Clinical Pharmacology & Toxicology Pearl of the Week

~ Drug induced extrapyramidal symptoms (EPS) ~

The EPS are a heterogenous group of disorders that share the common feature of abnormal muscular activity. Drug induced EPS are side effects of drugs with dopamine antagonism properties, such as

- Antipsychotics, especially first generation antipsychotics like haloperidol
- Antiemetics, such as metoclopramide, prochlorperazine, and droperidol
- Antidepressants, such as SSRIs, MAOIs, and TCAs
- Mood stabilizers, such as lithium

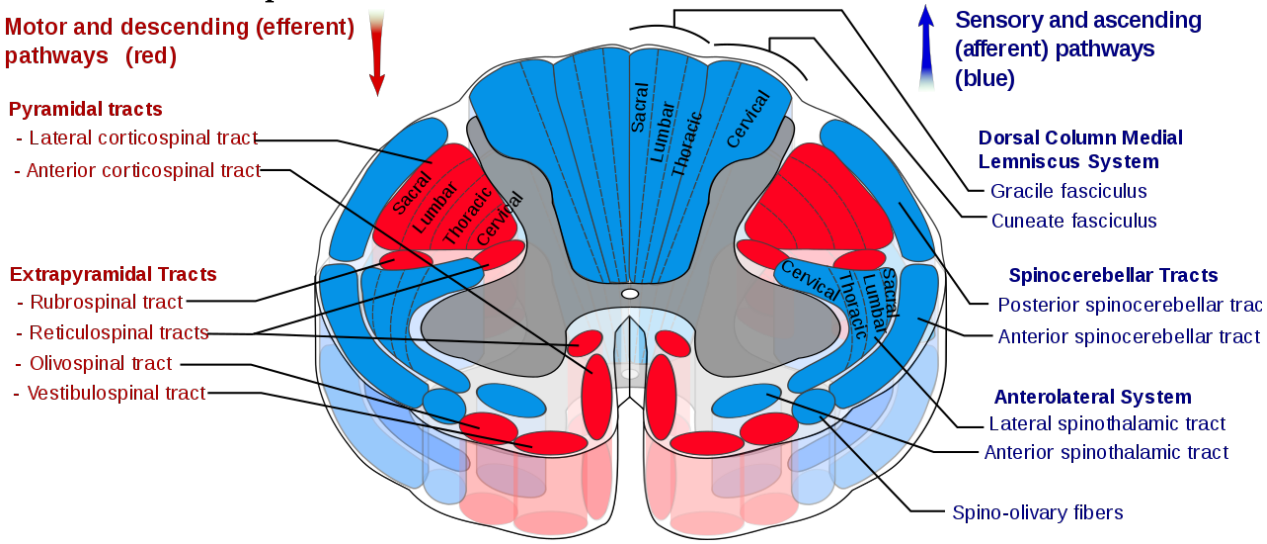
Anatomy

- The extrapyramidal system is a part of the motor system network causing involuntary actions
- The system is called extrapyramidal to distinguish it from the pyramidal tracts of the motor cortex that reach their targets by traveling through the pyramids of the medulla
- Extrapyramidal tracts are chiefly found in the reticular formation of the pons and medulla, and target lower motor neurons in the spinal cord that are involved in reflexes, locomotion, complex movements, and postural control
- These tracts are in turn modulated by various parts of the central nervous system, including the nigrostriatal pathway, the basal ganglia, the cerebellum, the vestibular nuclei, and different sensory areas of the cerebral cortex

Pathophysiology

- Dopamine is responsible for motor function in the nigrostriatal pathway. Abnormal dopaminergic transmission in this pathway can result in abnormal motor function
- The mechanism of most EPS is postulated to be due to dopamine blockade or imbalance of dopaminergic and cholinergic transmission. The exception is tardive dyskinesia which is postulated to be due to dopaminergic excess

Figure 1. Tracts of the Spinal Cord



Polarlys and Mikael Häggström. https://commons.wikimedia.org/w/index.php?curid=10909281

The extrapyramidal syndromes (Adapted from Goldfrank's Toxicologic Emergencies 11th edition):

	Acute dystonia	**Akathisia**	**Parkinsonism**	**Neuroleptic malignant syndrome**	**Tardive dyskinesia (TD)**
Timing	Hours to days	Hours to days	Weeks	2-10 days	3 months to years
Sx	Sustained, involuntary muscle contraction, torticollis, blepharospasm, oculogyric crisis	Restlessness and unease, inability to sit still	Bradykinesia, rigidity, shuffling gait, masklike facies, resting tremor	Altered mental status, motor symptoms, hyperthermia, autonomic instability, catatonia, mutism	Late onset involuntary choreiform movements, buccolingual-masticatory movements
Tx	Anticholinergics such as benztropine or diphenhydramine Benzodiazepines	Dose reduction Trial of alternative drugs Anticholinergics Benzodiazepines	Dose reduction Anticholinergics Dopamine agonist	Cooling Benzodiazepines Consider dopamine agonists (bromocriptine, amantadine) or dantrolene	Avoid anticholinergics (can *worsen* TD) Stop offending agent Cholinergics Can be highly resistant to treatment and irreversible

References:

1. Goldfrank's toxicologic emergencies 11th edition. Chapter 67. Antipsychotics.
2. D'Souza R.S., Hooten W.M. 2023. Extrapyramidal symptoms (EPS). StatPearls.

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.

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