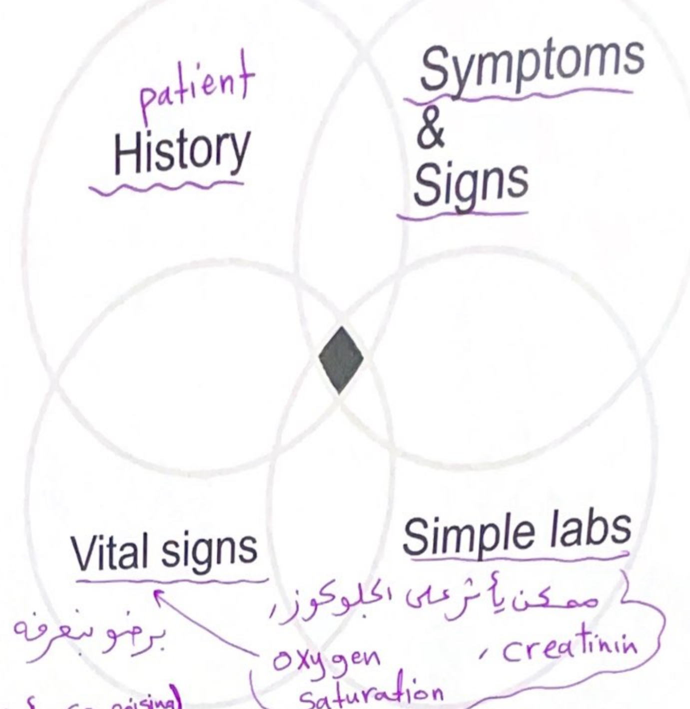
TOXIDROMES

TOXIDROMES

Collection of signs and symptoms that associated with exposing to a poisn

- ✓ THE ***IDENTIFICATION OF VARIOUS TOXIC SYNDROMES*** REQUIRES INTEGRATING OF DATA PROVIDED BY BOTH THE ***VITAL SIGNS AND PHYSICAL EXAMINATION*** TO ELICIT MANIFESTATIONS SPECIFIC TO AN INTOXICANT
- ✓ THIS COLLECTION OF MANIFESTATION (TOXICOLOGIC SYNDROMES) MAY ASSIST IN
- ✓ **1. THE DIAGNOSIS WHEN THE AGENT IS UNKNOWN** AND MAY HELP IN ← pinpoint ← مثلاً ال ← مؤشر لل opioid poisn pupil
- ✓ **2. ANTICIPATING MANIFESTATIONS THAT WILL DEVELOP.** symptoms and signs بتوقع ال يلي راح تصير

TOXIDROME



ممكن يأثر على الجلوكوز، creatinin
oxygen saturation

vital signs برضو نعرفه بال
يأثر على CO poising)
(RBC oxygen saturation

← certain toxins ممكن تسبب formation of toxic metabolite and we can detect that from lab test

نستنتج

TACKLING TOXIDROMES

كيف ممكن اتوقع ال toxin ؟

- Good history
- Directed physical examination
  - Vital signs, pupils, skin, bowel bladder
- Simple tests
  - Rapid glucose, ECG, ABG, UA, etc
- Simple interventions

* مثلاً لما قستله الضغط طلع عنده hypertension بحط احتمالات
شو ممكن يعمل hypertension مثلاً sympathomimetic
amphitamine
Coccain
nicotine

بنفس الوقت لقيت عنده mydriasis
برضو بحط الخيارات المحتملة وشوف شو المشترك

ANTIDOTE → block the recepter (antidote مش كل الادوية)

- ✓ Antidotal therapy involves antagonism or chemical inactivation of an absorbed poison

- ✓ Antidotes can significantly reduce morbidity and mortality rates but are potentially toxic if used for inappropriate reasons....their use requires correct identification of a specific poisoning or syndrome

* ex: naloxone antidote for opioids
flumazenil antidote for benzodiazepine

---

* B-blocker بتسبب hypoglycemia وكمان بتعمل symptoms mask of hypoglycemia بالتحديد الـ tachycardia بتعمل mask، ما عدا الـ sweating للمريض من الـ symptoms

ANTIDOTE لازم يتبع B-blocker في حالة كان مريض سكري وما

- ✓ The pharmacodynamics of a poison can be altered by competition ① at a receptor (naloxone therapy in the setting of heroin overdose)

- ✓ ② Physiological antidote (glucagon in the setting of propranolol overdose) (or other B-blocker) (reverse symptomes) ← بحيث يعكس الـ symptoms مثل: Bradycardia hypoglycemia

- ✓ ③ Anti-venoms and chelating agents bind and directly inactivate poisons (agents binds to the toxin in order to stop it's action) (برتبط مع الـ toxin وبثبط عمله)

مثل ارتباط الـ Iron مع الـ deferoxamine (مش ارتباط على recepter)

ANTIDOTE

- ✓ The **biotransformation** of a drug can also be altered by an antidote (fomepizole will inhibit alcohol dehydrogenase and stop the formation of toxic acid metabolites from ethylene glycol and methanol) fomepizole antidote for → methanol poising

methanol —alcohol dehydrogenase→ formaldehyde → formic acid (toxic)

- ✓ Many drugs used in the ***supportive care*** of a poisoned patient (anticonvulsants, vasoconstricting agents, etc.) may be considered nonspecific functional antidotes (for symptoms reversing)

fomepizle بثبط هاد الانزيم وبالتالي بثبط تكوّن alcohol metabolite toxic يلي معم

بـ من أدوية إذا منهم بسبّب convulsions بنعطيهم anti convulsant (benzodiazipene) أو مثلاً إذا سبّبت shock hypotension بنعطي vasoconstricter or anti-histamine

TOXIDROMES EXAMPLES

Cholinergic receptors stimulation

*Cholinergic agonist = drugs that binds to acetyl choline, muscarine recepter

TOXIDROMES: CHOLINERGIC

Symptoms and signs (toxidromes) مجموعة من تعبير راح تحصل ما

THREE WAYS TO ENHANCE CHOLINERGIC ACTIVITY:

(direct) 1. CHOLINERGIC MEDICATIONS

- PILOCARPINE = MIOSIS (glucoma) ← topically in the eye to treat glucoma
- BETHANECHOL = URINARY STIMULANT (to treat urinary retentison)

overdose منعم راح يحصل
and signs مجموعة من
symptoms

بالتالي بزيد تركيز الاستيل كولين وبزيد ال Stimulation for Cholinergic system

TOXIDROMES: CHOLINERGIC

(indirect) 2. ACETYL CHOLINESTERASE INHIBITORS: بتثبط هاد الانزيم بالتالي بيحصل block لل metabolism of acetyl choline
ORGANOPHOSPHATES & CARBAMATES

(direct) 3. PLANTS: AMANITA MUSCARIA (Certain mashroms) تحتوي على muscarine ← acetyl choline recepter agonist

CLITOCYBE

TOXIDROMES: CHOLINERGIC

DUMBELS (direct or indirect-AchEI)

(general parasympathatic stimulation)

- ✓ DEFECATION
- ✓ URINATION
- ✓ MIOSIS
- ✓ BRONCHOSPASM / BRADYCARDIA
- ✓ EXCESSIVE SALIVATION
- ✓ LACRIMATION
- ✓ SEIZURES, SECRETIONS, SWEATING

anticholinergic ←

- •ANTIDOTE: atropine / pralidoxime (PAM) ← reactivation for inhibited enzyme
- •Administer activated charcoal orally ← orally toxicity ازا صارت بسبب تناول

بنستخدمه في حالة (organophosphate + carbamates)

كل ما أسرعنا كل ما كان أحسن ولا بعدها تتشبط الانزيم بصير irreversible وما بنقدر نرجع نعمله reactivation

مثلا:
miosis → mydriasis
bradychardia → tachycardia
urination → urinary retension
salivation → dry mouth ← salivation بمانعها

في حال كانت toxicity من الـ ← راح تنعكس جدول الـ symptoms

TOXIDROMES: ANTICHOLINERGIC

THINK: ANTI AND ATROPINE

*drug classas that have anti cholinergic effect:-

- ANTIHISTAMINES ← first generation
- ANTIPSYCHOTICS → phenothiazine
- ANTISPASMODICS → reduce GI tract motelity
- ANTIEMETICS
- ANTIPARKINSON → مثل: benztropine and tralixaperidine
- TCAs → antideppressent
- PLANTS: *Atropa belladonna*, JIMSON WEED (*Datura stramonium*), HENBANE (*Hyoscyamus niger*)

[بمرض الباركنسون بنحاول نصلح balance اما بزيد dopamine أو بقلل acetyl choline]

TOXIDROMES

TABLE 34-2. ANTICHOLINERGIC SUBSTANCES

Antihistamines
- Ethanolamines
  - Dimenhydrinate (Dramamine)
  - Diphenhydramine (Benadryl)
- Ethylenediamines
  - Tripelennamine (Pyribenzamine)
- Alkylamines
  - Chlorpheniramine (Teldrin, Chlortrimeton)
- Piperazines
  - Cyclizine (Marezine)
  - Meclizine (Antivert)
- Phenothiazines
  - Promethazine (Phenergan)

Antiparkinsonian drugs
- Benztropine mesylate (Cogentin)
- Biperiden (Akineton)
- Ethopropazine (Parasidol)
- Trihexyphenidyl (Artane)
- Procyclidine (Kemadrin)

Antipsychotics
- Phenothiazines, particularly
  - Chlorpromazine (Thorazine)
  - Thioridazine (Mellaril)
  - Perphenazine (Trilafon)
- Nonphenothiazines
  - Molindone (Moban)
  - Loxapine (Loxitane)

Antispasmodics
- Clidinium bromide (Quarzan, Librax)
- Dicyclomine (Bentyl)
- Methantheline bromide (Banthine)
- Propantheline bromide (Pro-Banthine)
- Tridihexethyl (Pathilon)

Belladonna alkaloids and synthetic relatives
- Atropine (Hyoscyamine)
- Belladonna alkaloid mixtures
- Glycopyrrolate (Robinul)
- Homatropine (Dia-Quel, Malcotran)
- Methscopolamine (Pamine)
- Scopolamine (Hyoscine)

Ophthalmic products
- Atropine and scopolamine solutions
- Cyclopentolate (Cyclogyl)
- Tropicamide (Mydriacyl)

OTC medications (including antihistamines and belladonna alkaloids)
- Analgesics: Excedrin PM, Percogesic
- Cold remedies: Actifed, Allerest, Coricidin, Dristan, Flavihist, Romex, Sine-Off
- Hypnotics: Compoz, Sleep-Eze, Sominex, Unisom
- Menstrual products: Pamprin, Premesyn PMS

Plants (see Chapter 58)

Skeletal muscle relaxants
- Orphenadrine (Norflex)

Tricyclic antidepressants
- Amitriptyline (Elavil, Amitril, Endep, Emitrip)
- Desipramine (Norpramin, Pertofrane)
- Doxepin (Sinequan, Adapin)
- Imipramine (Tofranil, Pramine, Janimine, Tipramine)
- Nortriptyline (Aventyl, Pamelor)
- Protriptyline (Vivactil)
- Trimipramine (Surmontil)

(مش مطلوب)

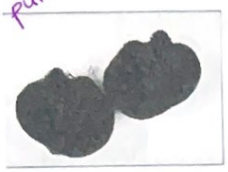
TOXIDROMES

ANTICHOLINERGIC (ATROPINE, ANTIHISTAMINES, TCA's)

(أعراض الـoverdose)

- HOT AS A HARE
- RED AS A BEET
- DRY AS A BONE
- BLIND AS A BAT
- MAD AS A HATTER
- The bowel and bladder lose their tone
- ....and the heart runs alone

(urinary retension and constipation)



higher doses can affect → dose dependent *
CNS and cause hallucination, agitation, tachycardia ---)
(atropine overdose considered as CNS excitatory agent) ⓥ

TOXIDROMES

ANTICHOLINERGIC

- Mydriasis
- Blurred vision → because of mydriasis and cycloplegia and dryness of the eye (serious complication)
- Fever
- Dry skin
- Flushing
- Ileus
- Urinary retention
- Tachycardia
- Hypertension
- Psychosis
- Myoclonus
- Seizures

ANTIDOTE:
physostigmine / treat symptoms

physostigmine → Cholinesterase inhibitor

بدي أحاول قدر ما أقدر انو امنع ال metabolism لل acetyl choline endogenous

acetyl choline ↑ ← وبالتالي بنافس ال atropin على ال binding site

وبالتالي بعمل reverse لل action لل atropine

MANAGEMENT

✓ Maintain an open airway and assist ventilation if needed

✓ Treat (if they occur):

- Hyperthermia….external rapid cooling → (atropine induced hyperthermia)
- Seizures…..benzodiazepine

NSAIDs غير فعّال بهاي الحالة ولا paracetamol

فقط بعمله general cooling (بغسل وجهو مثلاً)

← ليش بنختار physostigmine مش ال neostigmine لمعالجة atropine overdose ؟

لأنه ال physostigmine ← more lipid soluble to reverse CNS side effect

MANAGEMENT

- ✓ A small dose of **physostigmine** (0.5-1 mg IV in an adult), given to patients with severe toxicity
- ✓ *Precaution:* can cause AV block, asystole, and seizures, especially in patients with tricyclic antidepressant overdose
- ✓ **Decontamination:** administer activated charcoal orally (gastric lavage is not needed)

(مش مجبية)

TOXIDROMES: SYMPATHOMIMETIC

SYMPATHOMIMETIC (COCAINE, AMPHETAMINES), nicotine [indirect acting sympathomimetic agent]

- MYDRIASIS (no blurred vision)
- TACHYCARDIA
- HYPERTENSION
- FEVER
- SWEATING
- SEIZURES

ANTIDOTE:
benzodiazepines

TOXIDROMES

NARCOTIC

Papaver somniferum
" poppy plant"

TOXIDROMES

(opium poppy plant)

NARCOTIC (HEROIN, METHADONE) morphin

(in case of overdose)

- MIOSIS
- CNS DEPRESSION
- BRADYCARDIA
- HYPOTENSION
- HYPOVENTILATION (respiratory depression can lead to death
- HYPOTHERMIA
- COMA
- DEATH

ANTIDOTE:
naloxone

WITHDRAWAL

TOXIDROMES

WITHDRAWAL: (ALCOHOL, NARCOTICS, SEDATIVE - HYPNOTICS, antiHTN DRUGS

(overdose عكس ال)

- DIARRHEA
- CRAMPS
- MYDRIASIS
- LACRIMATION
- TACHYCARDIA
- SEIZURES
- HYPERTENSION
- HALLUCINATIONS

ANTIDOTE:

benzodiazepines → and other drugs to control seizures and CNS excitation

← اذا كان المريض مدمن وبدهم يسحبو منه المادة اللي هو بيعطيه naloxone ↳ will worse the Condition

Table 7. Common Toxidromes.

Cholinergic (organophosphates) (DUMBELS) **D**iarrhea, diaphoresis **U**rination **M**iosis **B**radycardia, bronchosecretions **E**mesis **L**acrimation **S**alivation	**Anticholinergic (antihistamines, TCAs)** Hyperthermia (HOT as a hare, RED as a beet) Dry skin (DRY as a bone) Dilated pupils (BLIND as a bat) Delirium, hallucinations (MAD as a hatter) Tachycardia Urgency retention	**Sympathomimetic (cocaine, amphetamines)** Diaphoresis Mydriasis Tachycardia Hypertension Hyperthermia Seizures	**Narcotic (heroin, methadone)** Miosis Hypoventilation Coma Bradycardia Hypotension **Withdrawal (from alcohol, opioids, benzodiazepines, barbiturates, antihypertensives)** Diarrhea Mydriasis Goose flesh Tachycardia Lacrimation Hypertension Yawning Cramps Hallucinations Seizures (with ETOH and benzodiazepine withdrawal)

احفظوبين بالسلايد

SPECIFIC ANTIDOTES

Table 8 *Specific Antidotes and Their Indications**

Antidote	Indication	Comments
Bicarbonate, sodium	TCA; For urine alkalinization in salicylate overdose; for severe metabolic acidosis from ASA, ethylene glycol, or methanol.	Use for TCA cardiotoxicity, not neurotoxicity. Urinary alkalinization may benefit rhabdomyolysis as well. Difficulty alkalinizing urine may be due to hypokalemia. Watch for complications from hypernatremia, volume overload, and serum pH above 7.5
Dantrolene Muscle relaxant	Malignant hyperthermia (muscle rigidity due to overactivation or release of Ca+2)	Give in patients who do not respond to neuromuscular paralysis, may aggravate respiratory depression.[43]
Diazoxide (prevent insuline release) K+ channel activator/vasodilator	Sulfonylureas hypoglycemia	Diazoxide inhibits insulin secretion. Use when serum glucose concentrations cannot be adequately maintained by IV 5% dextrose infusion
Digibind (digoxin antibodies)	Digoxin/ Digitalis/ Cardiac glycosides	Use for cases involving life-threatening arrhythmias or hyperkalemia (>5 meq/L)
Flumazenil	Benzodiazepines toxicity	Half-life = 40–80 min but duration of action 90 min.[44] Do not administer in any patient at risk for seizures or withdrawal.
N-acetylcysteine	Acetaminophen toxicity from 7– 10 g	Most effective administered within 8-10 h of ingestion. Controversy as to best route (IV vs oral) and duration of therapy. 36 h likely adequate in uncomplicated cases.[45]

① gastric lavage, Charcoal ② manipulation of urin pH to enhance barbeturates excreation

Nalmefene	Narcotics	Half-Life=8-10 h, but duration of effect approximately 4 h. Disadvantage is cost ($6.50/0.25 mg vs $0.30/ 0.4 mg of naloxone)
Naloxone	Narcotics	Half-life=1 hour, duration of effect 45 min. Beware of exposing the dangerous effects of coingestion such as cocaine or PCP[46]
Octreotide Somatostatin analogue / inhibit insulin	Sulfonylureas	A somatostatin analog suppresses insulin and C-peptide levels, permitting the plasma glucose to rise without additional dextrose support.
Pyridoxine (Vitamin B6)	Isoniazid Peripheral neuropathy due to pyridoxine depletion	Give in gram-to-gram ratio or 5 g empiric dose; consider as empiric therapy in unknown seizure overdose not responding to benzodiazepines.
Thiosulfate/nitrites Thiosulfate nitrites	Cyanide electron transport chain in mitochondria ATP blokage	Do not give nitrates in the setting of smoke inhalation since the resulting methemoglobinemia may exacerbate carbon monoxide poisoning.[47-49]
Vitamin K	Coumarin and indanedione derivatives (warfarin)	Must use Vitamin K1, not Vitamin K3. Even after IV dose, there is a 6-8 h delay before coagulation factors begin to achieve significant levels. Use fresh frozen plasma for immediate control of hemorrhage.
*TCA = tricyclic antidepressants.		

bind to cyanide ← Thiosulfate nitrites

↓ increase it's solubility to enhance it's excretion (cyanide toxicity ∴ charcoal ما نقدر استخدم)

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