Pesticides

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PERSPECTIVE

- *Pesticides*, a generic term used to refer to all pest-killing agents and include:
  - insecticides
  - Herbicides
  - Rodenticides
  - Fungicides
  - Fumigants
- Many are general protoplasmic poisons affecting a wide range of organisms, including humans.

ORGANOPHOSPHATE AND CARBAMATE INSECTICIDES

- Some of the most common pesticides for home and industrial use
- Organophosphorus insecticides are highly lipid soluble and are readily absorbed via dermal, GI, and respiratory routes
- This lipid solubility results in the storage of organophosphorus compounds in body fat, making toxic systemic levels possible from gradual or rapid accumulation from repeated low-level exposures

Principles of Disease

- The parent compound and its metabolites are acetylcholinesterase inhibitors

- Many parent organophosphorus compounds are less potent than their metabolites (e.g., parathion to paraoxon), which may result in delayed onset of clinical toxicity.

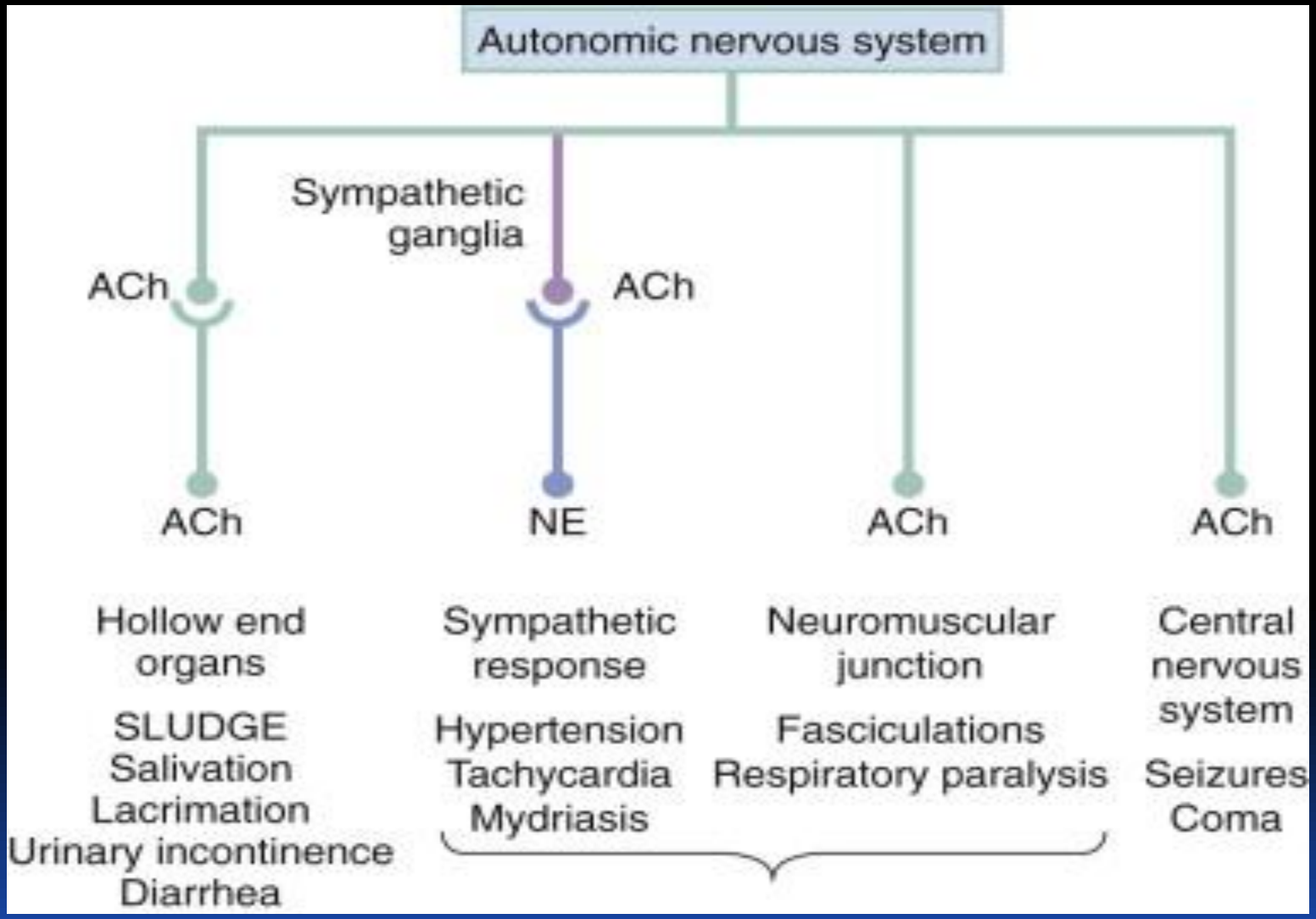
Principles of Disease

- They work by persistently inhibiting the enzyme acetylcholinesterase, the enzymatic deactivator of the neurotransmitter acetylcholine.
- Because of the global penetration of organophosphorus compounds, inhibition occurs at tissue sites (true acetylcholinesterase represented by erythrocyte cholinesterase) and in plasma (circulating pseudocholinesterase).

Principles of Disease

- Inhibition of cholinesterase results in the accumulation and subsequent prolonged effect of Acetylcholine at neurotransmitter receptors
  - Sympathetic & parasympathetic Ganglion (Nicotinic sites)
  - Postganglionic Cholinergic sympathetic and parasympathetic (Muscarinic sites)
  - skeletal muscle (Nicotinic sites)
  - central nervous system sites

Principles of Disease



Principles of Disease

Sympathetic nervous system (thoracolumbar outflow). The neurotransmitter in ganglia is acetylcholine (ACh). The neurotransmitter in the target organ is norepinephrine (NE).

Parasympathetic nervous system (craniosacral outflow), use ACh as the neurotransmitter in preganglionic and postganglionic target organs.

The ANS is divided further into the Muscarinic and Nicotinic receptors, Atropine can block Muscarinic receptors but not Nicotinic receptors.

Neuromuscular junction uses ACh as effector neurotransmitter.

In the brain, ACh is just one of several active neurotransmitters.

Clinical Features
Signs and Symptoms

- The accumulation of acetylcholine results in a classic cholinergic syndrome, manifested by hyperactivity of cholinergic responses at the receptor sites indicated previously.
- The clinical syndrome of muscarinic acetyl cholinesterase inhibition is commonly called the SLUDGE syndrome or DUMBELS.

SLUDGE Symptoms or DUMBELS

Salivation	Diarrhea/Diaphoresis
Lacrimation	Urination
Urinary incontinence	Miosis
Defecation	Bradycardia/Bronchorrhea/Bronchospasm
Gastrointestinal cramps	Emesis
Emesis	Lacrimation
	Salivation

Clinical Features
Signs and Symptoms

- Bradycardia is a classic sign of the cholinergic syndrome, but the increased release of norepinephrine from postganglionic sympathetic neurons precipitated by excess cholinergic activity at sympathetic ganglia may result in normal or even tachycardic heart rates (nicotinic effect).

Clinical Features
Signs and Symptoms

- CNS: A combination of sympathetic stimulation, involvement of the *N*-methyl-d-aspartate receptor, and enhanced acetylcholine concentrations can lead to seizures.
- NMJ: At the neuromuscular junction, excess acetylcholine causes hyper stimulation of the muscles with secondary paralysis.
- Because the diaphragm is affected, cholinesterase poisoning leads to respiratory arrest

Clinical Features
Signs and Symptoms

- clinical picture of acute organ ophosphorus poisoning is impressive,
- toxicity from gradual, cumulative exposure may be much more subtle. These patients commonly exhibit vague confusion or other central nervous system complaints; mild visual disturbances; or chronic abdominal cramping, nausea, and diarrhea.

Complications

- Seizure, bronchorrhea and bronchoconstriction are prominent mechanisms of early morbidity
- Obstruction of upper and lower airways produce hypoxia
- Muscle hyperactivity eventually gives way to muscle paralysis (including respiratory muscles and diaphragm)
- Respiratory insufficiency results in death if not anticipated and corrected

ENZYME COMPLEX AGING

- Unique effect of organophosphorus insecticides results from “aging,” the irreversible structural change that occurs in cholinesterase enzyme when the organophosphorus agent is bound to it for a prolonged time.
- On average, for commercial organophosphorus agents aging will occur by 48 hours, but may take longer.
- Once the enzyme has aged, an oxime antidote cannot regenerate the cholinesterase.

Diagnostic Strategies

- Known or suspected exposure to cholinesterase inhibitors should be confirmed by ordering plasma and erythrocyte (RBC)cholinesterase levels.
- In acute exposures, the plasma cholinesterase levels decrease first, followed by decreases in RBC cholinesterase levels.
- The RBC cholinesterase level is more indicative of what is occurring at the nerve terminal (tissue level).

Diagnostic Strategies

- Patients with chronic exposures may show only reduced RBC cholinesterase activity, with a normal plasma cholinesterase level.
- RBC cholinesterase levels recover at a rate of 1% per day in untreated patients and take approximately 6 to 12 weeks to normalize, whereas plasma cholinesterase levels may recover in 4 to 6 weeks.

Diagnostic Strategies

- Other studies should focus on the evaluation of pulmonary, cardiovascular, and renal function and fluid and electrolyte balance.

- Patients presenting with no acidosis, or only a metabolic acidosis on the arterial blood gas, have lower mortality than those presenting with a respiratory or mixed acidosis

Management

Treatment is directed toward four goals:

- (1) decontamination
- (2) supportive care
- (3)reversal of acetylcholine excess at muscarinic sites
- (4) reversal of toxin binding at active sites on the cholinesterase molecule.

- Decontamination should start in the out-of-hospital phase

Management

- Decontamination is particularly important in cases of dermal exposure; removal and destruction of clothing and thorough flushing of exposed skin may limit absorption
- Dermal decontamination can be done with dry agents, such as military resins, flour, sand, or bentonite.
- Caregivers are at risk from splashes or handling of contaminated clothing.
  - Should use universal precautions,

Management

- In the case of ingestion, GI decontamination procedures are of questionable benefit because of the rapid absorption of these compounds.
- Profuse vomiting and diarrhea are seen early in ingestion and may limit or negate any beneficial effect of additional GI decontamination.
- Equipment, but not tissues, may be washed with a 5% hypochlorite solution to inactivate the cholinesterase inhibitor.

Management

Supportive care should be directed primarily toward Airway management, Breathing and Circulation,

Airway management includes suctioning of secretions and vomitus, oxygenation, and, when necessary, intubation and ventilatory support,

Intravenous access and fluid boluses as needed for circulatory collapse

Seizure/Convulsions can be controlled by Benzodiazipine

Management

- The definitive treatment of acetylcholinesterase inhibition starts with Atropine.
- A competitive inhibitor of acetylcholine at muscarinic receptor sites, atropine reverses the clinical effects of cholinergic excess at parasympathetic end organs and sweat glands.
- Large doses of atropine may be required.
- Data suggest that the more rapid the atropinization, the faster control is obtained

Management

- Suggested dosing is 1 or 2 mg of atropine (0.02–0.05 mg/kg) IV, with doubling of each subsequent dose every 5 minutes until there is control of mucous membrane hypersecretion and the airway clears.
- If IV access is not immediately available, atropine may be administered IM

Management

- Tachycardia and mydriasis may occur at these doses, but they are not indications to stop atropine administration
- The endpoint of atropinization is drying of respiratory secretions, easing of respiration, and a mean arterial pressure greater than 60 mm Hg
- Atropine is not active at nicotinic sites and does not reverse the skeletal muscle effects (e.g., muscle fatigue and respiratory failure).

Management

- The second part of acetyl cholinesterase inhibition treatment is the use of an Oxime:
  - Pralidoxime (2-PAM, Protopam)
  - Obidoxime (Toxigonin)
- These degrade the organophosphate-acetylcholinesteras complex and restore the active cholinesterase form
- Work at muscarinic and nicotinic sites
- In the past, pralidoxime was only used within the first 24 hours because of aging of the organophosphate-acetylcholinesterase complex, but not all organophosphates behave in a similar manner

Management

- The medication may be given as repeated boluses or continuous infusion
- The infusion may need to be continued for several days for complete reversal of cholinesterase activity
- Indications for oxime therapy include
  - respiratory depression/apnea
  - fasciculations
  - seizures
  - arrhythmias, cardiovascular instability
  - Patients who need large amounts of atropine (2–4 mg) to completely reverse the signs and symptoms of intoxication
  - patient who requires repeated doses of atropine

Disposition

- Most patients with significant exposures require hospital admission including intensive care settings
- A person with chronic exposure, and mild visual or GI symptoms may be followed as outpatient
- Asymptomatic or mildly symptomatic patients with near normal cholineesterase levels may be discharged after 4 to 6 hours

- A secondary syndrome, the intermediate syndrome (IMS), occurs 24 to 96 hours after exposure and consists of proximal muscular weakness specifically of the respiratory muscles. It is believed to be an abnormality at the neuromuscular junction. Patients with IMS present with respiratory failure several days after the acute cholinergic symptoms have resolved and may require several weeks of ventilatory support.

- Organophosphorus-delayed neuropathy has been reported as a different entity and affects an axonal enzyme, neurotoxic esterase, and leads to a peripheral sensorimotor neuropathy 7 to 21 days after exposure.

CARBAMATE INSECTICIDES

- Carbamate insecticides are another class of acetylcholinesterase inhibitors and are differentiated from the organophosphorus compounds by their relatively short duration of toxic effects. Carbamates inhibit acetylcholinesterase for minutes to 48 hours, and the carbamate-cholinesterase binding is reversible. Although the clinical picture of acute carbamate poisoning may be identical to that of organophosphate poisoning,

- the toxic effects are limited in duration and patients may require only decontamination, supportive care, and treatment with adequate doses of atropine. Although the duration is limited in scope, patients may become just as sick and require assisted ventilation and seizure therapy. The use of pralidoxime is controversial in carbamate poisoning

Poison Center

Poison Control Centre

facility that provides immediate, free, and expert treatment advice in case of exposure to poisonous or hazardous substances.

Poison control center answer questions about potential poisons in addition to providing treatment management advice about household products, medicines, pesticides, plants, bites and stings, food poisoning, and fumes

More than 72% of poison exposure cases are managed simply by phone, reducing the need for costly hospital visits

GOALS:

- As source of rapid access to information for physicians which is valuable in assessing and treating poisonings timely and accurately
  - Training to the professional and paraprofessionals on first-aid, management and prevention of poisoning.
  - Provides toxicological laboratory services for therapeutic as well as forensic investigation
  - In developing contingency plans for chemical disaster with other responsible bodies.
  - The center carries out epidemiological and experimental studies

Poison Control Center - Riyadh
General Directorate of Health Affairs - Medial Province
Kingdom of Saudi Arabia

- Forensic Chemistry Unit
- Clinical Toxicology Unit
- Therapeutic Drug Monitoring Unit
- Drugs & Poisons Information Unit
- Studies & Research Unit

Departments

Therapeutic Drug Monitoring Unit

Estimate the number of drugs of interest such as some antibiotics, some medicines for heart disease, treatment of epilepsy and tumors that may exist in blood samples drawn from patients who need their cases treatment with these drugs in order to adjust the doses and avoid the side effects of the drugs.
In addition, this department is concern with diagnosis of non-compliance by taking those drugs from by some patients, which helps the physician to get a better therapeutic response to those drugs

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وزارة الصحة
Ministry of Health

Contact Numbers for Riyadh Poison Control Center (MOH)

Direct Number:

Phone Center: +966 112324189 / 112324180

Drug Information Unit Ext: 108

Fax Center: Ext: 106

Email: **pcc-riyadh@moh.gov.sa**

King Saud University Poison Control Service

- The Pharmacy Services Department of King Khalid University Hospital (KKUH) established a Poison control service in conjunction with their drug information center in October 1983

- Contact Detail 71500

King Saud University Poison Control Service

- offer expert advice from well-trained clinical pharmacists.
- The service was made available 24 hours a day (calls received from 7:30 am to 4:00 pm were managed by the Drug and Poison Information Center [DPIC], while after- hours consultations were managed by on-call clinical pharmacists).
- Information on poisoning management was targeted towards physicians,

DIFFERENCES BETWEEN DIC & PIC

Poison Information Center	Drug Information Center
CLIENTELE	
88% poison center calls are placed by public	9-10% calls are placed by public,but mostly by health care professionals.
CALL VOLUME	
103 calls per day, it ranges from 33 to 213 calls per day.depending upon service population size,poison center awareness in that area,poisoning rates.	Fewer than 7 calls per day

HOURS OF OPERATION/COST

- Operates 24hrs a day year round
- More expensive

STAFFING

- They use a wider variety of health care professionals

FUNDING

- Public funding

- Operates 9AM-5PM
- Less expensive
- They rely on pharmacists
- Sponsored by hospitals or medical centers

The data currently being tracked through the TESS include:

- General epidemiological data- date and time of call, reason for exposure
- Caller characteristics- site of caller, city and state
- Patient characteristics- age and sex, pregnancy status
- Exposure characteristics- substance, route of exposure, site of exposure, amount of exposure, time elapsed
- Clinical course- clinical manifestations and therapeutic interventions recommended and performed and outcome of exposure

RESOURCES: used as reference for exposures

- Micromedex's poisindex(a database of more than 8,00,000 household products, chemicals, and medications)
- General product formulations are found in Clinical Toxicology Of Commercial Products by Gosselin, Smith, and Hodge.
- In addition they often maintain manufacture files with recent product formulations
- Internal protocols, journals, medical literatures

Data from KKUH Poison Center

Table 1. The most common type of poisoning involving children <5 years old, 6-12 years old, and adults.

Categories	Substance ingested	Children <5 years (%)	Children 6-12 years (%)	Adults (%)
Drugs	CNS depressants	70		30
	Birth control pills	7.6		
	Iron/multivitamins	7.6		
	Paracetamol	5.7		
	NSAID	5.7	7.6	30
	Unknown	2.6	23	
	Antibiotics	2.6		
	Others	27	27.4	
Household products	Cosmetics			
	Chlorox	5.1		
	Disinfectant/ deodorizers	3.2		
	Elemental mercury	3.2		
	Naphthalene	2		
	Others	4.4		7
Industrial products		4.4		9
Bites/stings		1.2	30.4	12
Food poisonings and plants		<1		
Plants			7.6	

POISON INFORMATION SPECIALISTS

- They directly interact with the public and health care professionals.
- Poison information specialists must be both clinicians and counselors. They must elicit a complete history, correctly assess the potential severity of exposure using the most appropriate management plan to the caller.
- In addition, poison information specialists must be able to focus callers who are unable to give cohesive history.
- Specialists should be able to communicate in a calm , reassuring manner at all levels of education.
- Both nurses and pharmacists are suitable poison information specialists.