POISON PEARLS

Toxicology Topics for the Healthcare Team of a Poisoned Patient

For ALL patient recommendations call the Drug and Poison Information Center at 1-800-222-1222

Anticholinergics vs Sympathomimetics

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Background

Anticholinergic and sympathomimetic toxidromes share several overlapping clinical features, including tachycardia, hyperthermia, agitation, and mydriasis. Despite these similarities, the underlying pharmacologic mechanisms differ substantially and result in distinct clinical findings that can aid in bedside differentiation. Accurate recognition of these distinguishing features is critical for guiding appropriate management and minimizing the risk of complications.

Anticholinergic Agents

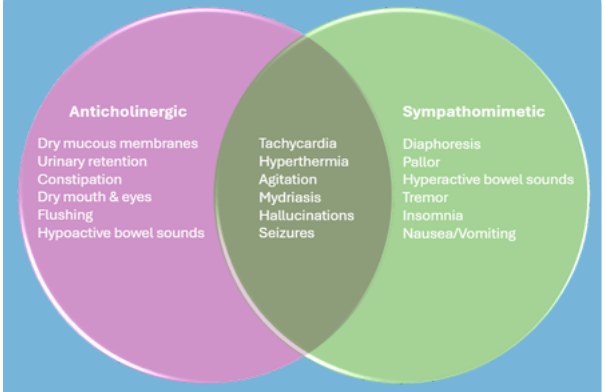
Mechanism of action: Anticholinergic agents inhibit the effects of acetylcholine at central and peripheral cholinergic receptors, thereby reducing parasympathetic nervous system activity. These agents may act through blockade of muscarinic receptors (antimuscarinic) or nicotinic receptors (antinicotinic), though most clinically relevant anticholinergic toxicities result from muscarinic receptor antagonism.
Examples: Some anticholinergic medications include atropine, antihistamines (diphenhydramine, hydroxyzine), antiemetics (scopolamine), antipsychotics (quetiapine, olanzapine), urinary incontinence agents (oxybutynin), Parkinson's disease agents (benztropine), and plants (jimson weed, Atropa belladonna).
Side effects: *Tachycardia*, xerostomia, blurred vision, constipation, urinary retention, decreased lacrimation (Ghossein et. al, 2023).
Overdose presentation: Flushing, anhidrosis, dry mucous membranes, *mydriasis*, altered mental status, *hyperthermia*, urinary retention, delirium, *hallucinations, agitation*, restlessness, confusion, *seizures, QT prolongation* (Broderick et. al, 2023).
Management: Management is primarily supportive and includes benzodiazepines for agitation or seizures, intravenous fluids, and external cooling for hyperthermia. Activated charcoal may be considered in appropriate early presentations. In select cases with severe anticholinergic delirium, physostigmine (no longer widely available in the US) or rivastigmine may be used.

Sympathomimetic Agents

Mechanism of Action: Sympathomimetic agents exert their effects by increasing catecholamine activity within the central and peripheral nervous systems. This may occur through enhanced release of catecholamines, inhibition of their reuptake or metabolism, or direct agonism at adrenergic receptors. The net effect is increased stimulation of the sympathetic nervous system, producing the physiologic "fight-or-flight" response (Farzam et al., 2023).
Examples: Some sympathomimetic agents include those used in the treatment of attention-deficit/hyperactivity disorder (mixed amphetamines, methylphenidate), nasal or sinus congestion (pseudoephedrine), and recreational (caffeine) or illicit substances (cocaine).
Side Effects: Loss of appetite, insomnia, weight loss, headache, nausea, vomiting, hypertension, tachycardia (SAMHSA, 1999).
Overdose Presentation: *Agitation*, tremor, hyperactivity, diaphoresis, pallor, *hyperthermia, mydriasis*, *seizures*, arrhythmias, *QT prolongation, hallucinations,* hyperactive bowel sounds (Shaffer & Richards, 2025; Farzam et al., 2023).
Management: Management is largely supportive and guided by the specific agent and clinical manifestations. Benzodiazepines are first-line therapy for agitation and to mitigate sympathetic overactivity. Intravenous fluids and external cooling measures are used to treat hyperthermia and reduce the risk of rhabdomyolysis. In cases of cocaine toxicity, β-blockers are generally avoided due to concern for unopposed α-adrenergic stimulation (Smollin et al., 2019). Ongoing monitoring is essential for early detection and management of complications (Farzam et al., 2023).

Key Differences

A key distinction between these toxidromes lies in the autonomic pathways involved. Anticholinergic toxicity results from inhibition of parasympathetic activity, whereas sympathomimetic toxicity reflects excessive stimulation of the sympathetic nervous system. Clinically, several bedside findings can help differentiate the two. Anticholinergic toxicity is typically associated with dry skin and mucous membranes, decreased bowel sounds, and flushing, while sympathomimetic toxicity presents with diaphoresis, hyperactive bowel sounds, and pallor. With sympathomimetics, patients may have normal bowel sounds, and in general, bowel sounds may not be a reliable way to distinguish between the two toxidromes. Management strategies for anticholinergics and sympathomimetics often overlap, with supportive care and benzodiazepines serving as key therapies.



Key Points:

- Anticholinergics and Sympathomimetic overdoses can present similarly
- Distinguishing features of anticholinergics:
  - dry skin, flushed skin, hypoactive bowel sounds
- Distinguishing features of sympathomimetics:
  - diaphoresis, pallor, hyperactive (or normal) bowel sounds
- Treatment for both anticholinergics and sympathomimetics are similar:
  - Patients need supportive care
  - They may require cooling measures
  - Benzodiazepines may help with agitation, tachycardia, seizures or hallucinations
  - Physostigmine or rivastigmine may be used in the setting of anticholinergic delirium

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