Clinical

Toxicological Emergencies
for the Urgent Care Physician

Urgent message: Several specific toxicological emergencies are most likely to be encountered in the urgent care setting. Prompt recognition of their clinical presentation, understanding the pathophysiology/natural disease progression, and initiation of treatment are critical factors in decreasing morbidity (and potential mortality) in these cases.

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Introduction

Beginning in 2004, poisonings rank second to motor vehicle accidents as the leading cause of accidental death in the U.S., with unintentional ingestions constituting the largest component of poisoning deaths.[1] The most common fatal ingestants included sedative hypnotics/antipsychotics, opioids, antidepressants, cardiovascular drugs, acetaminophen (with or without combinations), alcohols, and street drugs/stimulants.[2]

Utilizing a case-based format, this article will seek to:

- formulate general management guidelines for evaluation and treatment of toxicologic emergencies
- appraise evidence-based recommendations for acute decontamination
- describe and differentiate among common ingestions and drugs of abuse
- demonstrate the role of initial laboratory tests and radiographs in the management of these patients
- provide clinical pearls and mnemonics to aid in identification of commonly encountered poisons.

Urgent Care Management

Because the natural history of ingestions has a wide and variable clinical presentation with dynamic changes in a patient's status (e.g., asymptomatic and benign to fatal), management of these patients in the urgent care setting needs to prompt and selective, with the evaluation of all patients immediately upon arrival.

Table 1. Acutely Poisoned Patient: General Management Guidelines	
A-B-C-D-E-F	*A: Airway* – ensure airway is protected *B: Breathing* – provide supplemental oxygen as needed and ensure adequate ventilation *C: Circulation* – ensure adequate perfusion; initiate IV therapy with NS bolus (20 cc/kg in children); multiple boluses may be required for hypotensive patients *D: Decontamination* – administer activated charcoal (AC) for most ingestions unless otherwise contraindicated (1g/kg; 60-90g for most adults) *E: ECG* – evaluate for any dysrhythmias; treat as appropriate *F: Fingerstick* – assess for hypoglycemia; treat if indicated
Monitor	Place patient on cardiac monitor; assess vitals frequently
Seizures	Avoid secondary insult (e.g., aspiration, trauma), provide supplemental oxygen, benzodiazepines if available
Miscellaneous	• Expose patient to assess for secondary injury (e.g., trauma) • Assess for suicidal intent • Administer specific antidote if available and the patient is clinically toxic (e.g., naloxone for opiate intoxication, sodium bicarbonate for patients intoxicated with tricyclic antidepressants)

This assumes management is appropriate for a given urgent care center, and will vary according to availability of resources (e.g., lab support, staff personnel).

Patients who present with or develop altered mental status (e.g., Glasgow Coma Scale score ≤14, confusion, and agitation), abnormal vital signs, suicidal ideation, repeated vomiting, abnormal ECG findings, or those who will require extended observation require immediate transfer to the emergency department.

In contrast, most alert, stable patients can remain in a clinic setting safely as management decisions are being made.

Consultation with a local/regional Poison Control Center (1-800-222-1222) can aid in the evaluation/disposition of these patients.

For those patients with confirmed/suspected intentional ingestions, clinicians should make disposition decisions in coordination with a psychiatric consultant.

Acute Decontamination

Ipecac syrup

Ipecac syrup (IS) has, historically, been a mainstay of gastrointestinal (GI) decontamination. However, current literature does not favor the use of induced emesis due to the low benefit-to-risk ratio coupled with significant contraindications and adverse effects of its administration.[3] This notion was furthered by the American Academy of Pediatrics, which recommended against use of IS as a routine home treatment following ingestion, as well as for disposal of ipecac in the home.[4]

There are several complications involved with evoked emesis, including aspiration, airway compromise, and injury to the esophagus.

A 2005 position paper from the American Academy of Clinical Toxicology/European Association of Poisons Centres and Clinical Toxicologists stated that IS should not be administered routinely to poisoned patients and to consider ipecac only in an alert, conscious patient who has ingested a potentially toxic amount of a poison within the past 60 minutes.[5]

Absolute contraindications include nontoxic/acid/alkali/hydrocarbon/sharp object ingestions, as well as use in patients who are altered/comatose, actively vomiting, have no protective airway reflex, have known/suspected increased intracranial pressure, are pregnant, within hypertensive crisis, and/or expected to deteriorate.

Activated charcoal

Activated charcoal (AC) is the most common method of GI decontamination (recommended dosage: 1 g/kg) in poisoned patients.[6] Toxins absorb to AC in the small intestine and then are excreted.

Exceptions include alcohols, lithium, acids/alkalis, pesticides, hydrocarbons, iron, arsenic, and other small, ionized and water-soluble compounds.

In situations where multiple co-ingestants may be present (including corrosives), AC should still be given if there is a risk of systemic toxicity.

AC is contraindicated in patients who have no bowel sounds, risk for GI perforation/hemorrhage, active vomiting, loss of protective airway reflexes, or when endoscopic visualization is anticipated.

If a patient is obtunded, the airway must first be secured; then AC can be administered through an orogastric or nasogastric tube.

Avoid using cathartics mixed with the activated charcoal, since electrolyte imbalances can occur.

General management guidelines for the acutely poisoned patient are described in **Table 1**.

Case #1

An 8-year-old male presents with a complaint of blood-tinged vomiting. Mom was tending to her newborn baby when he began to develop these symptoms.

Iron toxicity

Iron overdose is a common and potentially fatal ingestion in two patient populations: children and expectant mothers.

Iron toxicity is common in children due to an iron tablet's close resemblance to candy, and the lack of recognition by the caretaker of iron as a poison.[7] Pregnant females also are at higher risk for iron toxicity, given the recommendation of utilizing prenatal vitamins (which contain iron) to promote embryonic development.

The primary organ systems involved in iron toxicity include the gastrointestinal and cardiovascular system, but it can also affect other organ systems as a re-

Table 2. Ferrous Salt–Iron Content Conversion Chart

Salt	*% elemental iron content*
Sulfate (most common preparation)	20%
Gluconate	12%
Fumarate	33%
Children's chewable tablets	18 mg/tablet

Table 3. Determination of Iron Toxicity Based on Elemental Iron Ingested

Non-toxic	<20 mg/kg
Mild to moderate toxicity	20-60 mg/kg
Severe toxicity	>60 mg/kg

sult of metabolic acidosis.

Within the GI system, iron is directly toxic due to its corrosive effect on the stomach, which can lead to vomiting, diarrhea, and GI bleeding. Hepatotoxicity results from free radical production and oxidative damage.[8]

In the cardiovascular system, iron directly damages blood vessels, causes vasodilatation, and blocks oxidative phosphorylation.

In addition, iron is a negative inotrope, and directly toxic to the myocardium. Metabolic acidosis is produced through lactic acid production (secondary to interference of oxidative phosphorylation and hypotension) and through the conversion of iron from the ferrous state (Fe^{2+}) to the ferric state (Fe^{3+}), which releases a hydrogen ion (see **Table 2**).[7]

To calculate the amount of elemental iron ingested, the following formula can be utilized:

$$\frac{(\#\ tabs\ ingested) \times (mg\ iron\ \frac{salts}{tab}) \times (\%\ elemental\ iron)}{patient\ weight\ (kg)}$$

For example, consider the 8-year-old boy described in this case. He weighed 30 kg, and ingested 20 tablets of 325 mg ferrous sulfate tablets. Therefore, applying the formula would yield the following:

$$\frac{(20) \times (325) \times (20\%)}{30\ (kg)} = 43\ \frac{mg}{kg}\ of\ elemental\ iron\ ingested$$

(Note, however, that if the patient is pregnant, pre-pregnancy weight should be used in the calculation.[7])

In general, level of iron toxicity can be determined by the amount of elemental iron ingested (**Table 3**).

Other diagnostic modalities that can assist in iron toxicity include an electrolyte panel to evaluate for anion gap metabolic acidosis (AGA) and abdominal radiographs to evaluate for radiopaque pill fragments. Radiographs can be helpful in the acute setting when the ingestion is unknown; however, their yield is inversely proportional to time from ingestion. A negative x-ray does not exclude a possible ingestion. (See **Table 4** for radiopaque compounds on x-ray).

Management follows standard protocol (see **Table 1**), and includes decontamination if other co-ingestants are suspected. Supportive management of hypotension with IV fluids and treatment of nausea and vomiting are the major cornerstones of initial management. Definitive management includes deferoxamine; a published consensus guideline recommends that all patients with ≥4 episodes of vomiting, ingestion of 40 mg/kg of elemental iron, and/or suspected toxic ingestion should be immediately transferred to the nearest ED.[7]

The following questions should be answered if iron toxicity is suspected:

1. Any history of emesis?
2. How many episodes of emesis? (More than four episodes of emesis suggests systemic toxicity.)
3. What type of iron was ingested (sulfate, fumarate, gluconate) and in what form (e.g., tablet/liquid/ chewables)?

Case #2

A 55-year-old male presents with left shoulder pain after a lifting injury. He has been taking a pain reliever for the last two days without any relief. The patient presents to the clinic for a stronger pain medication, but also complains of "ringing in his ears" and nausea for the last few hours.

Salicylate toxicity

Salicylates (i.e., aspirin, methyl salicylate) are commonly used for analgesia, but also as antipyretic, anti-inflammatory, and anti-platelet agents, and are easily accessible to the general public.

Salicylate poisoning can be either acute or chronic in nature, and clinicians must maintain a high index of suspicion in these patients. In 2004, there were over 21,000 aspirin and non-aspirin salicylate exposures reported to U.S. poison centers. Of those, 43 cases resulted in death and 12,968 patients required hospital treatment.[9]

Systemic effects occur secondary to inhibition of oxidative phosphorylation, direct stimulation of the central respiratory center, GI irritation, and increased capillary and pulmonary endothelial permeability. This leads to the classic findings of a respiratory alkalosis with a metabolic acidosis, hyperventilation, GI effects (e.g., vomiting, GI bleed), hypotension, altered mental status, seizures, and kidney and liver damage.

Patients may also complain of tinnitus, which may be an early indicator of CNS toxicity.[9] Chronic toxicity is most commonly seen in the elderly population due to declining renal function and utilization of multiple medications that may contain aspirin. It is characterized by a non-specific presentation, and can be confused with a sepsis syndrome, dementia/psychosis, and pulmonary edema.

Acute management is supportive (**Table 1**), and immediate transfer to an ED is indicated if >150mg/kg of aspirin is ingested, and/or the patient is clinically toxic.

In addition to supportive treatment, the patient should be decontaminated with activated charcoal (1 g/kg). The patient will need immediate transfer to a higher level of care for the administration of sodium bicarbonate to help alkalinize the urine. This helps facilitate excretion of salicylate, while also helping to prevent absorption into organ tissues (i.e., the central nervous system [CNS]).

Diagnosis of salicylate toxicity must also include the possibility of co-ingestants. An electrolyte panel will show an AGA—specifically, a mixed respiratory alkalosis with metabolic acidosis; however, this is best displayed on ABG.

Glucose may be decreased and the patient may also have hyperkalemia and renal insufficiency/failure secondary to the direct and indirect effects on the renal system.

In chronic ingestions, a CBC may show anemia from an underlying GI bleed. A chest x-ray should be obtained if the patient has any respiratory symptoms and/or signs of pulmonary edema.

Obtain an ECG for any possible dysrhythmias, especially to evaluate for any changes related to hyperkalemia.

The following clinical questions should be answered if salicylate toxicity is suspected:

1. How much salicylate was ingested?
2. Does the patient have tinnitus?
3. Is the patient tachypneic (compensation for acidosis)?

Case #3

A 24-year-old female presents to the clinic after her mother found her lying on the ground and vomiting. The patient admits to taking a large quantity of pills that were found in the medicine cabinet.

Non-steroidal anti-inflammatory drug (NSAID) toxicity

Similar to aspirin, NSAIDs are widely available and utilized for a variety of conditions, rendering them common ingestants. Over 107,000 case mentions due to NSAID ingestions were reported to Poison Control Centers in 2008.[2]

Drug absorption is rapid and will produce effects within two hours of taking the medication.

The effects of NSAIDs are due to competitive inhibition of the cyclooxygenase enzyme involved in prostaglandin synthesis. In an overdose, these effects become exaggerated and eventually impair the GI, renal, hepatic, and central nervous systems.

Patients most commonly present with GI symptoms (e.g., abdominal pain, vomiting, GI bleed) but can also have CNS depression and seizures, depending on the severity of ingestion and/or class of drug ingested (e.g., mefenamic acid).[10]

Patients with a history of GI bleed, peptic ulcer disease, and/or alcohol abuse are at greatest risk for developing an acute GI bleed—the most common cause of mortality in such cases. Elderly patients are also at higher risk for toxicity secondary to a decreased baseline renal function. An electrolyte panel may help to determine the baseline renal function, as well as any electrolyte abnormalities and AGA.

Most patients will improve with supportive care (**Table 1**), and ingestions of less than 100 mg/kg are unlikely to result in toxicity. The patient should be transferred if she is clinically toxic (e.g. GI, renal, hepatic, CNS dysfunction) or if reported ingestion of ibuprofen is >400 mg/kg, since the patient may require hemodialysis for definitive removal of the agent.[10]

The following clinical questions should be answered if NSAID toxicity is suspected:

1. How many pills were taken and what strength were the tablets?
2. Does the patient have any melena/bright red blood per rectum/hematemesis?
3. Does the patient have a history of baseline kidney dysfunction?

Case #4

A 30-year-old male presents complaining of nausea, vomiting, and abdominal pain. He states he took "some pills" last night with heavy amounts of alcohol in an attempt to commit suicide.

Acetaminophen toxicity

Acetaminophen (APAP) toxicity is one of the most common causes of potentially toxic ingestions, and alone or in combination therapy accounts for >161,000 case mentions reported to U.S. Poison Centers in 2008. Over half of all deaths attributed to analgesics are due to APAP.[2]

APAP toxicity is the leading cause of acute liver failure in western countries and contributes to the majority of admissions to liver transplant units.[11] Acetaminophen is metabolized primarily in the liver into sulfate and glucuronide conjugates, which are nontoxic and excreted in the urine.

Table 4. Must-know Mnemonics

Compound	*Mnemonic*	
Radiopaque substances on x-ray	**CHIPES** **C**: Calcium, cocaine, condoms, chloral hydrate **H**: Heavy metals **I**: Iron, iodide **P**: Psychotropics, bezoar **E**: Enteric coated pills **S**: Solvents (CCl_4)	
Cholinergic toxicity	**DUMBBELS** **D**: Diarrhea **U**: Urination **M**: Miosis **B**: Bronchospasm, bronchorrhea **B**: Bradycardia **E**: Emesis **L**: Lacrimation **S**: Salivation, seizure	
Anion gap metabolic acidosis - AGA	**CAT MUDPILES** **C**: Carbon monoxide, cyanide **A**: Alcoholic ketoacidosis **T**: Toluene **M**: Methanol, metformin **U**: Uremia **D**: DKA **P**: Paraldehyde **I**: INH/Iron toxicity **L**: Lactic Acidosis **E**: Ethylene glycol, EtOH **S**: Salicylate intoxication	
Anticholinergic toxicity	"Hot as a hare" "Blind as a bat" "Dry as a bone" "Mad as a hatter" "Red as a beet"	Hyperthermia Mydriasis Dry mucus membranes, decreased sweating Mental status changes Skin flushing

Table 5. Predicted Effect Based on QRS Duration[15]

QRS Duration	*Clinical effect*
<100 msec	No significant clinical toxicity
>100 msec	⅓ will have seizures; 14% ventricular dysrhythmias
>160 msec	½ will have ventricular dysrhythmias

A small percentage is metabolized by the cytochrome P-450 system into N-acetyl-p-benzoquinone imine (NAPQI), which is then reduced from this toxic form by glutathione into a nontoxic conjugate.

In overdose situations, the sulfation and glucuronidation pathways become saturated and the pathway shifts to the cytochrome P-450 system. This results in increasing amounts of NAPQI, which in turn depletes glutathione stores. Once the glutathione supply is depleted, the NAPQI compound becomes abundant and causes intracellular damage, primarily in hepatocellular cells.[11]

There are four stages of acute APAP toxicity:

1. 0-24 hours: GI irritation (e.g., nausea, vomiting, abdominal pain)
2. 24-48 hours: resolution of GI symptoms with elevation of liver function tests
3. 48-96 hours: severe hepatic dysfunction (coagulopathy, acidosis, hypoglycemia, cerebral edema, and death can occur in this stage)
4. 5-14 days: recovery.

In patients with APAP ingestion, the most reliable time of ingestion must be determined. If unclear, the earliest time of ingestion should be utilized or corroborated with others (e.g., family). This will help with the assessment of the need for antidote administration when the patient is transferred to the ED.

Treatment of acute APAP toxicity involves supportive management (**Table 1**), as well as decontamination with charcoal and its antidote, N-acetylcysteine (NAC). NAC is a precursor for glutathione, which helps reduce NAPQI to a non-toxic substance and decrease hepatotoxicity.

In patients with a suspected or confirmed APAP ingestion (≥150 mg/kg), immediate transfer to the ED should be initiated, since lab testing and possible NAC administration may be warranted.

Because APAP is a common co-ingestant and has potentially devastating hepatotoxic effects, APAP ingestion should be considered in all patients presenting to urgent care centers with

drug ingestion of any kind. Rates of potentially hepatotoxic levels without history of ingestion have been found to be 0.3% even in patients without history of ingestion.[12]

Subacute/chronic toxicity should also be suspected in those who have risk factors for hepatotoxicity (e.g., EtOH consumption) and consume >4g/d since APAP is a component of numerous medications.[13]

The following clinical questions should be answered if acetaminophen toxicity is suspected:

1. What time did the ingestion occur?
2. How much acetaminophen was ingested (toxic dose in both children and adults is ≥150mg/kg)?
3. What form of acetaminophen was ingested (e.g., tablet/liquid/chewable/sustained release)?

Case #5

A 65-year-old female with a history of chronic neuropathy presents after seizure. Her husband reports she has had episodes of confusion and sometimes takes extra doses of her medications.

Tricyclic antidepressants

Antidepressants are the third most common cause of fatalities due to ingestion; tricyclic antidepressants (TCAs) account for >11,000 case mentions to U.S. Poison Centers.[2] The resurgence of TCAs may in part be due to treatment of neuropathies, chronic pain, and refractory depression.

The mechanisms of action for TCAs are extensive; in an overdose, these effects are enhanced and lead to potentially deadly consequences, including catecholamine depletion and relative hypotension, anticholinergic effects, seizures, coma, and cardiac dysrhythmias/conduction disturbances.[14]

Management of these patients includes supportive care (**Table 1**), with emphasis on fluid resuscitation for hypotension. An ECG should be obtained immediately to evaluate for widening of the QRS, since this can predict the effects of the TCA poisoning better than serum concentrations.

Other findings on ECG include a terminal R wave in aVR >3mm, and R/S >0.7 in aVR,[16] though life-threatening complications can occur in the absence of ECG abnormalities.

AC should be administered, and the patient should be started on sodium bicarbonate (1 to 2 mEq/kg) if the QRS measures >100 msec on ECG (**Table 5**).

These patients can decompensate rapidly; any suspicion of TCA ingestion in patients who are symptomatic should prompt immediate transfer to an ED. Benzodiazepines should be administered in patients who have seizure activity.[14]

The following clinical questions should be answered if tricyclic antidepressant toxicity is suspected:

1. How many tablets were ingested?

2. Does the patient have any EKG changes?
3. Is there any seizure activity?

Case #6

A 22-year-old male was at a party in college and was found by some friends to be having hallucinations and acting inappropriately. The patient appears profusely diaphoretic and febrile. The patient had taken some "tablets" at the party.

Ecstasy (MDMA) ingestion

Ecstasy is an amphetamine-derived compound that is used primarily for its euphoric effects by teenagers and young adults. It works primarily by increasing the release of dopamine, norepinephrine, and serotonin while also inhibiting their re-uptake. This results in a sympathomimetic response which can produce the following effects:

- tachycardia
- hyperthermia
- anxiety
- diaphoresis
- cardiovascular instability.

In addition, serotonin syndrome can develop due to the increase in circulating serotonin. Symptoms of serotonin syndrome include CNS effects (e.g., altered mental status, hallucinations), autonomic effects (e.g., diaphoresis, hypertension, tachycardia), and neuromuscular instability (e.g., myoclonus, hyperreflexia), ultimately leading to life-threatening hyperthermia.[17]

Serotonin syndrome can be a life-threatening complication of ecstasy and drugs of abuse such as LSD or cocaine, as well as many commonly used over-the-counter drugs (e.g., Robitussin) and prescription medications (e.g., SSRIs, monoamine oxidase inhibitors, lithium). Having a high degree of suspicion is needed to help diagnose this clinical syndrome.

The patient should be transferred to the ED if any vital signs are abnormal (e.g., tachycardia, hypertension, and fever), or if you find muscle rigidity, seizures, and/or changes seen on ECG.

Primary treatment of ecstasy (stimulant) ingestion is supportive; however, management is focused on fluid resuscitation, prevention of seizures with benzodiazepines, and cooling the hyperthermic patient.

If the patient has overdosed, AC can be given to help increase absorption.

A secondary concern with ecstasy ingestion is rhabdomyolysis, which can lead to electrolyte abnormalities (e.g., hyperkalemia, hypocalcemia), cardiovascular compromise, renal insufficiency/failure, and death.

Treatment of hyperthermia requires aggressive cooling measures to help decrease core temperature. Cooling modalities such as a cool mist fans, wet blankets, ice packs to the groin and axillae, and infusion of cool normal saline can help with the patient's temperature while awaiting transfer.

The following clinical questions should be answered if ecstasy (MDMA) ingestion toxicity is suspected:

1. Does the patient have a fever and/or sympathomimetic features?
2. Does the patient have myoclonus and/or hyperreflexia?
3. What type, amount, and route of medication ingested?

Summary

The ability to quickly identify the substance and amount ingested by a patient who appears to be suffering the effects of toxicity is critical to quick action and subsequent positive outcomes. Typically, such patients can be treated effectively in the urgent care center, with transfer or follow-up referral employed as needed. ■

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