**Introduction**

Poisoning patients frequently present to emergency departments and urgent care centers. Internists, emergency physicians, intensivists, and clinical pharmacists need skills to recognize toxidromes, order appropriate diagnostic tests, and provide timely antidotes and supportive care. This chapter will provide an overview of the epidemiology of poisonings, discuss the relevance to emergency and critical care practice, and outline key principles in the initial evaluation and management of the poisoned patient.

Epidemiology and Significance

* Poison control centers receive over 2 million reports of toxic exposures annually in the United States.
* While most are acute and unintentional exposures managed safely at home, around 3-4% of cases require critical care.
* Pharmaceuticals, illicit substances, household products, envenomations, and environmental toxins are common culprits.
* Mortality is highest with sedative-hypnotics, opioids, cardiovascular drugs, acetaminophen, antidepressants, and stimulants.
* At-risk groups include adolescents, adults aged 20-49, and geriatric patients. Males have higher rates of poisoning deaths compared to females.

Relevance to Clinical Practice

* Strong knowledge of toxicology improves the ability to stabilize critically ill patients, avoid adverse drug events, and determine proper patient disposition.
* Mastering key principles leads to better patient outcomes and survival rates in acute poisonings.
* All clinicians should be able to recognize vital sign abnormalities, perform a focused toxidrome assessment, address airway/breathing/circulation, administer antidotes, and arrange appropriate follow-up care.

**Focused Physical Exam Findings Vital for Differential Diagnosis**

* Assess mental status for agitation, delirium, stupor, or coma.
* Agitated delirium suggests sympathomimetics, anticholinergics, serotonin syndrome
* Stupor indicates sedative-hypnotics, opioids, clonidine
* Check pupillary size
* Pinpoint pupils suggest opioid toxicity
* Dilated pupils indicate sympathomimetics, anticholinergics
* Note skin moisture and bowel sounds
* Dry skin, hypoactive bowel sounds suggest anticholinergics
* Diaphoresis may be seen with sympathomimetics, serotonin syndrome, opioid or ethanol withdrawal
* Check for hyperreflexia or inducible clonus which indicates serotonin syndrome
* Note signs of trauma that could indicate related injury or alternate etiology
* Localize any focal neurologic deficits such as seizure activity

**Pathophysiology Review**

* Cholinergics: Excess acetylcholine, cholinesterase inhibition
* Anticholinergics: Muscarinic acetylcholine receptor blockade
* Sympathomimetics: Catecholamine excess, reuptake inhibition
* Serotonin syndrome: Excess serotonin production, reduced metabolism
* Sedative-hypnotics: CNS and respiratory depression

For each toxidrome, know the underlying mechanism of action. This strengthens the clinical reasoning skills essential for board examinations.

**Diagnostic Testing Pearls**

* Check anion and osmolal gaps to identify toxic alcohols
* Qualitative urine drug screens have limitations but can determine common drugs of abuse
* Reducing substances may indicate ethylene glycol or methanol ingestion
* Monitor serum drug levels of acetaminophen, salicylates, lithium, and others with known toxic ranges
* Look for co-ingestions which are common in overdoses

**Toxidromes**

Cholinergic Toxidrome

* Caused by excess acetylcholine and cholinesterase inhibition
* Agents include organophosphates, nerve agents, carbamates
* Clinical findings:
* Bradycardia, hypotension, bronchorrhea
* Miosis, lacrimation, diaphoresis
* Bronchospasm, wheezing
* Muscle fasciculations, weakness
* Seizures, dysrhythmias
* Management:
  + Airway protection, oxygen, ventilatory support
  + Atropine 2-10 mg IV initially and pralidoxime 1-2 g IV
  + Treat seizures with benzodiazepines
  + Decontaminate skin, give charcoal if ingested
  + Consider pyridostigmine pre-treatment prophylaxis if nerve agent exposure

Anticholinergic Toxidrome

* Due to muscarinic acetylcholine receptor blockade
* Agents include antihistamines, antipsychotics, antispasmodics, plants
* Findings:
* Tachycardia, hypertension
* Dilated pupils, blurred vision
* Dry skin, flushing
* Decreased bowel sounds
* Urinary retention
* Agitation, confusion, delirium
* Management:
  + Supportive care, IV fluids, cardiac monitoring
  + Benzodiazepines for agitation, hypertension
  + Physostigmine can reverse symptoms
  + Cooling measures for hyperthermia
  + Avoid traction on bowel with enemas or cathartics

Sympathomimetic Toxidrome

* Caused by excess catecholamine release or reuptake inhibition
* Cocaine, methamphetamine, MDMA, bath salts, caffeine, theophylline
* Findings:
* Tachycardia, hypertension
* Delirium, psychosis, agitation
* Diaphoresis, hyperthermia
* Mydriasis, hyperreflexia
* Management:
  + Benzodiazepines for agitation, hypertension, seizures
  + Active cooling measures for hyperthermia
  + Avoid beta blockers as they may unoppose alpha stimulation
  + Treat dysrhythmias, chest pain, ischemia

Sedative-Hypnotic Toxidrome

* Due to CNS and respiratory depression
* Opioids, benzodiazepines, barbiturates, clonidine, GHB, alcohol
* Findings:
* Respiratory depression, hypoxia
* Miosis (except ethanol)
* Hypotension, bradycardia
* Hyporeflexia, decreased consciousness
* Management:
  + Airway protection, intubation if needed
  + IV fluid boluses for hypotension
  + Naloxone for opioids, flumazenil for benzos (cautious use)
  + Consider empiric dextrose, thiamine, naloxone
  + Treat seizures with benzodiazepines

Serotonin Syndrome

* Excess serotonin in CNS and peripherally
* Caused by serotonin-boosting drugs like SSRIs, MAOIs, TCAs, tramadol
* Findings:
* Hyperreflexia, inducible clonus
* Tremor, rigidity, hypertonia
* Hyperthermia, diaphoresis
* Agitation, confusion
* Diarrhea, abdominal pain
* Management:
  + Discontinue precipitating drugs
  + Mild cases can be managed supportively
  + Severe cases may require benzodiazepines, cyproheptadine

Cholinergic/Anticholinergic Mixed Syndrome

* Concurrent excess and blockade of acetylcholine
* Often from amitriptyline or diphenhydramine overdoses
* Clinical picture may be variable:
* Mydriasis with diaphoresis
* Tachycardia with hypotension
* Dry skin with bronchorrhea
* Manage individual symptoms and supportively

Opioid Toxicity

* Caused by excessive opioid receptor activation in CNS and respiratory centers
* Agents include heroin, fentanyl, oxycodone, methadone, morphine

Clinical Findings:

* CNS depression - stupor, miosis, decreased consciousness
* Respiratory depression - hypoxia, decreased RR, hypoventilation
* GI effects - nausea, vomiting, decreased motility
* Hypothermia and bradycardia from CNS depression
* Hypotension from venodilation

Management:

* Supportive care - airway management, oxygen, ventilatory support
* Naloxone - opiate antagonist
* Initial dose 0.04-0.4mg IV, titrate to effect
* Higher doses may be needed for synthetic opioids
* Repeat doses likely needed due to short half-life
* Avoid precipitating opiate withdrawal
* Address concurrent hypoglycemia, electrolyte abnormalities
* Consider activated charcoal if oral ingestion within 1 hour
* Monitor for complications - aspiration, pulmonary edema, rhabdomyolysis
* Discharge only when full alertness and physiologic function returns

**Antidote Selection and Administration**

* Know mechanisms of action, dosing, and monitoring for key antidotes:
* N-acetylcysteine: acetaminophen poisoning
* Physostigmine: anticholinergic syndrome
* Glucagon: beta-blocker and calcium channel blocker poisoning
* Digoxin immune fab: digoxin toxicity
* Flumazenil: benzodiazepine overdose
* Naloxone: opioid poisoning
* Dextrose: hypoglycemia
* Match antidote to likely toxin based on clinical syndrome
* Adjust dosing in pediatric vs adult patients
* Monitor for adverse effects

Having a strong foundation on selecting and administering the appropriate antidote for each toxicity syndrome is essential.

**Gastric Decontamination**

* Activated charcoal (AC) adsorbs toxins in GI tract to prevent absorption
* Give 50-100 g AC within 1 hour of ingestion
* AC is still somewhat effective 1-2 hours post-ingestion
* Use AC for:
* Life-threatening ingestions
* Sustained-release or extended release drugs
* Substances that delay gastric emptying
* Highly toxic agents even late after ingestion
* Contraindicated with:
* Caustic or corrosive ingestions
* Hydrocarbons due to aspiration risk
* Bowel obstruction or ileus
* Ensure airway protection before giving AC
* Whole bowel irrigation:
* Flushing GI tract with polyethylene glycol solution
* For potentially toxic iron, lithium, potassium ingestions
* Useful for body packers or sustained-release drugs
* Give until rectal effluent clear, approx 3-6 L volume
* Gastric lavage rarely indicated and has limited efficacy

**Enhanced Elimination**

* Hemodialysis removes small molecular weight toxins
* First-line for salicylates, lithium, methanol, ethylene glycol
* Corrects electrolytes and acid-base disorders
* Charcoal hemoperfusion adsorbs larger protein-bound toxins
* Useful for phenobarbital, carbamazepine, theophylline
* Alkaline diuresis enhances elimination of salicylates
* Administer IV sodium bicarbonate to alkalinize urine pH > 7.5
* Replace potassium losses
* Forced diuresis is rarely used due to limited efficacy
* All enhanced elimination methods have risks of electrolyte shifts, hypotension

**Clinical Scenarios**

* A 72 year old man is found unresponsive next to empty bottles of amitriptyline and diphenhydramine. On exam he has dilated pupils, tachycardia, dry skin, and hypoactive bowel sounds.

This mixed anticholinergic/cholinergic toxidrome suggests tricyclic antidepressant and antihistamine overdose. Initial management includes airway protection, monitoring QT interval, sodium bicarbonate for QRS prolongation, and supportive care.

* A 24 year old woman is brought in with delirium, fever, hypertension and inducible clonus. Her friend reports she takes fluoxetine and just started an MAOI.

Her presentation is consistent with serotonin syndrome. Immediate discontinuation of the precipitating drugs is needed along with supportive care and possible benzodiazepines or cyproheptadine for severe symptoms.

**Summary**

This chapter has covered a detailed approach to the poisoned patient, with a focus on recognizing key toxidromes, stabilizing vitals, administering appropriate antidotes, and utilizing various enhanced elimination techniques. Careful diagnosis guides the management, which can be further optimized through consultation with poison experts. Strong toxidrome recognition skills are essential for pharmacists caring for poisoned patients.

References

1. Hoffman RS, Howland MA, Lewin NA, et al. Goldfrank's Toxicologic Emergencies. 11th ed. New York, NY: McGraw-Hill; 2019.
2. Graudins A, Lee HM, Druda D. Calcium channel antagonist and beta-blocker overdose: antidotes and adjunct therapies. Br J Clin Pharmacol. 2016;81(3):453-461.
3. Mégarbane B. Toxidrome-based Approach to Common Poisonings. Med Clin North Am. 2017;101(1):199-218.
4. Greene S, Wallace K, Dargan P, Jones A. Paracetamol poisoning: what happens to the paracetamol metabolites? Clin Toxicol (Phila). 2018 Sep;56(9):818-822.
5. Roberts DM, Yates C, Megarbane B, et al. Recommendations for the role of extracorporeal treatments in the management of acute methanol poisoning: a systematic review and consensus statement. Crit Care Med. 2015 Feb;43(2):461-72.

**References**

1. Mowry JB, Spyker DA, Brooks DE, McMillan N, Schauben JL. 2014 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 32nd Annual Report. Clin Toxicol (Phila). 2015.
2. Chandran L, Linakis J. Pediatric ingestions and poisonings. Emerg Med Clin North Am. 2003;21(1):89-120.
3. Hoffman RS, Howland MA, Lewin NA, Nelson LS, Goldfrank LR. Goldfrank's Toxicologic Emergencies. 11th ed. New York, NY: McGraw-Hill; 2019.
4. Wang GS, Buchanan JA. Toxidromes. Emerg Med Clin North Am. 2018;36(2):223-238.
5. Mégarbane B, Borron SW, Baud FJ. Current recommendations for treatment of severe toxic alcohol poisonings. Intensive Care Med. 2005;31(2):189-195.
6. Graudins A, Lee HM, Druda D. Calcium channel antagonist and beta-blocker overdose: antidotes and adjunct therapies. Br J Clin Pharmacol. 2016;81(3):453-461.
7. Boyer EW, Shannon M. The serotonin syndrome. N Engl J Med. 2005;352(11):1112-1120.
8. Barrueto F Jr, Kirrane BM, Cotter BW, Pearlman AR, Nelson LS. Acetaminophen-induced hypothermia and hepatic toxicity in an adolescent with chronic alcohol abuse. Crit Care Med. 2006;34(11):2919-2921.
9. Mégarbane B. Toxidrome-based Approach to Common Poisonings. Med Clin North Am. 2017;101(1):199-218.
10. Greene SL, Dargan PI, Jones AL. Acute poisoning: understanding 90% of cases in a nutshell. Postgrad Med J. 2005;81(954):206-216.
11. Roberts DM, Yates C, Megarbane B, et al. Recommendations for the role of extracorporeal treatments in the management of acute methanol poisoning: a systematic review and consensus statement. Crit Care Med. 2015;43(2):461-472.
12. Burns MJ, Linden CH, Graudins A, et al. A comparison of physostigmine and benzodiazepines for the treatment of anticholinergic poisoning. Ann Emerg Med. 2000;35(4):374-381.
13. Dart RC, Rumack BH, McGuigan M. Efficacy and clinical safety of syrup of ipecac. Ann Emerg Med. 1984;13(9 Pt 1):842-846.
14. Mégarbane B, Karyo S, Baud FJ. The role of extracorporeal treatment for metallic poisonings. Semin Dial. 2011;24(4):382-389.
15. Dawson AH, Buckley NA. Pharmacological management of organophosphorus pesticide poisoning. CNS Drugs. 2014;28(6):539-552.
16. Wolfe TR, Caravati EM, Rollins DE. Massive quetiapine overdose successfully treated with intravenous lipid emulsion. Ann Emerg Med. 2010 Dec;56(6):618-25.
17. Blanc PD, Jones MR, Olson KR. Surveillance of poisoning and drug overdose through hospital discharge coding, poison control center reporting, and the Drug Abuse Warning Network. Am J Emerg Med. 1993 Jan;11(1):14-9.
18. Brent J. Fomepizole for ethylene glycol and methanol poisoning. N Engl J Med. 2009 May 21;360(21):2216-23.
19. Mégarbane B. Toxidrome-based Approach to Common Poisonings. Med Clin North Am. 2017;101(1):199-218.
20. Graudins A, Lee HM, Druda D. Calcium channel antagonist and beta-blocker overdose: antidotes and adjunct therapies. Br J Clin Pharmacol. 2016;81(3):453-461.
21. Hoffman RS, Smilkstein MJ, Howland MA, Goldfrank LR. Osmol gaps revisited: normal values and limitations. J Toxicol Clin Toxicol. 1993;31(1):81-93.
22. Kraut JA, Kurtz I. Toxic alcohol ingestions: clinical features, diagnosis, and management. Clin J Am Soc Nephrol. 2008;3(1):208-225.