Fine tremor
Muscle weakness
Drowsiness

**MODERATE**
Confusion/stupor,
Fasciculation
Increased reflexes
Myoclonic jerks,
Choreoathetosis

**SEVERE**
Coma Convulsions
Irreversible CNS damage
Cardiac toxicity
(Heart block, low BP)
Renal failure