



Clinical Pharmacology & Toxicology Pearl of the Week

~ Carbamazepine ~

- ✓ Carbamazepine (CBZ) is an antiepileptic drug commonly prescribed for seizure disorders, trigeminal neuralgia, neuropathic pain, schizophrenia & bipolar disorder
- ✓ It is structurally related to the Tricyclic Antidepressants (amitriptyline, imipramine, nortriptyline)
- ✓ Its mechanism of action involves:
 - Antagonism of inactivated voltage-dependent Na⁺ channels
 - Antagonism of L-type voltage-gated Ca⁺² channels
 - Adenosine receptor agonism (at therapeutic doses) & antagonism (at toxic doses)
 - Anticholinergic properties (antimuscarinic)
 - Serotonin reuptake inhibition
 - Inhibition of glutamate neurotransmission
- ✓ At therapeutic doses CBZ is well absorbed, highly protein bound and has a Vd of 0.8-2.0 L/kg
- ✓ CBZ is largely metabolized by CYP3A4, has several active metabolites that are excreted mostly via the kidneys and should be avoided in CrCl < 60
- ✓ CBZ is a **strong** CYP & P-glycoprotein inducer and has MANY drug interactions; it should NOT be taken with grapefruit juice
- ✓ HLA-B*1502 testing should be considered prior to starting CBZ, especially in patients with ancestry from China, India and Southeast Asia, as these patients are at a significantly increased risk of SJS/TEN
- ✓ Carbamazepine undergoes enterohepatic recirculation, and as such is amenable to multi-dose activated charcoal therapy after overdose
- ✓ Carbamazepine is moderately dialyzable. Dialysis may be considered for severe poisonings, particularly those with recurrent seizures or dysrhythmias

Table 1. Complications of Carbamazepine at Therapeutic Doses and in Toxic Ingestions

<u>Adverse Effects of Carbamazepine Therapy</u>		<u>Acute Carbamazepine Toxicity</u>	
		<u>System/Toxidrome</u>	<u>Signs/Symptoms</u>
Common	Dizziness Drowsiness Ataxia Nausea Vomiting Constipation Rash &/or photosensitivity SIADH	Neurologic	Confusion Drowsiness Ataxia Dysmetria Nystagmus Myoclonus, Dyskinesia Seizure Coma
Less common / Severe	Vitamin D deficiency Osteomalacia SJS/TEN DRESS, AGEP Myelosuppression (can be severe) Elevated liver enzymes & hepatitis		Cardiovascular
		Anticholinergic toxidrome	
		Serotonin Syndrome	

The Clinical Pharmacology physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. Clinical Pharmacology consultations are also available through the Netcare e-referral process and through Specialist Link. Our service is also listed in the [Alberta Referral Directory](#). Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found [HERE](#).

More CPT Pearls of the Week can be found [HERE](#).