24 - D. Mood stabilisers

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© SPMM Course D. Mood stabilisers Lithium is orally well absorbed but not metabolized in the liver; it is renally excreted. Lithium carbonate and citrate are not bioequivalent preparations; hence the careful prescribing practice is required. Lithium is rapidly and completely absorbed after oral administration. Lithium takes 45 days to achieve a steady state in healthy young males. It is not protein bound. Lithium's plasma half-life is around 18 hours initially but later after 1 year of chronic use increases to 36 hours. Lithium is excreted via the proximal tubules where sodium is also filtered. Hence, any loss of body sodium can increase lithium reabsorption as compensation in error leading to toxicity. Hence maintaining sodium homeostasis is important in patients on lithium therapy.

Agents increasing lithium levels Agents decreasing lithium levels Toxicity with normal levels ACE inhibitors Osmotic diuretics Carbamazepine – increased antithyroid effect and neurotoxicity Loop diuretics Caffeine Atracurium – increased neuromuscular blockade Fluoxetine Aminophylline Haloperidol, clozapine – increased neurotoxic effects NSAIDs Theobromine, Theophylline Calcium channel blockers – increased neurotoxicity Thiazides Carbonic anhydrase inhibitors Metronidazole – increased neurotoxicity Valproate is available as semisodium compound (divalproex) and as sodium salt of the valproic acid. Divalproex consists of half valproic acid and half sodium valproate. Semisodium compound is somewhat better tolerated. Valproate is well absorbed, with a bioavailability close to 100%. It is quite hydrophilic, with a low volume of distribution. Valproate has t1/2 of 9 to 16 hours and is highly (90%) protein bound. This binding is saturable so that at higher doses a greater percentage of the drug may be in the free form. At higher doses, the increased free fraction may remain in the plasma compartment (rather than escaping into the tissues) and thus be cleared by the liver. This may yield ‘‘sublinear’’ kinetics so that with higher plasma concentrations, greater increases in dose may be required to yield the desired increase in plasma level (Graves, 1995). Binding interactions occur so that VPA can increase free diazepam. Carbamazepine has a tricyclic structure and undergoes hepatic metabolism. It has an erratic absorption and a bioavailability of about 80%. It is about 75% bound to plasma proteins. Carbamazepine induces its own breakdown. Before autoinduction of the epoxide pathway (via induction of CYP3A3/4), the half-life of CBZ is about 24 hr, and the clearance is about 25 mL/ min. After autoinduction (2 to 4 weeks into therapy), the half-life falls to about 8 hr, and clearance rises

Revision #1
Created 2026-01-04 20:04:19 UTC by Omar Ayman
Updated 2026-01-04 20:04:19 UTC by Omar Ayman