# Identification, Availability & Storage of Antidotes Against Highly Toxic Substances


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**Diploma in Clinical Toxicology(Australia)**
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## Lessons from history...

- A young princess ate part of an apple given to her by a wicked witch
- She was found comatose and unresponsive, as if in a deep sleep
- Airway positioning and mouth to mouth ventilation were performed, and she recovered fully

Lesson

# Best antidote Good Supportive Care

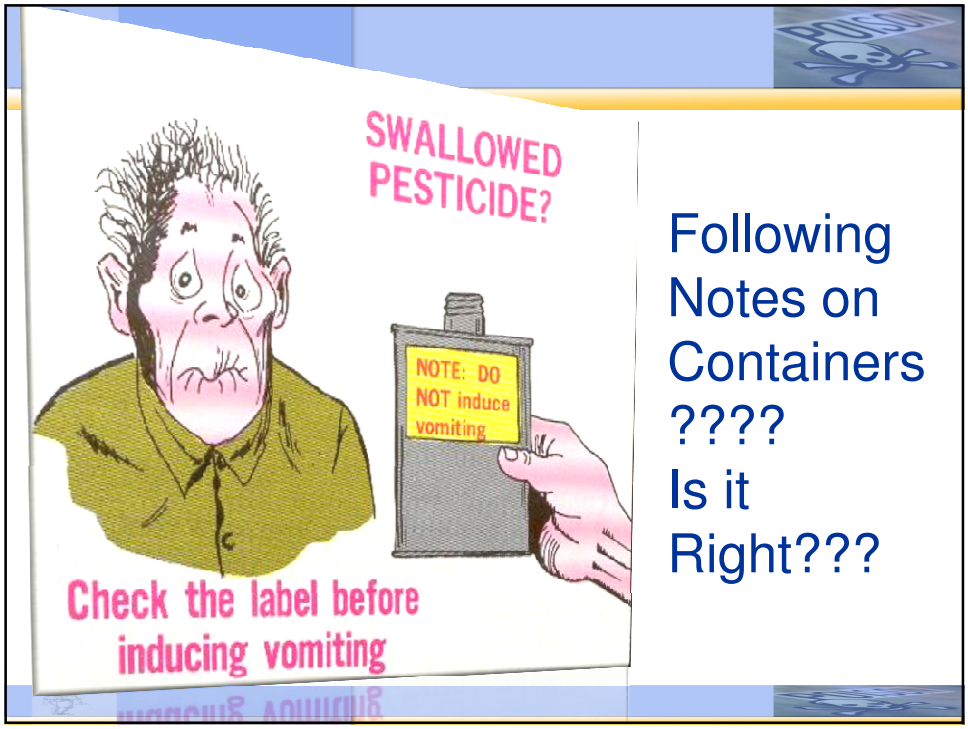
## Antidotes

Definition:

- An **antidote** is a substance which can counteract a form of poisoning. The term ultimately derives from the Greek αντιδιδοναι *antididonai*, "given against".

or

- A therapeutic substance used to counteract the toxic action(s) of a specified xenobiotic



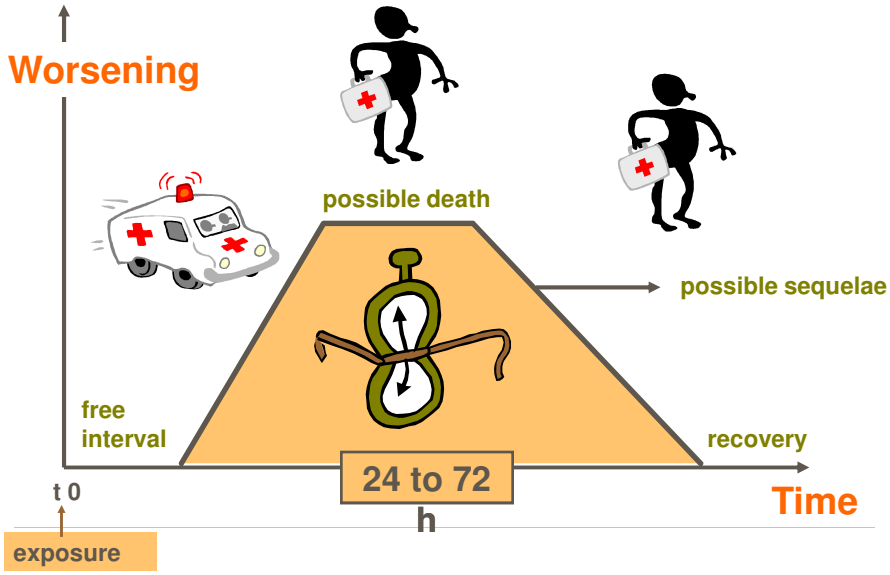

Following Notes on Containers ???? Is it Right???

## Background

'Fewer than 1% of people who present with self poisoning develop severe clinical effects.
One of the main challenges in managing poisoned patients is to identify this group as early as possible so that appropriate supportive, and if necessary, specific management steps can be instituted to prevent serious complications.'

A L Jones, P I Dargan. Advances, challenges, and controversies in poisoning. Emerg Med J 2002;19:190–191

## Acute poisoning, a dynamic process




## Use of antidotes?

- Guidelines for hospital/ED antidotes availability
  - ✓ International Program on Chemical Safety (OMS – 1997)
  - ✓ US experts panel (2000)
  - ✓ UK experts panel (2006)
  - ✓ French and Belgian experts (2006, 2007)
- No specific guidelines for prehospital use of antidotes
  - ✓ apart from some French guidelines (1997, 2000) and studies (1993 – 2006)
  - ✓ likely to be a subset of antidotes needed in the ED

# Availability? IPCS (OMS) 1997

**Evaluation of Antidotes: Activities of the International Programme on Chemical Safety***

Jenny Pronczuk de Garbino; John A. Haines; Dag Jacobsen; Tim Meredith

*Geneva, Switzerland (JPdG; JAH); Oslo, Norway (DJ); Nashville, Tennessee (TM)*

Clinical Toxicology, 35(4), 333–343 (1997)

Availability of antidotes:

**A. within 30 minutes**

B. within 2 hours

C. within 6 hours

**1. effectiveness well documented**

2. widely used, but …

3. questionable usefulness

# Availability? IPCS (OMS) 1997

**Evaluation of Antidotes: Activities of the International Programme on Chemical Safety***

Jenny Pronczuk de Garbino; John A. Haines; Dag Jacobsen; Tim Meredith

*Geneva, Switzerland (JPdG; JAH); Oslo, Norway (DJ); Nashville, Tennessee (TM)*

**21 'antidotes'**

Clinical Toxicology, 35(4), 333–343 (1997)

**Availability < 30 min**

**Well documented effectiveness**

Atropine
Beta-blockers
Calcium gluconate
Dicobalt edetate
Digoxin antibodies
Ethanol
Glucagon
Glucose
Hydroxocobalamin
Isoprenaline
4-methylpyrazole

Methylene blue
Naloxone
Oxygen
Phentolamine
Physostigmine
Prenalterol
Protamin sulphate
Sodium nitrite
Sodium nitroprusside
Sodium thiosulfate

# Availability? USA, 2000

Combined Evidence-Based Literature Analysis and Consensus Guidelines for Stocking of Emergency Antidotes in the United States

ANNALS OF EMERGENCY MEDICINE 36:2 AUGUST 2000

**Evaluation of 20 antidotes**

See Appendix for author affiliations.

Received for publication October 28, 1999. Revision received March 22, 2000. Accepted for publication April 28, 2000.

Presented in abstract form at the American College of Emergency Physicians Research Forum, Las Vegas, NV, October 1999.

Supported by the United States Health Resource Services Administration and

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Lewis R. Goldfrank, MD
Peter A. Chyka, PharmD
Donna Lotzer, RPh, CSPI
Alan D. Woolf, MD, MPH
Jude McNally, RPh, ABAT
Wayne R. Snodgrass, MD, PhD
Kent R. Olson, MD
Elizabeth Scharman, PharmD, ABAT
Robert J. Geller, MD

**Study objective:** To develop guidelines for the stocking of antidotes at hospitals that accept emergency admissions using combined evidence-based and consensus methods.

**Methods:** Study participants were 12 medical care providers from disciplines that are affected by insufficient stocking of emergency antidotes (clinical pharmacology, critical care, clinical pharmacy, emergency medicine, hospital pharmacy, internal medicine, managed care pharmacy, clinical toxicology, pediatrics, poison control centers, pulmonary

individuals for
revious antidote
ase and use of
dote was sys-
e files, current

1. Is the antidote effective?
2. Is the antidote needed within one hour?
3. How many patients should a facility prepare for …?
4. What amount of the antidote is needed to treat a 70-Kg patient?

# Availability? USA, 2000

Combined Evidence-Bas
and Consensus Guideline
Emergency Antidotes in t

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Daniel Spyker, MD, PhD
Monica Kraft, MD
Robert Lipsy, PharmD

**16 recommended 'antidotes'**:
Acetylcysteine
Atropine
Crotalid snake anvenim
Calcium salts
Cyanide antidote kit
Deferoxamine
Digoxin antibodies
Dimercaprol
Ethanol
Fomepizole
Glucagon
Methylene blue
Naloxone
Pralidoxime
Pyridoxine
Sodium bicarbonate

2 not recommended:
. Black widow antivenin
. CaNa2 EDTA

No consensus:
. Flumazenil
. Physostigmine

ANNALS OF EMERGENCY MEDICINE 36:2 AUGUST 2000

## Antidote recommendations for stocking at facilities that accept emergency patients in USA.

*ANNALS OF EMERGENCY MEDICINE, VOLUME 54 NO 3 SEPTEMBER 2009*

RICHARD C. DART, MD, PHD, STEPHEN W. BORRON, MD, MS, E. MARTIN CARAVATI, MD, MPH, DANIEL J. COBAUGH, PHARM D, STEVEN C. CURRY, MD, JAY L. FALK, MD, LEWIS GOLDFRANK, MD, SUSAN E. GORMAN, PHARM D, MS, STEPHEN GROFT, PHARM D, KENNON HEARD, MD, KEN MILLER, MD, PHD, KENT R. OLSON, MD, GERALD O'MALLEY, DO, DONNA SEGER, MD, STEVEN A. SEIFERT, MD, MARCO L. A. SIVILOTTI, MSC, MD, TAMMI SCHAEFFER, DO, ANTHONY J. TOMASSONI, MD, MS, ROBERT WISE, MD, GREGORY M.BOGDAN, PHD, MOHAMMED ALHELAIL, MD JENNIE BUCHANAN, MD, JASON HOPPE, DO, ERIC LAVONAS, MD SARA MLYNARCHEK, MPH, DONG-HAUR PHUA, MD SEAN RHYEE, MD, MPH, SHAWN VARNEY, MD, AMY ZOSEL, MD

Antidote recommendations for stocking at facilities that accept emergency patients.

| Antidote | Poisoning Indication | Should be stocked | Available within 60 minutes | Immediately available |
|---|---|---|---|---|
| Acetyl cysteine | Acetaminophen | Yes | Yes | No |
| Antivenin* | Snakebite | Yes | Yes | No |
| Atropine Sulphate | OPs and N-methyl carbamate pesticides | Yes | Yes | Yes |
| Botulinum antitoxin | Botulism | No | NA | NO |
| Botulism immune globulin | Infant botulism | No | NA | NA |
| Calcium chloride | Ca channel blockers, HF | Yes | Yes | Yes |
| Calcium gluconate | Ca channel blockers, HF | Yes | Yes | Yes |
| Calcium Sodium EDTA | Lead | Yes | Yes | Yes |
| Calcium DTPA | Internal contamination with Plutonium, Americium, Curium | Yes | No | No |
| Cyanide antidote kit | Cyanide poisoning | Yes | Yes | Yes |
| Hydroxocobalamin | Cyanide poisoning | Yes | Yes | Yes |

Antidote recommendations for stocking at facilities that accept emergency patients.

| Antidote | Poisoning Indication | Should be stocked | Available within 60 minutes | Immediately available |
|---|---|---|---|---|
| Deferoxamine mesylate | Acute iron poisoning | Yes | Yes | No |
| Digoxin Immune Fab | Cardiac glycosides/steroid Toxicity | Yes | Yes | Yes |
| Dimercaprol | Heavy metal toxicity (arsenic, mercury, lead | Yes | Yes | No |
| Ethanol OR Fomepizole | Methanol, or ethylene glycol poisoning | Yes | Yes | No |
| Flumazenil | Benzodiazepine toxicity | Yes | Yes | Yes |
| Glucagon hydrochloride | β-Blocker, calcium channel blocker | Yes | Yes | Yes |
| Methylene blue | Methemoglobinemia | Yes | Yes | Yes |
| Naloxone hydrochloride | Opioid and opiate drugs | Yes | Yes | Yes |

Antidote recommendations for stocking at facilities that accept emergency patients.

| Antidote | Poisoning Indication | Should be stocked | Available within 60 minutes | Immediately available |
|---|---|---|---|---|
| Octreotide acetate | Sulfonylurea-induced hypoglycemia | Yes | Yes | No |
| Physostigmine salicylate | Anticholinergic syndrome | Yes | Yes | Yes |
| Potassium iodide | Thyroid radioiodine protection | Yes | Yes | No |
| Pralidoxime chloride | Organophosphorus insecticide poisoning | Yes | Yes | NC |
| Pyridoxine hydrochloride | Isoniazid, hydrazine and derivatives | Yes | Yes | Yes |
| Prussian blue | Thallium/radiocesium | NC | NC | NC |
| Sodium bicarbonate | Sodium channel blocking drugs, urine or serum alkalization | Yes | Yes | Yes |

Dart et al: Annals *of Emergency Medicine,* Volume 54 NO 3 September 2009

# Availability? UK, 2006

Guideline on Antidote Availability for Accident and Emergency Departments
June 2006

FOR
EMERGENCY MEDICINE

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Guy's and St Thomas' NHS
NHS Foundation Trust

Guy's and St Thomas' Poisons Unit
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Website: www.medtox.org

- **Those that should be immediately available within A&E**
- Those that should be available for use within one hour or four hours
- Those that are either not critically time dependent or are used rarely and could be held supra-regionally

# Availability? UK, 2006

**Those that should be immediately available within A&E: 18 'antidotes'**

Guy's and St Thomas' NHS
Foundation Trust

Guy's and St Thomas' Poisons Unit
☎0870 2432241

*Registered Charity No 273876*

CHURCHILL HOUSE
2ND FLOOR, 35 RED LION SQUARE
LONDON, WC1R 4SG, UNITED KINGDOM

**Guy's and St Thomas' Poisons Unit**
Avonley Road
London

- Acetylcysteine
- Activated charcoal
- Atropine
- Benzatropine
- Calcium salts
- Hydroxocobalamin
- Diazepam
- Dicobalt edetate
- Ethanol
- Flumazenil
- Glucagon
- Glyceryl trinitrate
- Methylene blue
- Naloxone
- Procyclidine injection
- Sodium bicarbonate
- Sodium nitrite
- Sodium thiosulfate

# Belgian and French authors

Réanimation 15 (2006) 383–389

Réanimation

Antidotes

P. Hantson[a,*], R. Bédry[b]

[a] Département des soins intensifs, centre de toxicologie clinique, cliniques Saint-Luc, université
10, avenue Hippocrate, 1200 Bruxelles, Belgique
[b] Service de réanimation polyvalente et de toxicologie médicale, clinique mutualiste, 46, avenue Docteur-

**Antidotes** EMC

V. Danel, C. Tournoud, P. Lheureux, P. Saviuc, P. Hantson,

Antidotes. EMC (Elsevier Masson SAS, Paris), Méde
d'urgence, 25-030-A-30, 2007.

- Acetylcysteine
- Atropine
- Calcium salts
- Diazepam
- Flumazenil
- Hydroxocobalamin
- Naloxone
- Phytomenadione
- Pralidoxime
- Sodium bicarbonate
- Tropatepine

# Prehospital availability? French data

Petit P. Antidotes, antagonistes et épuration des toxiques en préhospitalier. Septième Symposium de Réanimation Préhospitalière de Montluçon. *Rev SAMU* 1997:61-7.

'Antidotes' needed

in a Medical Emergency Care Unit

(France, 1997)

- Activated charcoal
- Adrenaline
- Atropine
- Calcium salts
- Dobutamine
- Flumazenil
- Hydroxocobalamin
- Hypertonic glucose
- Isoprenaline
- Naloxone
- Propranolol
- Thiosulfate

# Prehospital availability?

LA REVUE DES SAMU

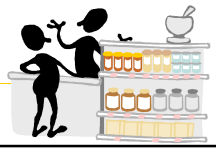
N°145 ISSN 1148-8115 2000 TOME XXII N° 2 AVRIL

- *Le choix des antidotes.*
  *F. Lapostolle, C. Lapandry*
- *Modalités d'utilisation des principaux antidotes.*
  *F. Lapostolle, F. Adnet, C. Lapandry*

NUMÉRO SPÉCIAL FORMATION CONTINUE
TOXICOLOGIE - Deuxième partie

# Which antidotes are actually used?

- French data:
  Acute poisoning = 3 → 10 % MECU interventions
  - ✓ Dherbecourt V. Indication d'administration des antidotes sur les lieux d'intervention ou pendant les transferts par le SAMU. Thèse Université de Lille, 1993
  - ✓ Lardeur et al. Régulation et prise en charge des intoxications volontaires par un SAMU.
    Presse Medicale 2001; 30: 626-630.
  - ✓ Labourel et al. Analyse épidemiologique des intoxications médicamenteuses volontaires aiguës: prise en charge par un SMUR.
    Rev Med Liège 2006:61: 3: 185-189.



## Which antidotes?

- Most used:
  - ✓ Flumazenil
  - ✓ Hydroxocobalamin
  - ✓ Hypertonic glucose
  - ✓ Naloxone
  - ✓ Sodium bicarbonate/lactate

- *Rarely used:*
  - ✓ *acetylcysteine, adrenaline, atropine, diazepam, digoxin antibodies, ethanol, fomepizole, glucagon*

## Use of antidotes in Poisoning Cases

- In the United States in 2006, more than 2.4 million people reported to poison centers, of which approximately 3.5% required specific antidotal therapy.
- Only five antidotes (benzodiazepines, N-acetylcysteine [NAC], naloxone, calcium, and atropine) accounted for 87% of the antidote use in such cases
- There is no such data from India but the above data is unlikely to be applicable as the poisoning scenario is quite different

## Role of antidotes in Poisoning


## Other therapeutic agents useful in the treatment of Poisoning

| Agent | Indications |
|---|---|
| Corticosteroids | Acute allergic reactions, bronchoconstriction, laryngeal edema |
| Diazepam | Convulsions, excitation, anxiety, hypertonia |
| Adrenaline | Anaphylactic shock, cardiac arrest |
| Furosemide | Fluid retention, LVF |

## Other therapeutic agents useful in the treatment of Poisoning

| Agent | Indications |
|---|---|
| Glucose | Hypoglycemia |
| Oxygen | Hypoxia |
| Magnesium Sulfate | Cardiac arrhythmias |
| Mannitol | Cerebral oedema, Fluid retention |
| Dopamine | Hypotension |

## Cholinesterase Inhibitors

Most likely agent in accidental release:

Organophosphorus pesticides

Most likely agent in act of Terrorism:

Sarin and VX

Routes of Entry: These agents are absorbed by inhalation, by ingestion and even through skin. Even one drop of agent VX on skin can be lethal

## Cholinesterase Inhibitors

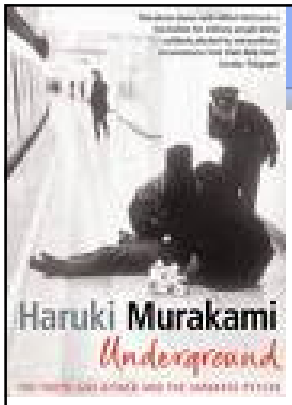
Two main groups:

- Organophosphorus insecticides
- Nerve gases used in warfare

On Monday 20 March 1995, five members of Aum Shinrikyo launched a chemical attack on the Tokyo Metro, one of the world's busiest commuter transport systems, at the peak of the morning rush hour . The chemical agent used, liquid sarin, was contained in plastic bags wrapped in newspaper. At prearranged stations, the sarin packets were dropped and punctured several times with the sharpened tip of the umbrellas.

Shoko Asahara

Aum Shinrikyo is the former name of a controversial group now known as Aleph. The prosecution said that it was an attempt to bring down the government and install Shoko Asahara, the group's founder, as the "emperor" of Japan.




| | |
|---|---|
| Location | Tokyo, Japan |
| Date | (March 20, 1995) 7:00-8:10 a.m. |
| **Attack type** | Chemical warfare |
| **Weapon(s)** | Sarin |
| **Deaths** | 12 |
| **Injured** | 1,034 (*50 severe; 984 temporary vision problems*) |
| **Perpetrator (s)** | Aum Shinrikyo |

## Cholinesterase Inhibitors

Treatment: Supportive treatment includes oxygen, suctioning of secretions and mechanical ventilation

Antidotes: There are three antidotes.

Atropine works mainly at the muscarinic sites. In adults it is given in doses of 2 mg every 5 – 10 minutes and the dose is adjusted to minimize respiratory secretions, airway resistance and dose is adjusted by clinical judgement.

## Cholinesterase Inhibitors

Pralidoxime: Reactivates acetyl cholinesterase and thus works at nicotinic, muscarinic and central nervous system receptors. The initial dose is 1 gm administered over 20-30 minutes

Benzodiazepines: are highly effective anticonvulsant agents. They should be administered in all persons with severe intoxication


## Cyanide poisoning

- Cyanide - a rare source of poisoning;
- Cyanide poisoning - Industry, particularly in the metal trades, mining, electroplating, jewelry manufacturing, and x-ray film recovery.
- As suicidal agents, particularly among healthcare and laboratory workers
- Terrorist attack.
- Studies in France, Sweden, and Scotland, as well as the United States, document smoke inhalation as an important source of cyanide poisoning.

# CYANIDE

## INDUSTRY


ELECTROPLATING

HARDENING METALS

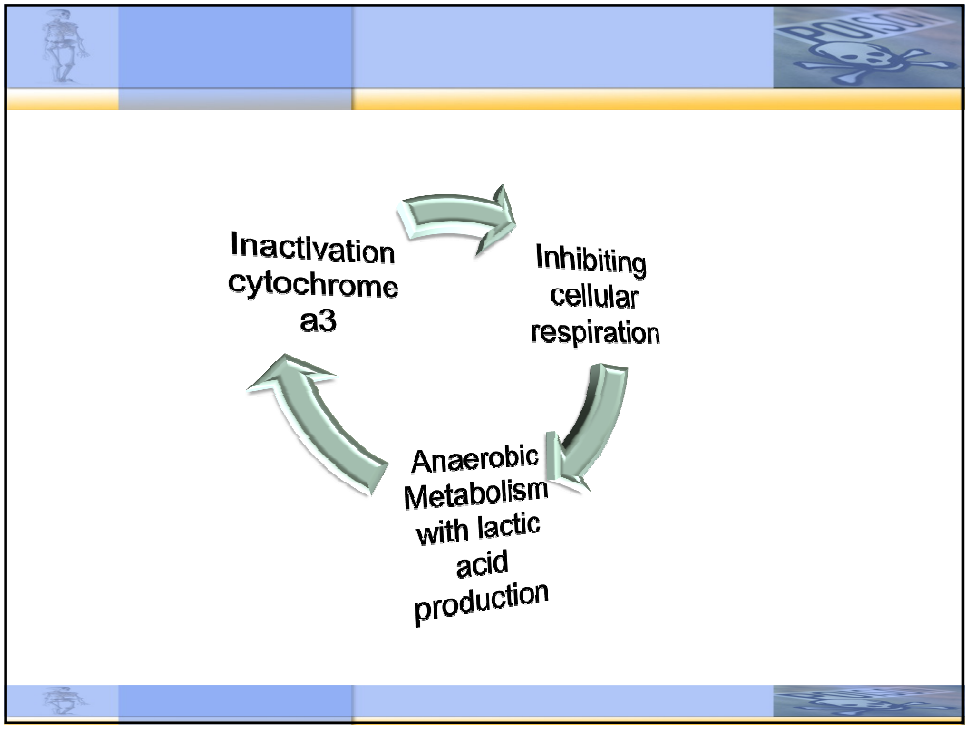
GOLD EXTRACTION

LABORATORIES

# CYANIDE

## FIRE

CYANIDE/CARBON MONOXIDE




## Management of Cyanide Poisoning

- Patients generally require admission to ICU for continuous cardiac monitoring, respiratory and cardiovascular support, and frequent neurologic evaluation.
- Acute poisoning from cyanogens (nitriles) and poorly soluble salts may not manifest or become life threatening for several hours after exposure.
- Monitor disease resolution by clinical criteria, serial plasma lactate concentrations, and arterial and venous blood gases.
- Perform serial ECGs for patients with cardiac dysrhythmias or complaints of chest pain.

## Cyanide Antidote Kit

- Cyanide Antidote Kit (CAK) contains amyl nitrite pearls, sodium nitrite, and sodium thiosulfate.
- Amyl and sodium nitrites induce methemoglobin in red blood cells, which combines with cyanide, thus releasing cytochrome oxidase enzyme. Inhaling crushed amyl nitrite pearls is a temporizing measure before intravenous administration of sodium nitrite.
- Sodium thiosulfate enhances the conversion of cyanide to thiocyanate ,

## Cyanide Antidote Kit(CAK)

- Avoid the sodium nitrite portion of the cyanide kit in patients with smoke inhalation unless carboxyhemoglobin concentration is very low (<10%). The induction of methemoglobinemia from the nitrites in addition to present carboxyhemoglobinemia significantly reduces the oxygen-carrying capacity of blood.
- Vasodilatation leading to hypotension is another adverse effect of CAK.

## Cyanide Antidote Kit

### Contents of Cyanide antidote kit (Troikaa )

Two ampoules of Sodium nitrite Injection USP 300 mg in 10 ml of sterile water for injection
1 vial of Sodium thiosulfate injection I.P., 25 gm in 50 ml of sterile water for injection

12 durules of Amyl nitrite Inhalant, 0.3 ml

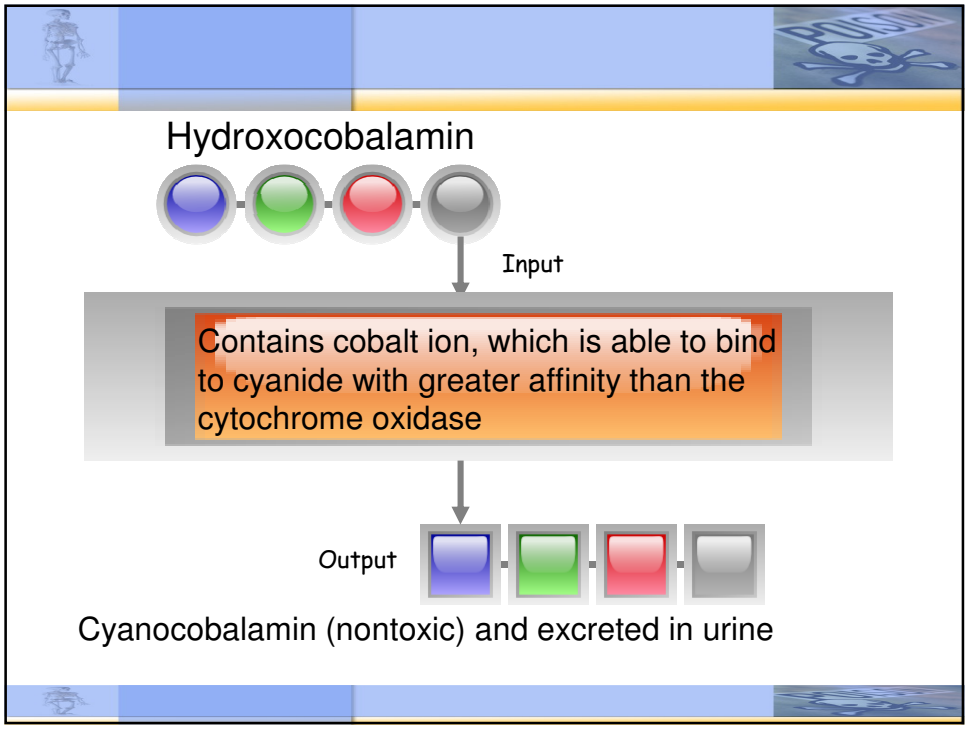
## Hydroxocobalamin as Cyanide antidote

- This antidote has been used in France since 1996.
- Individuals with smoke inhalation from enclosed space fires who have soot in the mouth or nose, altered mental status, or hypotension may have significant cyanide poisoning
- Cyanide poisoning also is responsible for significant morbidity and mortality in victims of fires and smoke inhalation, because hydrogen cyanide can be a combustion product in fires involving materials such as plastics, wool, silk, and polyurethane

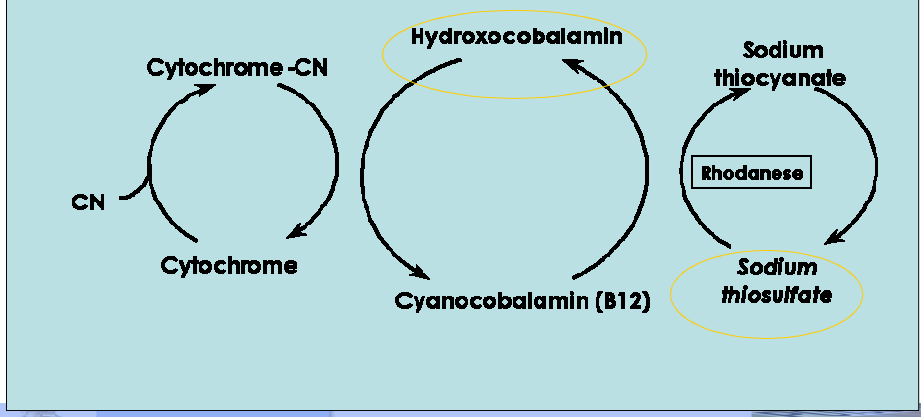
# Hydroxocobalamin

- The antidote kit containing nitrites and thiosulfate reduce the oxygen-carrying capacity of blood (by oxidizing hemoglobin).

- This constellation of problems has limited the utility of the classic antidote combination for cyanide, particularly in the prehospital setting.



## Hydroxocobalamin for CN




*Prehospital administration for victims of smoke inhalation.*

*IV 5 g (or 70 mg/kg in children) over 30 min*

*Few adverse effects*

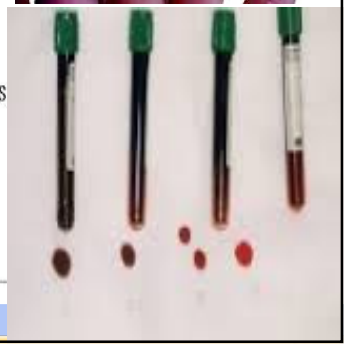
*Well tolerated*

*CO Poisoning*

## Acute Methemoglobinemia

| | | |
|---|---|---|
| Acetanilid | Hydroxylamine | Nitroprusside |
| Alloxan | Lidocaine | Paraquat/Diquat |
| Aniline(dyes, ink) | Menadione | Phenacetin |
| Antipyrine | Metoclopramide | Phenazopyridine |
| Arsine | Methylene blue | Phenol |
| Benzene derivatives | Naphthalene | Phenylhydrazine |
| Benzocaine | Nitrates* | Phenytoin |
| Chlorates | Nitric oxide | Prilocaine |
| Chlorobenzene | Nitrites | Primaquine |
| Chloroquine | Nitroalkanes | Smoke inhalation |
| Dapsone | Nitrochlorobenzene | Sulfonamide antibiotics |
| Dinitrophenol | Nitrofuran | Trinitrotoluene |
| Dinitrotoluene | Nitroglycerin | |

Many chemicals may have oxidizing properties and this list is not complete.
*Chemical and food sources.



## Methylene blue

Blue dye used in acute methemoglobinemia

Converts methemoglobin to hemoglobin

Not effective if deficiency of G-6PD

Available in 10ml ampules containing 10mg/ml

Dose : 1-2mg/kg slowly I/V over 5 minutes

Maximum dose : 7 mg/kg

# Can You Use Methylene Blue In Patients with G6PD Deficiency?

## Famous Textbook Quotes

- Methylene blue remains the first line therapy even in patients with known G6PD deficiency
  - Brent
- Should never be administered to someone with known G6PD deficiency
  - Shannon
- Should be used cautiously in patients with G6PD deficiency
  - Dart


## Antivenin

- The Indian antivenom manufacturers' "polyvalent anti-snake venom serum" (ASV) is raised in horses using the venoms of the four most important venomous snakes in India
- *Indian cobra, Naja naja;*
- *Indian krait, Bungarus caeruleus;*
- *Russell's viper, Daboia russelii;*
- *Saw-scaled viper, Echis carinatus*

- The decision to treat a snake bite with antivenin is largely based on clinical parameters
- Trying to capture, kill, or transport a snake for identification purposes seems of little value and possibly dangerous

**ASV is polyvalent**

**Syndromic approach helps in examination and investigations and outcome predictions**

WHO Library Cataloguing-in-Publication data

Warrel, David A.

Guidelines for the management of snake-bites

1. Snake Bites – education - epidemiology – prevention and control – therapy.

2. Public Health. 3. Venoms – therapy. 4. Russell's Viper. 5. Guidelines.

6. South-East Asia. 7. WHO Regional Office for South-East Asia

ISBN 978-92-9022-377-4 (NLM classification: WD 410)

# Indications for antivenom

- Antivenom treatment is recommended if and when a patient with proven or suspected snake-bite develops one or more of the following signs:

- **Systemic envenoming**
- *Haemostatic abnormalities:*
- Spontaneous systemic bleeding ,
- Coagulopathy **(20WBCT or other laboratory tests such as prothrombin time)** or thrombocytopenia (<100 x 109/litre or 100 000/cu mm)
- Neurotoxic signs: ptosis, external ophthalmoplegia, paralysis etc

**20-minute whole blood clotting test (20WBCT)**

- Place 2 mls of freshly sampled venous blood in a small, new or heat cleaned, dry, glass vessel.
- Leave undisturbed for 20 minutes at ambient temperature.
- Tip the vessel once.
- If the blood is still liquid (unclotted) and runs out, the patient has hypofibrinogenaemia ("incoagulable blood") as a result of venom-induced consumption coagulopathy (Fig. 61).
- In the South-East Asia region, incoagulable blood is diagnostic of a viper bite and rules out an elapid bite*.
- **If the vessel used for the test is not made of ordinary glass, or if it has been cleaned with detergent, its wall may not stimulate clotting of the blood sample (surface activation of factor XI – Hageman factor) and test will be invalid**
- If there is any doubt, repeat the test in duplicate, including a "control" (blood from a healthy person such as a relative)

- *Cardiovascular abnormalities:* hypotension, shock, cardiac arrhythmia, abnormal ECG.
- *Acute kidney injury (renal failure):* oliguria/anuria , rising blood creatinine/ urea.
- *(Haemoglobin-/myoglobin-uria:)* dark brown urine (clinical), urine dipsticks, other evidence of intravascular haemolysis or generalized rhabdomyolysis (muscle aches and pains, hyperkalaemia)

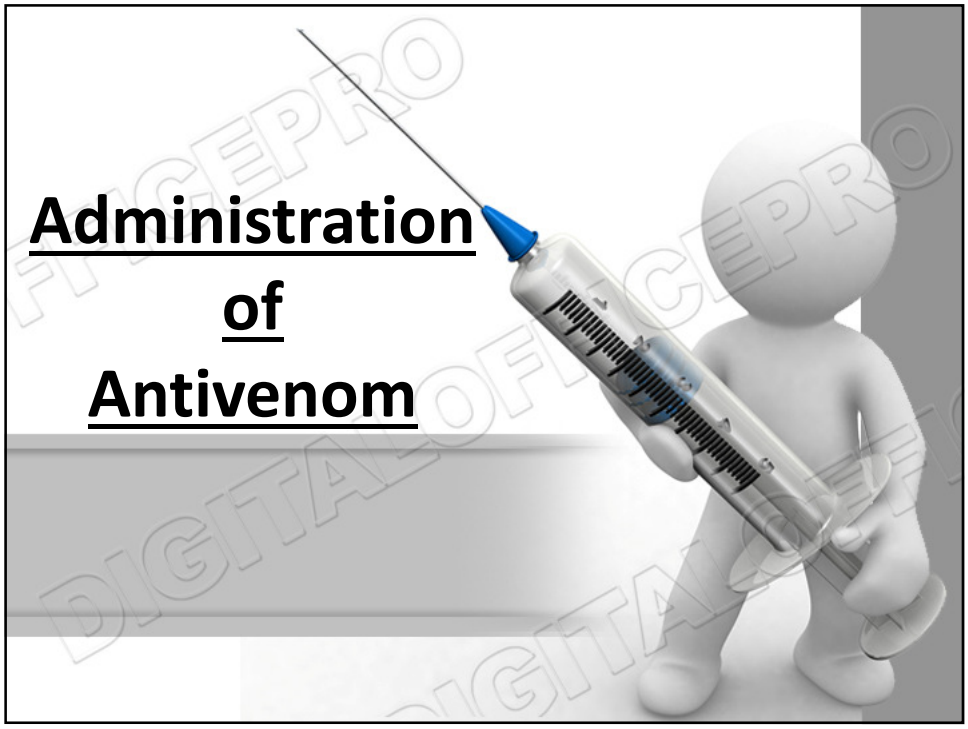
## Local envenoming

- Local swelling involving more than half of the bitten limb (in the absence of a tourniquet) within 48 hours of the bite. Swelling after bites on the digits (toes and especially fingers).
- Rapid extension of swelling (for example, beyond the wrist or ankle within a few hours of bite on the hands or feet).
- Development of an enlarged tender lymph node draining the bitten limb

- Antivenom treatment should be given as soon as it is indicated.
- It may reverse systemic envenoming even when this has persisted for several days or, in the case of haemostatic abnormalities, for two or more weeks.
- It is, therefore, appropriate to give antivenom for as long as evidence of the coagulopathy persists.

## Antivenom reactions

- ***Early anaphylactic reactions***: itching ,urticaria, dry cough, fever, nausea, vomiting, abdominal colic, diarrhoea and tachycardia.
- A minority of these patients may develop severe life-threatening anaphylaxis: hypotension, bronchospasm and angio-oedema.
- ***Pyrogenic (endotoxin) reactions:*** chills (rigors), fever, vasodilatation and a fall in blood pressure. Febrile convulsions
- ***Late (serum sickness type) reactions***: fever, nausea, vomiting, diarrhoea, itching, recurrent urticaria, arthralgia, myalgia, lymphadenopathy, periarticular swellings, mononeuritis multiplex, proteinuria with immune complex nephritis and, rarely, encephalopathy.




Epinephrine (adrenaline) should always be drawn up in readiness before antivenom is administered.

Antivenom should be given by the IV route whenever possible.

***Intravenous "push" injection***: Slow IV injection (not more than 2 ml/minute).

***Intravenous infusion***: Reconstituted freeze-dried or neat liquid antivenom is diluted in approximately 5-10 ml of isotonic fluid per kg body weight (i.e. 250-500 ml of isotonic saline or 5% dextrose in the case of an adult patient) and is infused at a constant rate over a period of about one hour.

## Administration of antivenom

- Closely observed *for at least one hour* after starting intravenous antivenom administration.
- Local administration of antivenom at the site of the bite is not recommended
- Intramuscular injection of antivenom: not recommended

## Dose of Polyvalent antivenoms

- Antivenoms are lyophilized (reconstituted to 10ml per vial) or liquid.
- Recommended initial dosage for all these antivenoms

| Indian cobra, Naja naja; | 10-20 vials |
|---|---|
| Indian krait, Bungarus caeruleus; | 10-20 vials |
| Russell's viper, Daboia russelii; | 10 vials |
| Saw-scaled viper, Echis carinatus | 5 vials |

**Note: venoms of other species (e.g. hump-nosed pit-viper Hypnale hypnale – South-West India and Sri Lanka) are not covered, nor are venoms by Naja, Daboia or Echis species or other species from outside India.**

***Criteria for giving more antivenom***

- Persistence or recurrence of blood incoagulability after 6 hours or of bleeding after 1-2 hours.
- Deteriorating neurotoxic or cardiovascular signs after 1-2 hours.

**Contraindications to antivenom:**

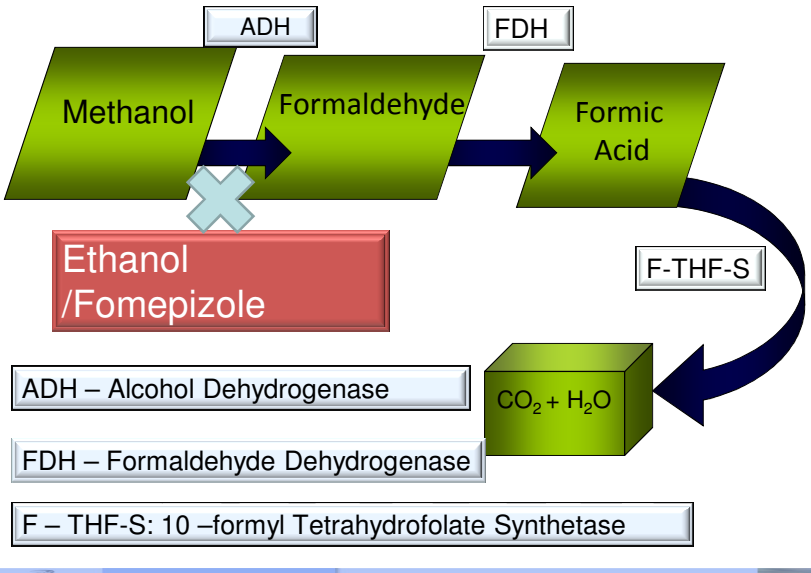
- No absolute contraindication
- Hypersensitivity or strong history of atopic disease.
- ***Available in India- polyvalent snake venom***


## FLUMAZENIL


## Ethanol & Fomepizole

- Antidotes for suspected methanol or ethylene glycol poisoning
- Ethanol is used therapeutically in the management of poisoning by ethylene glycol, methanol, and other toxic alcohols such as diethylene glycol, triethylene glycol, propylene glycol, and ethylene glycol butyl ethers.

## Metabolism of Methanol

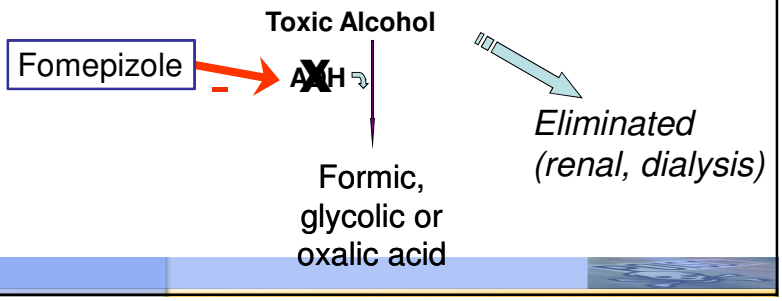



## **Fomepizole** (4-methypyrazole)

→ Approved by FDA for E.G. poisoning in 1997, and for methanol poisoning in 2000

## **Fomepizole** (4-methypyrazole)

- Introduced in 1986
- Competitive Inhibitor of Alcohol dehydrogenase
  (*in vitro*: 80,000 times affinity for ADH than methanol)




## Ethanol vs Fomepizole* in Methanol Poisoning

### Ethanol

Relatively inexpensive
Ethanol dosing is complex
Should be used with caution when pt has co ingested CNS depressant drugs
Frequent labs to maintain blood level above 100 mg/dL
IV administration of ethanol (phlebitis, fluid loads, hyponatremia, oversedation and hypoglycaemia esp in children

### Fomepizole

Expensive ($1,500 per 1.5 mL ampule)
Easier to administer and longer duration of action
Does not cause CNS depression
Does not require frequent labs
minor adverse effects (venous irritation, headache, nausea, dizziness).
* Not available in India

## Lots of problems with Ethanol!!

1. Oral Absorption is erratic (and difficult)
2. IV preparations rarely shelved
3. Math is challenging (many reports of errors)
4. Kinetics vary between pts. and in same pt.
5. Causes even more profound CNS depression
6. Need large volumes (1120 cc bolus of 5% etoh)
7. Etoh intoxication can cause hypoglycemia, gastritis, pancreatitis
8. Use of Ethanol mandates hourly ethanol and glucose checks in ICU
9. Duration can take as long as 100 hrs (depending on dialysis)

## Ethylene Glycol / Methanol

### Fomepizole – Advantages:

1. Does not require separate preparations
2. Therapeutic levels are reliably achieved
3. No Change in mental status
4. No risk of hypoglycemia, hepatotoxicity
5. Hemodialysis not needed in subgroup of patients

Main Disadvantage: Cost!

Apr. $1000 US per 1500 mg vial

Suggested shelf life of drug ~ 3 yrs
U.S. Manufacturer (Orphan Medical) will replace drug at no charge

## Dose & route of administration

- Ethanol : given orally or IV

| | Intravenous | | Oral |
|---|---|---|---|
| Dose | 5% | 10% | 50% |
| Loading | 15ml/kg | 7.5ml/kg | 2ml/kg |
| Maintenance | 2-4ml/kg/hr | 1-2ml/kg/hr | 0.2-0.4 ml/kg/hr |
| Maintenance during hemodialysis | 4-7 ml/kg/hr | 2-3.5 ml/kg/hr | 0.4-0.7 ml/kg/hr |

Obtain serum ethanol level after the loading dose and frequentally during maintenance therapy to ensure a concentration 100-150 mg/dl.

## Fomepizole

- Loading dose: 15mg/kg(up to 1gm) IV slowly over 30 minutes
- Maintenance therapy: 10 mg/kg every 12 hours for four doses then increase to 15mg/kg until methanol or ethylene glycol levels are below 20 mg/dl.

## Naloxone and opiate toxidrome

- Narcotic 'simple' overdose: miosis, bradypnea, bradycardia, CNS depression, needle tracks…
- Goal of prehospital naloxone therapy is to simply reverse respiratory depression
- No indication in the severe complicated overdose
- Should only be administered in **small, diluted and titrated doses**
- Short duration of a 'toxicodynamic' action: *we 'treat' the patient not the 'overdose'*

## Chelating Agents

- Certain organic compounds are capable of forming coordinate bonds with metals through two or more atoms of the organic compound; such organic compounds are called chelating agents. The compound formed by a chelating agent and a metal is called a chelate. A chelating agent that has two coordinating atoms is called bidentate; one that has three, tridentate;

## Chelating Agents

Penicillamine: available by oral route, effective in chelating lead, mercury and copper, may cause allergic reactions, weekly measurement of metals is needed to know the need for continued therapy, treatment may be given for 3 months

D-Penicillamine: Available in India as Cilamin, Artamin etc.

## Calcium disodium EDTA:

Calcium disodium EDTA is favored for the treatment of severe lead poisoning, in combination with dimercaprol.

- Children who are symptomatic
- Children whose lead levels are over 2.17 umol/L (45 ug/dL)
- Adults who have symptoms suggestive of encephalopathy
- Adults whose lead levels are over 4.8 umol/L (100 ug/dL)

## Chelating Agents

BAL (Dimercaprol, British antilewisite)
Used for arsenic, mercury and lead and gold poisoning, has to be given by deep I/M injection causes many adverse effects (Available in India)

DMSA (Succimer,2,3-dimercaptosuccinic acid)*
It is a water soluble analog of Dimercaprol. Used in lead and mercury poisoning. Also used in arsenic poisoning. Available both as oral and parenteral preparations. Less toxic as compared to BAL
(Not available in India)

## (Physostigmine) * for Anticholinergic Overdose

- Physostigmine is a specific therapeutic option in the management of anticholinergic toxicity.
- The current recommendation is for physostigmine use in the management of a severe anticholinergic syndrome, while it remains contraindicated for membrane-stabilizing effects (*eg*, prolonged QRS duration), particularly for cyclic antidepressant overdose.
- * Not available in India

## Botulinum antitoxins*

- Trivalent (against serotypes A,B,E)
- Bivalent (A,B)
- Monovalent (E) in Canada
- H-BAT is a heptavalent (A-G) antitoxin developed by US army. It is currently indicated for all serotypes of botulism.

* Not available in India

## Ca-DTPA and Zn-DTPA*

- Calcium-DTPA (Ca-DTPA) and Zinc-DTPA (Zn-DTPA) are drug products that have been used investigationally for over 40 years to speed up excretion of the transuranium elements plutonium, americium, and curium from the body. Ca-DTPA and Zn-DTPA bind to these elements and are then excreted in the urine.
- Ca-DTPA and Zn-DTPA do not treat contamination with radioactive iodine, uranium and neptunium, or the complications of radiation exposure (e.g., bone marrow suppression).
- Ca-DTPA (and Zn-DTPA) can chelate certain important minerals that the body needs (zinc, magnesium, and manganese).

* Not available in India

## Some recommendations for antidotes which should be available in India

- Fomepizole for Methanol poisoning
- Hydroxocobalamin for Cyanide poisoning
- Flumazenil
- Physostigmine for Datura poisoning

## Basic Rules of Chemical Safety

Rule #1

**Don't buy or store chemicals you do not need.**

Basic Rules of Chemical Safety

Rule #2

## Store chemicals in their original container.

Basic Rules of Chemical Safety

Rule #3

## Always wear appropriate safety gear and work in a safe environment.

Basic Rules of Chemical Safety

Rule #4

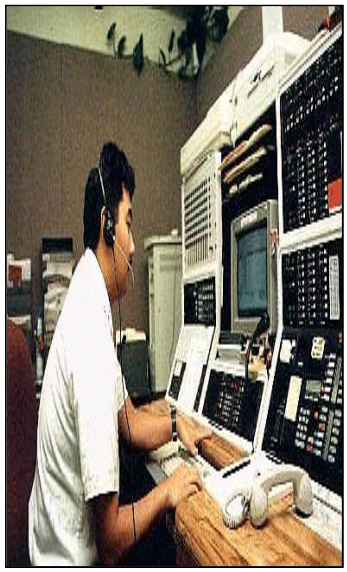
## Always dispose of chemicals safely.

## First Responder Requirements

- Understand What Hazardous Materials Are
- Know Risks of Hazardous Materials
- Understand Outcomes
- Recognize a Hazardous Materials Release
- Identify the Hazardous Material, If Possible
- Determine Need for Additional Resources
- Understand First Responder Roles

## First Responder's Capacity

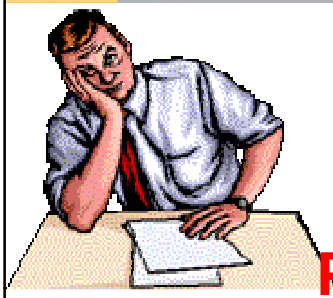
- Recognize Signs, Symptoms, and Indicators
- Know What to Tell
- Recognize Trends
- Know Whom to Contact
- Notify Technical Responders
- Provide Safety Guidance



## Organisation for the Prohibition of Chemical Weapons (OPCW)

- Destroying 80% of the world's chemical weapons deserved a Nobel peace prize

# Any Questions ?



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## Poison Help Line

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# Jay Hind