



# Clinical Pharmacology & Toxicology Pearl of the Week

## ~ Drug-Induced Seizures ~

Major mechanisms involved in drug induced seizures:

1. Antagonism of inhibitory neurotransmitters like GABA, glycine, adenosine, histamine
2. Agonism of excitatory neurotransmitters like glutamate and acetylcholine
3. Metabolic disturbances (hypo/hypernatremia, hypomagnesemia, hypocalcemia, hypoglycemia)
4. Sodium channel blockade

Table 1: Xenobiotics causing seizure by class (non-exhaustive list, **common causes bolded**)

Analgesics	Mefenamic acid (NSAID), salicylate, opioids (meperidine, propoxyphene, <b>tramadol</b> )
Anticonvulsants	Carbamazepine, topiramate
Cellular asphyxiants	CO, CN, H <sub>2</sub> S, azides
<b>Antidepressants</b>	<b>TCA</b> , <b>citalopram</b> /escitalopram (SSRI), <b>venlafaxine</b> /desvenlafaxine (SNRI), <b>bupropion</b> (NDRI)
Antipsychotics	Phenothiazines, butyrophenones, atypical (olanzapine, quetiapine). These lower seizure thresholds but usually not sole cause
Antihistamines	<b>Diphenhydramine</b> , doxylamine
Drugs of abuse	<b>Amphetamine</b> , MDMA, cocaine, phencyclidine, GHB
Hypoglycaemics	Insulin, sulfonylureas
Heavy metals	Arsenic, lead, thallium
Sodium channel blockers	Propranolol, local anesthetics, antimalarials (chloroquine, hydroxychloroquine, quinine), antidysrhythmics (flecainide)
Substance withdrawal	<b>Ethanol</b> , benzodiazepines, phenobarbital, baclofen, GHB
Plants, herbs, natural products	Water hemlock, <i>Gyromitra</i> mushroom, Ephedra, Nicotine
Miscellaneous	Boric acid, camphor, fluoride, <b>isoniazid</b> , iron, organophosphates, carbamates, organochlorine pesticides, rodenticides (bromethalin, zinc phosphide), methylxanthines (theophylline, caffeine)

Alternatively, the mnemonic OTISCAMPBELL may be used:

<b>O</b>	Organophosphate, oral hypoglycemics, opioid
<b>T</b>	TCA, theophylline
<b>I</b>	Isoniazid, Insulin
<b>S</b>	Salicylates, Sympathomimetics, Strychnine
<b>C</b>	Cocaine, Camphor, CO, CN
<b>A</b>	Amphetamines, anticholinergics, amantadine, antibiotics (beta-lactams)
<b>M</b>	Methylxanthines
<b>P</b>	Pesticides/insecticides, PCP, plants (water hemlock)
<b>B</b>	Benzodiazepine withdrawal
<b>E</b>	Ethanol Withdrawal
<b>L</b>	Lead, lithium, lindane,
<b>L</b>	Local anesthetics

### Management:

- ABC, rule out hypoglycemia, consider decontamination and elimination
- GABA agonists: Benzodiazepines (midazolam, diazepam, lorazepam) are indirect GABA agonists and are first line therapy. Phenobarbital and propofol are direct GABA agonists and can terminate seizures when benzodiazepines fail
- Avoid phenytoin as it is a sodium channel blocker which treats seizures with a structural focus. Drug induced seizures are generalized processes for which phenytoin is ineffective
- Consider pyridoxine (Vit B6) in suspected cases involving pyridoxine deficiency (INH, hydrazine, *Gyromitra* mushroom) overdose. Empiric dose is 5g IV in adult or 70mg/kg in children, or give gram per gram amount if ingested dose known



The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click [HERE](#) for clinical issues the CP service can assist with.



The Poison and Drug Information Service (**PADIS**) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.