

HIGHLIGHTS

- Highly toxic herbicides
- Affect hepatic, renal, and nervous systems

Signs and Symptoms:

- Sweating, thirst, fever, headache, confusion, malaise, and restlessness
- Hyperthermia, tachycardia, tachypnea in serious cases
- Characteristic bright yellow staining of skin and hair often present with topical exposure

Treatment:

- No specific antidote
- Replace oxygen and fluids, control temperature
- Decontaminate skin, hair, clothing

Contraindicated:

- Antipyretic therapy with salicylates
- Atropine

Nitrophenolic and Nitrocresolic Herbicides

These highly toxic chemicals have many uses in agriculture worldwide, as herbicides (weed-killing and defoliation), acaricides, nematocides, ovicides, and fungicides. Relatively insoluble in water, most technical products are dissolved in organic solvents and formulated for spray application as emulsions. There are some wettable powder formulations. Only dinocap continues to have active registrations in the United States.

Toxicology

Nitroaromatic compounds are highly toxic to humans and animals with LD_{50} s in the range of 25 to 50 mg/kg.¹ Most nitrophenols and nitrocresols are well absorbed by the skin, gastrointestinal tract, or lung when fine droplets are inhaled.² Fatal poisonings have occurred as a result of dermal contamination; more common is a moderate irritation of the skin and mucous membranes.

Nitrophenols and nitrocresols undergo some biotransformation in humans, chiefly reduction (one nitro group to an amino group) and conjugation at the phenolic site. Although nitrophenols and metabolites appear consistently in the urine of poisoned individuals, hepatic excretion is probably the main route of disposition. Elimination is slow with a documented half-life in humans between 5 and 14 days.¹ Blood and tissue concentrations tend to increase progressively if an individual is substantially exposed on successive days.

The basic mechanism of toxicity is stimulation of oxidative metabolism in cell mitochondria, by the uncoupling of oxidative phosphorylation. This leads to hyperthermia, tachycardia, headache, malaise, and dehydration, and in time, depletes carbohydrate and fat stores. The major systems prone to toxicity are the hepatic, renal, and nervous systems. The nitrophenols are more active as uncouplers than chlorophenols such as pentachlorophenol (described in chapter 10). Hyperthermia and direct toxicity on the brain cause restlessness and headache, and in severe cases, seizures, coma, and cerebral edema. The higher the ambient temperature, such as in an outdoor agricultural environment, the more difficult it is to dissipate the heat.^{1,2} Liver parenchyma and renal tubules show degenerative changes. Albuminuria, pyuria, hematuria, and azotemia are signs of renal injury.

Cataracts occur in laboratory animals given nitrophenols, and have occurred in humans, both as a result of ill-advised medicinal use and as a consequence of chronic, occupational exposure.³ Cataract formation is sometimes accompanied by glaucoma.

Signs and Symptoms of Poisoning

Most patients present within a few hours of exposure with generalized non-specific signs and symptoms including profuse sweating, thirst, fever, headache, confusion, malaise, and restlessness. The skin may appear warm and flushed as **hyperthermia** develops, along with tachycardia, and tachypnea, all of which indicate a serious degree of poisoning. Apprehension, anxiety, manic behavior, seizures, and coma reflect cerebral injury; seizures and coma signify an immediately life-threatening intoxication. Labored breathing and cyanosis are consequences of the stimulated metabolism and tissue anoxia. Renal failure may occur early in cases of severe exposure. Liver damage is first manifested by jaundice, and cell death can occur within 48 hours and is dose-dependent.⁴ Death may occur within 24 to 48 hours after exposure in cases of severe poisoning.² In cases of survival of severe poisoning, complete resolution of symptoms may be slow due to the toxicant's long half-life.^{1,5}

A characteristic bright yellow staining of skin and hair is often present with topical exposure and can be an important diagnostic clue to the clinician.^{1,2,5} Yellow staining of the sclerae and urine indicates absorption of potentially toxic amounts. Weight loss occurs in persons continually exposed to relatively low doses of nitrophenols or nitrocresols.^{1,3}

Confirmation of Poisoning

If poisoning is probable, do not await confirmation before beginning treatment. Save urine and blood specimens on ice at temperature below 20° C in the event confirmation is necessary later on. Unmetabolized nitrophenols and nitrocresols can be identified spectrophotometrically, or by gas-liquid chromatography, in the serum at concentrations well below those that have been associated with acute poisonings. The data on exposure and systemic levels of compounds in this group are limited, and most reports specify the compound dinitro-ortho-cresol. In general, blood levels of 10 mcg/dL or greater are usually seen when systemic toxicity is evident.^{1,6} One fatal case occurred with a level of 75 mcg/dL.⁶ Blood analysis is useful in confirming the cause of poisoning. Monitoring of levels should be done routinely during acute intoxication in order to establish a decay curve to determine when therapy can be safely discontinued.

Commercial Products

dinitrocresol*
Chemsect DNOC
DNC
DNOC
Elgetol 30
Nitrador
Selinon
Sinox
Trifocide
dinitrophenol*
Chermox PE
dinobuton*
Acrex
Dessin
Dinofen
Drawinol
Talan
dinocap
Crotothane
Karathane
dinopenton
dinoprop*
dinosam*
Chemox General
DNAP
dinoseb*
Basanite
Caldon
Chemox General
Chemox PE
Chemsect DNBP
Dinitro
Dinitro-3
Dinitro General Dynamyte
Dinitro Weed Killer 5
DNBP
Elgetol 318
Gebutox
Hel-Fire
Kiloseb
Nitropone C
Premerge 3
Snox General
Subitex
Unicrop DNBP
Vertac
Vertac General Weed Killer
Vertac Selective Weed Killer
dinoseb acetate*
Aretit
dinoseb methacrylate*
Acricid
Ambox
binapacryl

(Continued on the next page)

Commercial Products

(Continued)

Dapacryl
Endosan
FMC 9044
Hoe 002784
Morrocid
NIA 9044
dinosulfon*
dinoterb acetate*
dinoterb salts*
dinoterbon*

* All U.S. registrations have
been cancelled

Treatment

1. Supportive treatment and hyperthermia control. There is no specific antidote to poisoning with nitrophenolic or nitrocresolic herbicides. Treatment is supportive in nature and includes oxygen, fluid replacement, and temperature control.

Reduce elevated body temperature by physical means. Administer sponge baths and ice packs, and use a fan to promote air flow and evaporation.⁷ In fully conscious patients, administer cold, sugar-containing liquids by mouth as tolerated.

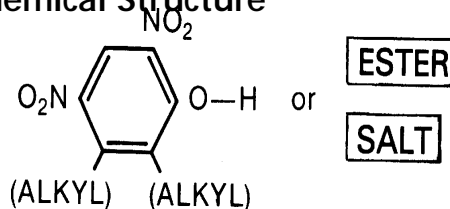
2. Contraindications. Antipyretic therapy with salicylates is strongly contraindicated as salicylates also uncouple oxidative phosphorylation. Other antipyretics are thought to be of no use because of the peripherally mediated mechanism of hyperthermia in poisoning of this nature. Neither the safety nor the effectiveness of other antipyretics has been tested.

Atropine is also absolutely contraindicated! It is essential not to confuse the clinical signs for dinitrophenol with manifestations for cholinesterase inhibition poisoning.²

3. Skin decontamination. If poisoning has been caused by contamination of body surfaces, bathe and shampoo contaminated skin and hair promptly and thoroughly with soap and water, or water alone if soap is not available. Wash the chemical from skin folds and from under fingernails. Care should be taken to prevent dermal contamination of hospital staff. See Chapter 2.

4. Other Treatment. Other aspects of treatment are identical to management of pentachlorophenol poisoning, detailed in Chapter 10.

General Chemical Structure



References

1. Leftwich RB, Floro JF, Neal RA, et al. Dinitrophenol poisoning: A diagnosis to consider in undiagnosed fever. *South Med J* 1982;75:182-5.
2. Finkel AJ. Herbicides: Dinitrophenols. In: Hamilton and Hardy's Industrial Toxicology, 4th ed. Boston: John Wright PSG, Inc., 1983, pp. 301-2.
3. Kurt TL, Anderson R, Petty C, et al. Dinitrophenol in weight loss: The poison center and public safety. *Vet Hum Toxicol* 1986;28:574-5.

4. Palmeira CM, Moreno AJ, and Madeira VM. Thiols metabolism is altered by the herbicides paraquat, dinoseb, and 2,4-D: A study in isolated hepatocytes. *Toxicol Lett* 1995;81:115-23.
5. Smith WD. An investigation of suspected dinoseb poisoning after agricultural use of a herbicide. *Practitioner* 1981;225:923-6.
6. NIOSH. Criteria document: Occupational exposure to dinitro-orthocresol. Cincinnati: NIOSH, 1978.
7. Graham BS, Lichtenstein MJ, Hinson JM, et al. Nonexertional heatstroke: Physiologic management and cooling in 14 patients. *Arch Intern Med* 1986;146:87-90.