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Skin effects

© SPMM Course Gastrointestinal effects Valproate inhibits hepatic enzymes; in some cases the acute liver injury may occur though this is rare in clinical practice. Of persons taking valproate, 5 to 40 percent experience a persistent but clinically insignificant elevation in liver transaminases up to three times the upper limit of normal, which is usually asymptomatic and resolves after discontinuation of the drug (termed ‘transaminitis’). Liver failure is reported with valproate, lamotrigine, topiramate and carbamazepine. Risk factors include young age and combination therapy. This is caused by 2 mechanisms: 1. Metabolic toxicity e.g. due to 4-en valproate, a metabolite of valproate. 2. Hypersensitivity - doseindependent effect is resulting in fulminant failure. Severe hepatic damage associated with valproate is seen especially in those with learning disability when undiagnosed urea cycle disorders are present (less than 2 years often). Another rare side effect of valproate is acute pancreatitis. This is a hypersensitivity reaction; dose reduction will not be helpful. Hyperammonemia can be associated with coarse tremor and carbamazepine co-prescription; it may respond to L-carnitine administration. Valproate competes with carnitine transport and can induce a state of carnitine depletion especially in children and in epileptics. Teratogenic effects The most common teratogenic effect of lithium involves cardiac valves especially Ebstein's anomaly of the tricuspid valves. The risk of Ebstein's malformation in lithium-exposed fetuses is 1 of 1,000 (20 times the risk in the general population). Lithium’s teratogenic effects are somewhat lower than that caused by the use of valproate or carbamazepine. Lithium is excreted into breast milk, and signs of lithium toxicity in infants include lethargy, cyanosis and sluggish neonatal reflexes. Valproate causes neural tube defects as a teratogenic effect in 1% to 4% mothers. Folate-vitamin B complex supplementation for all young women of childbearing potential may reduce risk though it is best to avoid valproate totally. Learning disability and low IQ in children is the most common teratogenic effect of valproate. Skin effects Exacerbation of acne and psoriasis are associated with lithium therapy. Alopecia / hair loss occurs in 5 to 10 percent. It is not clear if zinc and selenium supplementation can reverse or prevent the latter effect.

Revision #1
Created 2026-01-04 20:04:40 UTC by Omar Ayman
Updated 2026-01-04 20:04:40 UTC by Omar Ayman