

CLINICAL TOXICOLOGY

Unit 5

CUTM1648: Concepts of
Toxicology

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Introduction



Branch of toxicology which focuses on diseases that are caused by or are uniquely associated with toxic substances. Clinical toxicologists treat patients who are poisoned by drugs and other chemicals and develop new techniques for the diagnosis and treatment of such intoxications



HISTORY OF CLINICAL TOXICOLOGY



- The *Odyssey and Shastras* from approx. 600 BC contained references to antidotes.
- The first documentation of use of a specific antidote may be found in Homer's *Odyssey* where it is suggested to Ulysses that he take moli to protect himself from poisoning.



HISTORY OF CLINICAL TOXICOLOGY



- Galen (AD 129-200) wrote three books called *De Antidotis I*, *De Antidotis II*, and *De Theriaca ad Pisonem* that described the development of a universal antidote known as a alexipharmic or theriac by King Methridates VI of Pontus who lived from 132-63 BC.
- Advances in the field of clinical toxicology have paralleled the evolution of poison control centers.



CLINICAL STRATEGY FOR TREATMENT OF THE POISONED PATIENT



- General steps representing important elements of the initial clinical encounter for a poisoned patient: (in ED)
 1. Stabilization of the patient
 2. Clinical evaluation (HPLR))
 3. Prevention of further toxin absorption
 4. Enhancement of toxin elimination
 5. Administration of antidote
 6. Supportive care and clinical follow-up



1. Stabilization of the patient



- First priority.
- This is the so-called ABCs (Airway, Breathing, Circulation) of initial emergency treatment.
- The clinical procedures available to stabilize a critically ill poisoned patient include the initial and ongoing assessment and, if indicated, support of ventilation, circulation, and oxygenation.



Stabilization of the patient



- Once the poisoned patient is clinically stabilized, the remainder of the assessment and treatment steps proceed.
- In critically ill patients, sometimes treatment interventions must be initiated before a patient is truly stable.



Clinical evaluation



☯ Clinical History in the Poisoned Patient

The primary goal of taking a medical history in poisoned patients is to determine, whenever possible, what substance the poisoned patient has been exposed to and to determine the extent and time of exposure.



Clinical evaluation



Possible sources to obtain an accurate history include family members, emergency medical technicians at the scene, employer who can provide a list of chemicals that are in the work environment



Clinical evaluation



- In estimating the exposure level to the poison, generally one should maximize the possible dose received.
- With an estimate of dose, the toxicologist can refer to various information resources to determine what the range of expected clinical effects might be from the estimated exposure.



Clinical evaluation



- Estimating the timing of the exposure to the poison is also very crucial.
- Sometimes both info. is not available with the toxicologist.
- When this occurs, treatment proceeds empirically as an “unknown ingestion” poisoning.



Clinical evaluation

Physical Examination



- A thorough examination of the patient is required to assess the patient's condition, categorize the patient's mental status and, if altered, determine possible additional explanations for the abnormal mental status such as trauma or CNS infection.



Clinical evaluation



- A toxidrome is a constellation of clinical signs and symptoms that, when taken together, are likely associated with exposure from certain toxicologic classes of chemicals.
- The major toxic syndromes include narcotic, cholinergic, sympathomimetic, and anticholinergic



Clinical evaluation



Clinical Features of Toxic Syndromes

	BLOOD PRESSURE	PULSE	TEMPERATURE	PUPILS	LUNGS	ABDOMEN	NEUROLOGIC
Sympathomimetic	Incr.	Incr.	Slight Incr.	Mydriasis	NC	NC	Hyperalert, incr. reflexes
Anticholinergic	Slight incr. or NC	Incr.	Incr.	Mydriasis	NC	Decr. Bowel sounds	Altered mental status
Cholinergic	Slight decr. or NC	Decr.	NC	Miosis	Incr. bronchial sounds	Incr. bowel sounds	Altered mental status
Opioid	Decr.	Decr.	Decr.	Miosis	NC or rales (late)	Decr. Bowel sounds	Decr. level of consciousness

Clinical evaluation



- Categorization of the patient presentation into toxic syndromes allows for the initiation of rationale treatment based on the most likely category of toxin responsible.
- Occasionally a characteristic odor can be detected on the poisoned patient's breath or clothing which may point toward exposure or poisoning by a specific agent.



Clinical evaluation



Characteristic Odors Associated with Poisonings

ODOR	POTENTIAL POISON
Bitter almonds	Cyanide
Eggs	Hydrogen sulfide, mercaptans
Garlic	As, organophosphates, DMSO, Thallium
Mothballs	Naphthalene, camphor
Vinyl	Ethchlorvynol
Wintergreen	Methylsalicylate



Laboratory Evaluation



- A common misconception concerning the initial treatment of poisoned patients - definitive diagnosis of the specific agent or poison responsible for the patient's clinical presentation is frequently made by the clinical laboratory during the initial patient evaluation.
- The repertoire of specific assays for toxins available in clinical laboratories on a rapid turnaround basis (STAT, e.g., within 1 hour) is very limited.



Laboratory Evaluation

Drugs Commonly Measured in a Hospital Setting on a STAT Basis

Acetaminophen
Acetone
Carbamazepine
Carboxyhemoglobin
Digoxin
Ethanol
Ethyl alcohol
Gentamycin
Iron
Lithium
Methemoglobin
Osmolality
Phenobarbital
Phenytoin
Procainamide/NAPA
Quinidine
Salicylates
Theophylline
Tobramycin
Valproic acid



- This emphasizes the importance of recognizing clinical syndromes for poisoning & for the clinical toxicologist to be able to initiate general treatment and supportive care for the patient with poisoning from an unknown substance.



Laboratory Evaluation



- For some commonly ingested drugs, a nomogram has been established to predict the severity of the poisoning.

It is important in some cases to guide therapeutic intervention based on the measured plasma concentration of the drug and the time elapsed from the exposure.



Laboratory Evaluation



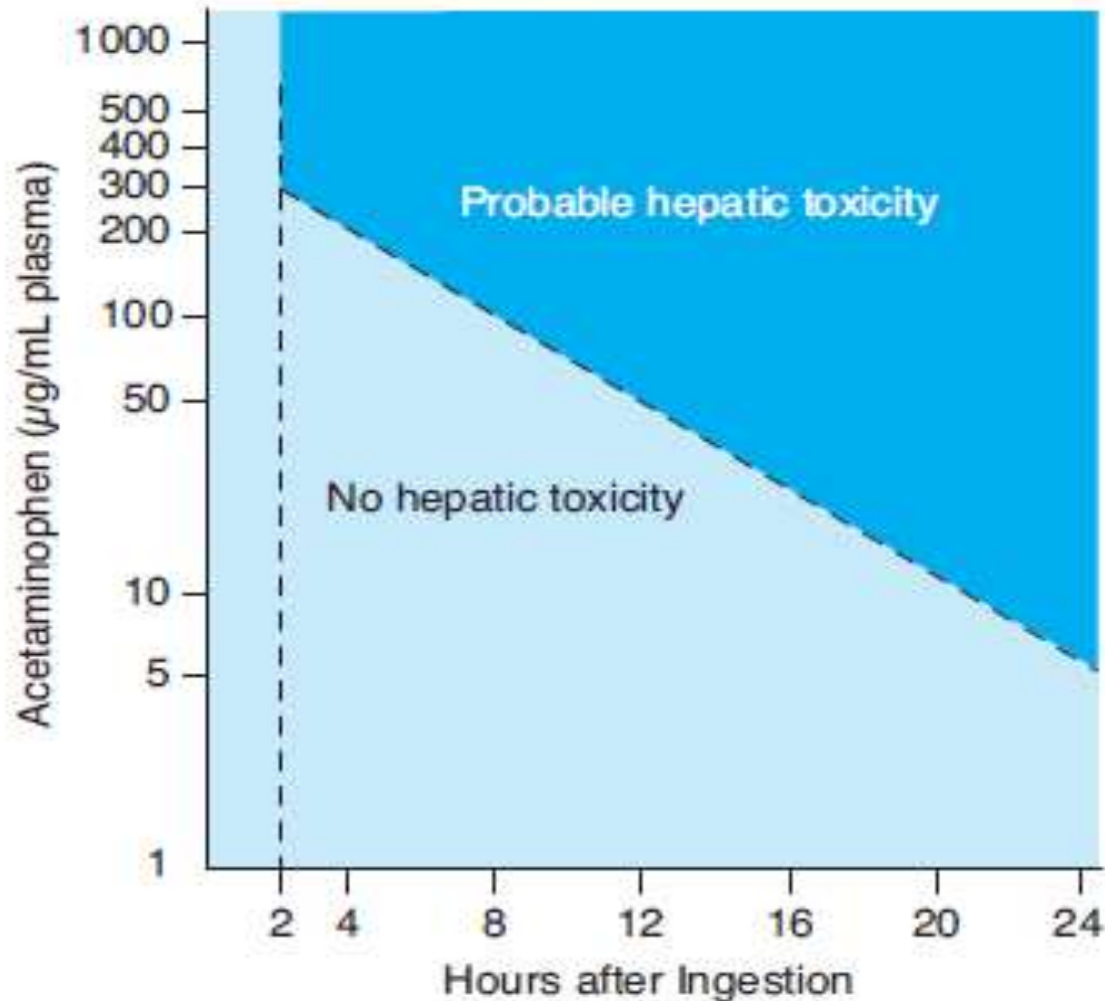
- Due to the limited clinical availability of “diagnostic” laboratory tests for poisons, toxicologists utilize specific, routinely obtained, clinical laboratory data to establish a differential diagnosis of what poisons may have been ingested



Laboratory Evaluation



Semilogarithmic Plot
of Plasma Acetaminophen Levels vs. Time



Laboratory Evaluation



- There are two calculations that toxicologists perform using clinical laboratory values routinely in an acute clinical setting are the **anion gap** and the **osmol gap**.
- Both are diagnostic aids when the clinical history suggests poisoning & the patient's condition is consistent with exposure to agents known to cause elevations of these parameters



Laboratory Evaluation



Differential Diagnosis of Metabolic Acidosis with Elevated Anion Gap: "AT MUD PILES"

A	Alcohol (Ethanol ketoacidosis)
T	Toluene
M	Methanol
U	Uremia
D	Diabetic ketoacidosis
P	Paraldehyde
I	Iron, Isoniazid
L	Lactic Acid
E	Ethylene Glycol
S	Salicylate



- An abnormal anion gap or osmol gap suggests a differential diagnosis for significant exposure of a poisoned patient.

Laboratory Evaluation



- **Anion Gap = $[Na \text{ mEq/L} - (Cl \text{ mEq/L} + HCO_3 \text{ mEq/L})]$**
- Normal Anion Gap ≤ 12
- **OsmoGap = Measured Serum Osmolality (mOsm) – Calculated Serum Osmolarity**
- Where, calculated serum osmolarity = $2 \times Na \text{ mEq/L} + Glucose \text{ mg/dL} / 18 + BUN \text{ mg/dL} / 2.8$.
- Normal osmol gap $< 10 \text{ mOsm}$.



Radiographic Examination



- The utility to diagnose specific poisonings relatively limited due primarily to the lack of radiopacity of many oral forms of medication.
- Most useful radiographs ordered in an overdose or poisoned patient include the chest and abdominal radiographs and the computed head tomography study.





- Abdominal plain radiographs are helpful in the setting where foreign bodies are detected in the GIT.



Laboratory Evaluation



The four primary methods currently available for this purpose are:

1. Induction of emesis with like syrup of ipecac,
2. Gastric lavage,
3. Oral administration of activated charcoal
4. Whole bowel irrigation.



Prevention of Further Poison Absorption



- During the early phases of poison treatment or intervention for a toxic exposure via the oral, inhalation or the topical route, the treatment team may have an opportunity to prevent further absorption of the poison to minimize the total amount that reaches the systemic circulation.



Enhancement of Poison Elimination



- Several methods available to enhance the elimination of specific poisons or drugs absorbed into the systemic circulation.
- The primary methods employed for this today include:
 1. alkalization of the urine,
 2. hemodialysis,
 3. hemoperfusion,
 4. hemofiltration,
 5. plasma exchange or exchange transfusion,
 6. serial oral activated charcoal.



Use of Antidotes in Poisoning



- Antidotes : A remedy that stops or controls the effects of a poison.
- A relatively small number of specific antidotes are available for clinical use in the treatment of poisoning.



Antidotes

Acetaminophen

Anticholinergics

Benzodiazepines

Beta blockers

Carbamates

Calcium channel blockers

Carbon Monoxide

Cyanide

Digoxin

Ethylene glycol/methanol

N-acetylcysteine

Physostigmine

Flumazenil

Glucagon

Atropine

Calcium, glucagon,
insulin/glucose

Oxygen

Amyl Nitrite, sodium nitrite,
sodium thiosulfate

Fab fragments

Ethanol, fomepizole

Use of Antidotes in Poisoning



Antidotes

Iron

Isoniazid

Metals

Nitrates/nitrites

Opiates

Organophosphates

Snakes

Deferoxamine

Pyridoxine

**BAL, EDTA, DMSA
(Succimer), d-
penicillamine**

Methylene Blue

Naloxone, nalmefene

Atropine, Pralidoxime

Antivenin, CroFab



Use of Antidotes in Poisoning



- The development of human monoclonal antibodies directed against specific toxins has significant potential therapeutic value → snake bite, marine animal bite.



Cottonmouth (water moccasin)



Marine Animals



- Stingray





Jellyfish



Supportive Care of the Poisoned Patient



- Very important phase .
- Poisoned patients who are unstable or at risk for significant clinical instability are generally admitted to a medical intensive care unit for close monitoring.
- In addition, patients who are excessively sedated due to poisoning or those who require mechanical ventilation or invasive hemodynamic monitoring are usually candidates for an intensive care stay.



Supportive Care of the Poisoned Patient



- Similar to other ill, hospitalized patients, patients admitted for continued treatment of poisoning are at risk for nosocomial infections, iatrogenic fluid and electrolyte disturbances as well as potential harmful effects from the initial therapies that they received for treatment of their poisoning.



Supportive Care of the Poisoned Patient



- Another important component of the supportive care phase of poison treatment is the psychiatric assessment.
- For intentional self poisonings, a formal psychiatric evaluation of the patient should be performed prior to patient discharge.
- In many cases, it is not possible to perform a psychiatric interview of the patient during the early phases of treatment and evaluation. Once the patient has been stabilized and is able to communicate, the psychiatric evaluation should be obtained in this



Supportive Care of the Poisoned Patient



- Once the patient has been stabilized and is able to communicate, the psychiatric evaluation should be obtained in this setting.
- Generally a patient who has attempted suicide should be constantly monitored until they have been evaluated by the psychiatric consultant and judged to be “safe” to remove from constant surveillance.





Thank You