



## 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<sup>+</sup> channels
  - Antagonism of L-type voltage-gated Ca<sup>+2</sup> 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 V<sub>d</sub> 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. See the EXTRIP website for more details.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching "Pharmacology" from the ARD home page. 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 in [Alberta Referral Directory](#) (ARD) by searching "Toxicology" from the ARD home page.

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

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**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
			Cardiovascular
Less common / Severe	Vitamin D deficiency Osteomalacia SJS/TEN DRESS, AGEP Myelosuppression (can be severe) Elevated liver enzymes & hepatitis	Anticholinergic toxidrome	
		Serotonin Syndrome	