

Chapter 21 : Medicinal Poisons

Introduction :

• Large doses of any medicine may cause cardiotoxicity or neurotoxicity but when toxicity occurs it usually does so as a result of the drug's shared ability to stimulate the same set of brain receptors as are stimulated by abused drugs. **For example :**

- Analgesics such as oxycodone and hydrocodone bind to the same set of **μ receptors** as 'morphine'.
- Antitussives, such as dextromethorphan, bind the same set of **N-methyl-D-aspartate (NMDA) receptors** as any other 'dissociative anaesthetic'.
- Members of the benzodiazepine family bind the benzodiazepine receptor located on the **γ -aminobutyric acidA (GABA A) receptor** acting synergistically with 'opiates' to depress respiration.
- Second- and third-generation antidepressants cause '**serotonin syndrome**', but the underlying MOA is just the same as that of cocaine – the antidepressants prevent the reuptake of serotonin, leading to the accumulation of excess serotonin in the synaptic cleft between nerve endings, two disorders have come to predominate most **discussion: serotonin syndrome and QT interval prolongation.** (Our main discussion)

Serotonin syndrome

✓ What is serotonin syndrome ?

It's a potentially life-threatening adverse drug reaction that occurs when excess serotonin accumulates within the synaptic cleft of neurons in the central nervous system.

✓ Symptoms :

In full-blown serotonin syndrome symptoms include:

- 1- **Cognitive effects** (mental confusion, hypomania, hallucinations, agitation, headache, coma),
- 2- **Autonomic effects** (shivering, sweating, hyperthermia, hypertension, tachycardia, nausea and diarrhoea)
- 3- **Somatic effects** (myoclonus, hyper-reflexia and tremor).

Box 21.1 Drugs known to cause serotonin syndrome

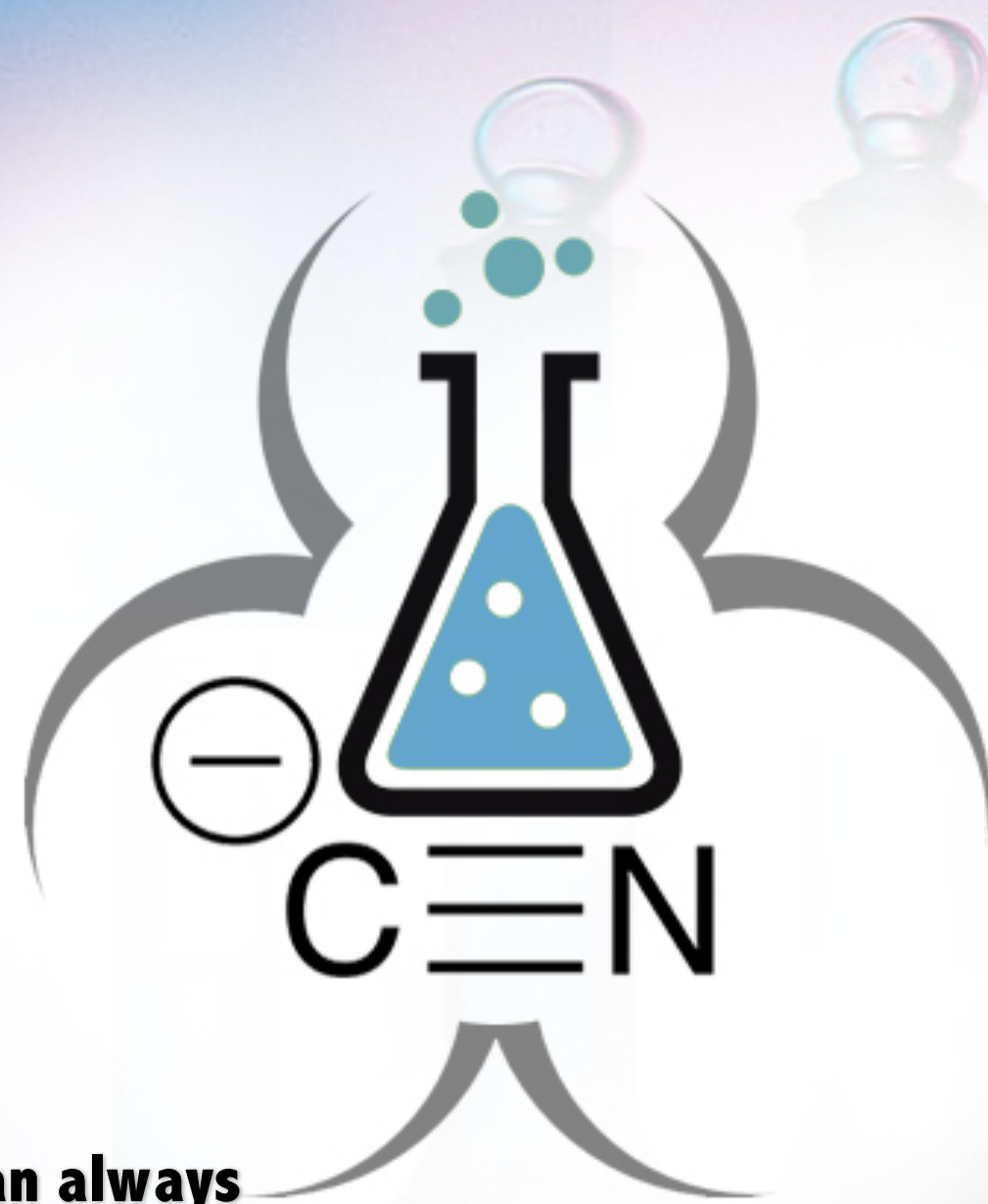
- Antidepressants
 - Monoamine oxidase inhibitors
 - Selective serotonin reuptake inhibitors
 - Tricyclic antidepressants
 - Bupropion
 - Trazadone
- Opiates
 - Buprenorphine
 - Fentanyl
 - hydrocodone
 - Meperidine
 - Oxycodone
 - Pentazocine
- Stimulant drugs
 - Cocaine
 - All amphetamines
 - Methylphenidate
- Migraine treatments
 - All triptans (agents that bind type 1 serotonin receptors)
- Psychedelics
 - LSD (lysergic acid diethylamide)
 - MDMA (3,4-methylenedioxymethamphetamine, commonly known as ecstasy)
 - MDA (3,4-methylenedioxyamphetamine)
- Miscellaneous agents (many different types of drugs fall into this category)
 - Chlorpheniramine
 - Dextromethorphan
 - Lithium
 - Olanzapine
 - Risperidone
 - Ritonavir

QT interval prolongation (long QT syndrome) :

- The normal rate-adjusted length for the QT interval is less than **440 milliseconds**.
- A prolonged QT interval favours the occurrence of a lethal form of ventricular tachycardia known as **torsades des pointes**.
- **Acquired** LQTS is the result of a drug interaction between a drug and one of the channels that controls the orderly sequence of depolarization within the heart's individual cardiomyocytes.
- This structure in question is called the **'rapid delayed repolarizing channel'**, abbreviated as **(hERG)**.
- ❖ Routine toxicology screening will not reveal whether this interaction has occurred, **and there will be no detectable changes at autopsy**, making a thorough review of the medical history mandatory; even then the diagnosis may be impossible to make at autopsy .

Drugs with unique modes of action:

- ✓ **Phenacetin** → Poisoning with phenacetin is now an exceedingly rare event because its proclivity to produce renal disease is well known. However, it is an effective pain reliever by virtue of its actions on the sensory tracts of the spinal cord.
- ✓ **Lithium** → In fact, its mode of action is not known with certainty. There is some evidence that an excitatory neurotransmitter could be involved.
 - Most recently it has been proposed that lithium might restore normal brain function to those with bipolar disorder, and that it somehow does so by deactivating an enzyme **called GSK-3B**.
 - Another feature of lithium poisoning is delayed cardiotoxicity (bradychardia) .
 - Diagnosis of poisoning is by measurement of **blood lithium concentrations**.
- ✓ **Insulin** → Insulin overdose can cause fatal brain damage , but if overdose is suspected it can be confirmed by several different methods.



**If you have any questions You can always
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