Clinical Toxicology

Dr. Asaad H.Alzaidy
PhD pharmacology & toxicology

Clinical toxicology: focuses on the effects of substances in patients caused by accidental poisoning or intentional overdoses of medications, drugs of abuse, household products , or various other chemicals.

Intoxication : toxicity associated with any chemical substance.

Poisoning : a clinical toxicity secondary to accidental exposure .

Overdoses : an intentional exposure with intent of causing self injury or death .

Toxidromes : a group of signs , symptoms, and laboratory findings that suggest a specific ingestion .

Vital signs and toxic syndromes

vital signs

pulse rate,
respiratory rate,
temperature,
blood pressure ,
oxygen saturation,
capillary blood glucose, and
pain severity

Age	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	Pulse (beats/min)	Respirations (breaths/min)[b]
Adult	≤120	<80	60–100	16–24
16 years	≤120	<80	80	16–30
12 years	119	76	85	16–30
10 years	115	74	90	16–30
6 years	107	69	100	20–30
4 years	104	65	110	20–30
4 months	90	50	145	30–35
2 months	85	50	145	30–35
Newborn	65	50	145	35–40

[a] The normal rectal temperature is defined as 95°F to 100.4°F (35°C–38°C) for all ages. For children 1 year of age or younger, these values are the mean values for the 50th percentile. For older children, these values represent the 90th percentile at a specific age for the 50th percentile of weight in that age group.

[b] These values were determined in the emergency department and may be environment and situation dependent.

A poisoning case can present to the hospital in any one of
a number of ways. Broadly, there are four types of presentation:

1. **Fulminant**—Produced by a massive dose. Death occurs very rapidly, sometimes without preceding symptoms, the patient appearing to collapse suddenly.

2. **Acute—**Produced by a single dose or several small doses taken in a short period. Onset of symptoms is abrupt.

3. **Chronic**—Produced by small doses taken over a long period. Onset is insidious.

4. **Subacute—**Characterised by a mixture of features of acute and chronic poisoning.

toxic syndromes ?

Table 2 describes the most typical toxic syndromes. This table includes only vital signs that are thought to be characteristically abnormal or pathognomonic and directly related to the toxicologic effect of the xenobiotic

	Vital Signs								
Group	BP	P	R	T	Mental Status	Pupil Size	Peristalsis	Diaphoresis	Other
Anticholinergics	–/↑	↑	±	↑	Delirium	↑	↓	↓	Dry mucous membranes, flush, urinary retention
Cholinergics	±	±	–/↑	–	Normal to depressed	±	↑	↑	Salivation, lacrimation, urination, diarrhea, bronchorrhea, fasciculations, paralysis
Ethanol or sedative–hypnotics	↓	↓	↓	–/↓	Depressed, agitated	±	↓	–	Hyporeflexia, ataxia
Opioids	↓	↓	↓	↓	Depressed	↓	↓	–	Hyporeflexia
Sympathomimetics	↑	↑	↑	↑	Agitated	↑	–/↑	↑	Tremor, seizures
Withdrawal from ethanol or sedative–hypnotics	↑	↑	↑	↑	Agitated, disoriented hallucinations	↑	↑	↑	Tremor, seizures
Withdrawal from opioids	↑	↑	–	–	Normal, anxious	↑	↑	↑	Vomiting, rhinorrhea, piloerection, diarrhea, yawning

↑ = increases; ↓ = decreases; ± = variable; – = change unlikely; BP, blood pressure; P, pulse; R, respirations; T, temperature.

Table 2.1: Toxic Syndromes

Anticholinergic syndrome

Causes: Antihistamines, antiparkinsonian drugs, atropine, scopolamine, amantadine, antipsychotic drugs, antidepressants, antispasmodics, skeletal muscle relaxants, many plants (especially Datura), and fungi (e.g. *Amanita muscaria*)

Symptomatology: Delirium with mumbling speech, tachycardia, dry hot skin, mydriasis, myoclonus, urinary retention, decreased bowel sounds. Convulsions and arrhythmias in severe cases

Cholinergic syndrome

Causes: Organophosphates, carbamates, parasympathomimetic drugs, and some mushrooms

Symptomatology: Confusion, CNS depression, salivation, lacrimation, urinary and faecal incontinence, vomiting, sweating, fasciculations, seizures, miosis, pulmonary oedema, tachy/bradycardia

Sympathomimetic syndrome

Causes: Cocaine, amphetamines, upper respiratory decongestants (phenylpropanolamine, ephedrine, and pseudoephedrine)

Symptomatology: Paranoia, delusions, tachycardia, hypertension, hyperpyrexia, sweating, mydriasis, seizures, arrhythmias

Sedative syndrome

Causes: Opiates, barbiturates, benzodiazepines, ethanol, methaqualone, meprobamate, ethchlorvynol, glutethimide, clonidine

Symptomatology: Miosis, hypotension, bradycardia, hypothermia, CNS depression, hyporeflexia, coma, rarely convulsions

In some instances, an unexpected combination of findings may be particularly helpful in identifying a xenobiotic or a combination of xenobiotics.

For example, an increase in pulse with a decrease in blood pressure (cyclic antidepressants or phenothiazines),

or the presentation of a decrease in pulse with an increase in blood pressure (ergot alkaloids) may be extremely helpful in diagnosing a toxic etiology.

BLOOD PRESSURE

Xenobiotics cause hypotension by four major mechanisms:

1-decreased peripheral vascular resistance,
2-decreased myocardial contractility,
3-dysrhythmias
4-depletion of intravascular volume.

Many xenobiotics can initially cause orthostatic hypotension, and any xenobiotic that affects autonomic control of the heart or peripheral capacitance vessels may lead to orthostatic hypotension. Hypertension from xenobiotics may be caused by CNS sympathetic overactivity, increased myocardial contractility or increased peripheral vascular resistance, or a combination of these.

PULSE RATE

Extremely useful clinical information can be obtained by evaluating the pulse rate. The normal heart rate for adults was defined by consensus more than 50 years ago as a regular rate greater than 60 beats/min and less than 100 beats/min.

Because pulse rate is the net result of a balance between sympathetic (adrenergic) and parasympathetic (muscarinic and nicotinic) tone, many xenobiotics that exert therapeutic or toxic effects or cause pain syndromes, hyperthermia, or volume depletion also affect the pulse rate. With respect to temperature, there is a direct correlation between pulse rate and temperature in that pulse rate increases approximately 8 beats/min for each 1.8°F (1°C) elevation in temperature.

The inability to differentiate easily between sympathomimetic and anticholinergic xenobiotic effects by vital signs alone illustrates the principle that no single vital sign abnormality can definitively establish a toxicologic diagnosis. In trying to differentiate between a sympathomimetic and anticholinergic toxic syndrome, it should be understood that although tachycardia commonly results from both sympathomimetic and anticholinergic xenobiotics, when tachycardia is accompanied by diaphoresis or increased bowel sounds, adrenergic toxicity is suggested, but when tachycardia is accompanied by decreased sweating, absent bowel sounds, and urinary retention, anticholinergic toxicity is likely.

RESPIRATIONS

Establishment of an airway and evaluation of respiratory status are the initial priorities in patient stabilization. Although respirations are typically assessed initially for rate alone, careful observation of the depth and pattern is essential for establishing the etiology of a systemic illness or toxicity.

The term *hyperventilation* may mean tachypnea (an increase in ventilatory rate), hyperpnea (an increase in tidal volume), or both

. Hyperventilation may result from the direct effect of a CNS stimulant, such as the direct effect of salicylates, on the brainstem.

Bradypnea may occur when a CNS depressant acts on the brainstem.

A progression from fast to slow breathing may also occur in a patient exposed to increasing concentrations of cyanide or carbon monoxide.

TEMPERATURE

Temperature evaluation and control are critical. However, temperature assessment can be done only if safe and reliable equipment is used. The risks of inaccuracy are substantial when an oral temperature is taken in a tachypneic patient, an axillary temperature or a temporal artery temperature is taken in any patient (especially those found outdoors), or a tympanic temperature is taken in a patient with cerumen impaction. Obtaining rectal temperatures using a nonglass probe is essential for safe and accurate temperature determinations in agitated individuals and is considered the standard method of temperature determination in this text.

The core temperature or deep internal temperature (T) is relatively stable (98.6° ± 1.08°F; 37° ± 0.6°C) under normal physiologic circumstances. Hypothermia (T <95°F; <35°C) and hyperthermia (T >100.4°F; >38°C) are common manifestations of toxicity.

PRINCIPLES OF MANAGING THE ACUTELY POISONED OR OVERDOSED PATIENT

Similar to the management of any seriously compromised patient, the clinical approach to the patient potentially exposed to a xenobiotic begins with the recognition and treatment of life-threatening conditions, including airway compromise, breathing difficulties, and circulatory problems such as hemodynamic instability and serious dysrhythmias.

After the "ABCs" (airway, breathing, and circulation) have been addressed, the patient's level of consciousness should be assessed because this helps determine the techniques to be used for further management of the exposure.

Management of patients with altered mental status:

Altered mental status (AMS) is defined as the deviation of a patient's sensorium from normal. Although it is commonly construed as a depression in the patient's level of consciousness, a patient with agitation, delirium, psychosis, and other deviations from normal is also considered to have an AMS. After airway patency is established or secured, an initial bedside assessment should be made regarding the adequacy of breathing. If it is not possible to assess the depth and rate of ventilation, then at least the presence or absence of regular breathing should be determined. In this setting, any irregular or slow breathing pattern should be considered a possible sign of the incipient apnea, requiring ventilation with 100% oxygen by bag–valve–mask followed as soon as possible by endotracheal intubation and mechanical ventilation. Endotracheal intubation may be indicated for some cases of coma resulting from a toxic exposure to ensure and maintain control of the airway and to enable safe performance of procedures to prevent GI absorption or eliminate previously absorbed xenobiotics.

Within the first 5 minutes of managing a patient with an AMS, four therapeutic interventions should be *considered*, and if indicated, administered:

1. High-flow oxygen (8–10 L/min) to treat a variety of xenobiotic-induced hypoxic conditions

2. Hypertonic dextrose: 0.5–1.0 g/kg of D50W for an adult or a more dilute dextrose solution (D10W or D25W) for a child; the dextrose is administered as an IV bolus to diagnose and treat or exclude hypoglycemia

3. Thiamine (100 mg IV for an adult; usually unnecessary for a child) to prevent or treat Wernicke encephalopathy

4. Naloxone (0.05 mg IV with upward titration) for an adult or child with opioid-induced respiratory compromise.

The clinician must consider that hypoglycemia may be the sole or contributing cause of coma even when the patient manifests focal neurologic findings; therefore, dextrose administration should only be omitted when hypoglycemia can be definitely excluded by accurate rapid bedside testing.

Also, while examining a patient for clues to the etiology of a presumably toxic-metabolic form of AMS, it is important to search for any indication that trauma may have caused, contributed to, or resulted from the patient's condition.

Characteristic breath or skin odors may identify the etiology of coma. The fruity odor of ketones on the breath suggests diabetic or alcoholic ketoacidosis but also the possible ingestion of acetone or isopropyl alcohol, which is metabolized to acetone. The pungent, minty odor of oil of wintergreen on the breath or skin suggests methyl salicylate poisoning. The odors of other substances such as cyanide ("bitter almonds"), hydrogensulfide ("rotten eggs"), and organic phosphorus compounds ("garlic") are summarized in Table 3.

Figure 3: *Odors Suggestive of a Xenobiotic.* **(You have to memorize this table)**

Odor	Xenobiotic
Bitter almond	Cyanide
Carrots	Cicutoxin (water hemlock)
Disinfectants	Creosote, phenol
Eggs (rotten)	Carbon disulfide, disulfiram, hydrogen sulfide, mercaptans, *N*-acetylcysteine
Fish or raw liver (musty)	Aluminum phosphide, zinc phosphide
Fruit	Nitrites (amyl, butyl)
Garlic	Arsenic, dimethyl sulfoxide (DMSO), organic phosphorus compounds, phosphorus, selenium, tellurium, thallium,
Hay	Phosgene
Mothballs	Camphor, naphthalene, *p*-dichlorobenzene,
Pepper	*O*-chlorobenzylidene malonitrile
Rope (burnt)	Marijuana, opium
Shoe polish	Nitrobenzene
Sweet fruity	Acetone, chloral hydrate, chloroform, ethanol, isopropanol, lacquer, methylbromide, paraldehyde, trichloroethane
Tobacco	Nicotine
Vinegar	Acetic acid
Violets	Turpentine (metabolites excreted in urine)
Wintergreen	Methyl salicylate

Table 4: *Antidotes and Therapeutics for the Treatment of Poisonings and Overdoses* **(You have to memorize this table)**.

Therapeutics[b]	Uses
Activated charcoal (p. 108)	Adsorbs xenobiotics in the GI tract
Antivenom (*Crotalinae*) (p. 1608)	Crotaline snake envenomations
Antivenom (*Elapidae*) (p. 1308)	Coral snake envenomations
Antivenom (*Latrodectus mactans*) (p. 1582)	Black widow spider envenomations
Atropine (p. 1473)	Bradydysrhythmias, cholinesterase inhibitors (organic phosphorus compounds, physostigmine) muscarinic mushrooms (*Clitocybe, Inocybe*) ingestions
Benzodiazepines (p1109)	Seizures, agitation, stimulants, ethanol and sedative–hypnotic withdrawal, cocaine, chloroquine, organic phosphorus compounds
Botulinum antitoxin (ABE-trivalent) (p. 695)	Botulism
Calcium chloride, calcium gluconate (p. 1381)	Fluoride, hydrofluoric acid, ethylene glycol, CCBs, hypomagnesemia, β-adrenergic antagonists
L-Carnitine (p. 711)	Valproic acid
Cyanide kit (nitrites, p. 1689; sodium thiosulfate, p. 1692)	Cyanide
Dantrolene (p. 1001)	Malignant hyperthermia
Deferoxamine mesylate (Desferal) (p. 604)	Iron
Dextrose in water (50% adults; 20% pediatrics; 10% neonates) (p. 728)	Hypoglycemia
Digoxin-specific antibody fragments (Digibind and Digifab) (p. 946)	Cardioactive steroids
Dimercaprol (BAL, British anti-Lewisite) (p. 1229)	Arsenic, mercury, gold, lead
Diphenhydramine	Dystonic reactions, allergic reactions
DTPA (p. 1779)	Radioactive isotopes
Edetate calcium disodium (calcium disodium versenate, $CaNa_2$ EDTA) (p. 1290)	Lead, other selected metals
Ethanol (oral and parenteral dosage forms) (p. 1419)	Methanol, ethylene glycol
Fat emulsion (Intralipid 20% (p. 976)	Cardiac arrest, local anesthetics
Flumazenil (Romazicon) (p. 1072)	Benzodiazepines
Folinic acid (Leucovorin) (p. 783)	Methotrexate, methanol
Fomepizole (Antizole) (p. 1414)	Ethylene glycol, methanol
Glucagon (p. 910)	β-Adrenergic antagonists, CCBs
Glucarpidase (p. 787)	Methotrexate
Hydroxocobalamin (Cyanokit) (p. 1695)	Cyanide
Insulin (p. 893)	β-Adrenergic antagonists, CCBs, hyperglycemia
Iodide, potassium (SSKI) (p. 1775)	Radioactive iodine (I^{131})
Ipecac, syrup of (p. 104)	Induces emesis
Magnesium sulfate or magnesium citrate (p. 114)	Induces catharsis
Magnesium sulfate injection	Cardioactive steroids, hydrofluoric acid, hypomagnesemia, ethanol withdrawal, torsades de pointes
Methylene blue (1% solution) (p. 1708)	Methemoglobinemia
N-acetylcysteine (Acetadote) (p. 500)	Acetaminophen and other causes of hepatotoxicity
Naloxone hydrochloride (Narcan) (p. 579)	Opioids, clonidine
Norepinephrine (Levophed)	Hypotension (preferred for cyclic antidepressants)
Octreotide (Sandostatin) (p. 734)	Oral hypoglycemic induced hypoglycemia
Oxygen (Hyperbaric) (p. 1671)	Carbon monoxide, cyanide, hydrogen sulfide
D-Penicillamine (Cuprimine) (p. 1261)	Copper
Phenobarbital	Seizures, agitation, stimulants, ethanol and sedative–hypnotic withdrawal
Phentolamine (p. 1096)	Cocaine, MAOI interactions, epinephrine, and ergot alkaloids
Physostigmine salicylate (Antilirium) (p. 759)	Anticholinergics
Polyethylene glycol electrolyte solution (p. 114)	Decontaminates GI tract
Pralidoxime chloride, (2-PAM-chloride; Protopam) (p. 1467)	Acetylcholinesterase inhibitors (organic phosphorus agents and carbamates)
Protamine sulfate (p. 880)	Heparin anticoagulation
Prussian blue (Radiogardase) (p. 1334)	Thallium, cesium
Pyridoxine hydrochloride (Vitamin B_6) (p. 845)	Isoniazid, ethylene glycol, gyromitrin-containing mushrooms
Sodium bicarbonate (p. 520)	Ethylene glycol, methanol, salicylates, cyclic antidepressants, methotrexate, phenobarbital, quinidine, chlorpropamide, type 1 antidysrhythmics, chlorphenoxy herbicides
Sorbitol (p. 114)	Induces catharsis
Starch (p. 1349)	Iodine
Succimer (Chemet) (p. 1284)	Lead, mercury, arsenic
Thiamine hydrochloride (Vitamin B_1.) (p. 1129)	Thiamine deficiency, ethylene glycol, chronic ethanol consumption (“alcoholism”)
Vitamin K_1 (Aquamephyton) (p. 876)	Warfarin or rodenticide anticoagulants

[a] Each emergency department should have the vast majority of these antidotes immediately available, some of these antidotes may be stored in the pharmacy, and others may be available from the Centers for Disease Control and Prevention, but the precise mechanism for locating each one must be known by each staff member.
[b] A detailed analysis of each of these agents is found in the text in the Antidotes in Depth section on the page cited to the right of each antidote or therapeutic listed.
CCB, calcium channel blocker; DTPA, diethylenetriaminepentaacetic acid; EDTA, ethylenediamine tetraacetic acid; GI, gastrointestinal; MAOI, monoamine oxidase inhibitor; SSKI, saturated solution of potassium iodide.