First Yale New Haven International Congress on Disaster Medicine and Emergency Management

September 12-13, 2005

Omni New Haven Hotel
155 Temple Street
New Haven, Connecticut, USA

The conference will provide hospital, pre-hospital, public safety, public health and emergency management professionals with:

- Current best practices in health emergency management, including healthcare and public health organizations
- Recent progress in clinical disaster medicine
- Lessons learned from recent international and national disasters
- Latest research and development in disaster medicine and emergency management

Registration will begin on April 15, 2005 and can be accessed through our Web site at: http://yalenewhavenhealth.org/emergency/commu/natlconf.html

Abstracts are being accepted until June 1, 2005 at: http://yalenewhavenhealth.org/emergency/commu/call_abstracts.html

Contact:
203-688-3224 or center@ynhh.org

Conference Co-sponsors:

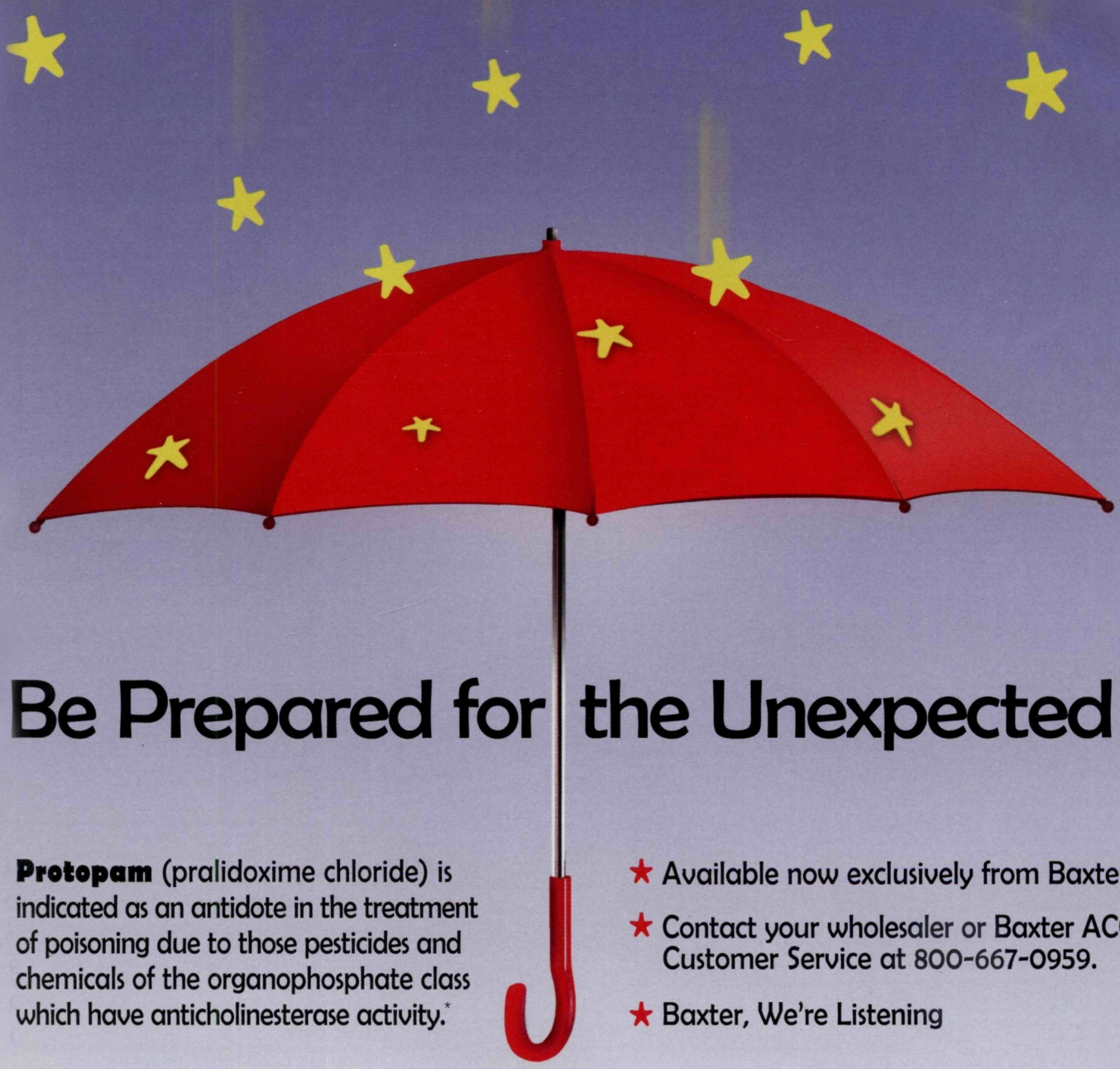
Yale New Haven Health

Pan American Health Organization
Regional Office of the World Health Organization

Yale University School of Medicine

World Association for Disaster and Emergency Medicine

https://doi.org/10.1017/S1049023X00002338 Published online by Cambridge University Press



Be Prepared for the Unexpected!

Protopam (pralidoxime chloride) is indicated as an antidote in the treatment of poisoning due to those pesticides and chemicals of the organophosphate class which have anticholinesterase activity.*

- ★ Available now exclusively from Baxter
- ★ Contact your wholesaler or Baxter ACC Customer Service at 800-667-0959.
- ★ Baxter, We're Listening

Protopam is not effective in the treatment of poisoning due to phosphorous, inorganic phosphates, or organophosphates not having anticholinesterase activity. **Protopam** is **not** indicated as an antidote for intoxication by pesticides of the carbamate class since it may increase the toxicity of carbaryl.

When atropine and pralidoxime are used together, the signs of atropinization (flushing, mydriasis, tachycardia, dryness of the mouth and nose) may occur earlier than might be expected when atropine is used alone.

Protopam Chloride
(pralidoxime chloride)

Baxter

Baxter Healthcare Corporation
95 Spring Street, New Providence, NJ 07974
1-800-ANA-DRUG (262-3784)

*For complete information on indications, please refer to Full Prescribing Information. Please see brief summary of Prescribing Information on the adjacent page.

PROTOPAM Chloride

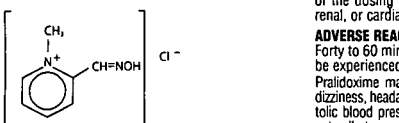
(pralidoxime chloride) for Injection

℞ only

DESCRIPTION

Chemical name: 2-formyl-1-methylpyridinium chloride oxime. Available in the United States as PROTOPAM Chloride, pralidoxime chloride is frequently referred to as 2-PAM Chloride.

Structural formula:



$C_7H_9ClN_2O$ M.W. 172.61

Pralidoxime chloride occurs as an odorless, white, nonhygroscopic, crystalline powder which is soluble in water. Stable in air, it melts between 215° and 225° C, with decomposition.

The specific activity of the drug resides in the 2-formyl-1-methylpyridinium ion and is independent of the particular salt employed. The chloride is preferred because of physiologic compatibility, excellent water solubility at all temperatures, and high potency per gram, due to its low molecular weight.

Pralidoxime chloride is a cholinesterase reactivator.

PROTOPAM Chloride for intravenous injection or infusion is prepared by crydesiccation. Each vial contains 1g of sterile pralidoxime chloride, and NaOH to adjust pH, to be reconstituted with 20 mL of Sterile Water for Injection, USP. The pH of the reconstituted solution is 3.5 to 4.5. Intramuscular or subcutaneous injection may be used when intravenous injection is not feasible.

CLINICAL PHARMACOLOGY

The principal action of pralidoxime is to reactivate cholinesterase (mainly outside of the central nervous system) which has been inactivated by phosphorylation due to an organophosphate pesticide or related compound. The destruction of accumulated acetylcholine can then proceed, and neuromuscular junctions will again function normally. Pralidoxime also slows the process of "aging" of phosphorylated cholinesterase to a nonreactivatable form, and detoxifies certain organophosphates by direct chemical reaction. The drug has its most critical effect in relieving paralysis of the muscles of respiration. Because pralidoxime is less effective in relieving depression of the respiratory center, atropine is always required concomitantly to block the effect of accumulated acetylcholine at this site. Pralidoxime relieves muscarinic signs and symptoms, salivation, bronchospasm, etc., but this action is relatively unimportant since atropine is adequate for this purpose.

Pralidoxime is distributed throughout the extracellular water; it is not bound to plasma protein. The drug is rapidly excreted in the urine partly unchanged, and partly as a metabolite produced by the liver. Consequently, pralidoxime is relatively short acting, and repeated doses may be needed, especially where there is any evidence of continuing absorption of the poison.

The minimum therapeutic concentration of pralidoxime in plasma is 4 µg/mL; this level is reached in about 16 minutes after a single injection of 600 mg PROTOPAM Chloride. The apparent half-life of PROTOPAM Chloride is 74 to 77 minutes.

It has been reported[1] that the supplemental use of oxime cholinesterase reactivators (such as pralidoxime) reduces the incidence and severity of developmental defects in chick embryos exposed to such known teratogens as parathion, bidrin, carbachol, and neostigmine. This protective effect of the oximes was shown to be dose related.

INDICATIONS AND USAGE

PROTOPAM is indicated as an antidote: (1) in the treatment of poisoning due to those pesticides and chemicals of the organophosphate class which have anticholinesterase activity and (2) in the control of overdosage by anticholinesterase drugs used in the treatment of myasthenia gravis.

The principal indications for the use of pralidoxime are muscle weakness and respiratory depression. In severe poisoning, respiratory depression may be due to muscle weakness.

CONTRAINDICATIONS

There are no known absolute contraindications for the use of PROTOPAM. Relative contraindications include known hypersensitivity to the drug and other situations in which the risk of its use clearly outweighs possible benefit (see **PRECAUTIONS**).

WARNINGS

PROTOPAM is not effective in the treatment of poisoning due to phosphorus, inorganic phosphates, or organophosphates not having anticholinesterase activity.

PROTOPAM is **not** indicated as an antidote for intoxication by pesticides of the carbamate class since it may increase the toxicity of carbaryl.

PRECAUTIONS

General

Pralidoxime has been very well tolerated in most cases, but it must be remembered that the desperate condition of the organophosphate-poisoned patient will generally mask such minor signs and symptoms as have been noted in normal subjects.

Intravenous administration of PROTOPAM should be carried out slowly and, preferably, by infusion, since certain side effects, such as tachycardia, laryngospasm, and muscle rigidity, have been attributed in a few cases to a too-rapid rate of injection. (See **DOSAGE AND ADMINISTRATION.**)

PROTOPAM should be used with great caution in treating organophosphate overdosage in cases of myasthenia gravis since it may precipitate a myasthenic crisis.

Because pralidoxime is excreted in the urine, a decrease in renal function will result in increased blood levels of the drug. Thus, the dosage of pralidoxime should be reduced in the presence of renal insufficiency.

Laboratory Tests

Treatment of organophosphate poisoning should be instituted without waiting for the results of laboratory tests. Red blood cell, plasma cholinesterase, and urinary paranitrophenol measurements (in the case of parathion exposure) may be helpful in confirming the diagnosis and following the course of the illness. A reduction in red blood cell cholinesterase concentration to below 50% of normal has been seen only with organophosphate ester poisoning.

Drug Interactions

When atropine and pralidoxime are used together, the signs of atropinization (flushing, mydriasis, tachycardia, dryness of the mouth and nose) may occur earlier than might be expected when atropine is used alone. This is especially true if the total dose of atropine has been large and the administration of pralidoxime has been delayed.[2-4]

The following precautions should be kept in mind in the treatment of anticholinesterase poisoning, although they do not bear directly on the use of pralidoxime: since barbiturates are potentiated by the anticholinesterases, they should be used cautiously in the treatment of convulsions; morphine, theophylline, aminophylline, succinylcholine, reserpine, and phenothiazine-type tranquilizers should be avoided in patients with organophosphate poisoning.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Since pralidoxime chloride is indicated for short-term emergency use only, no investigations of its potential for carcinogenesis, mutagenesis, or impairment of fertility have been conducted by the manufacturer, or reported in the literature.

Pregnancy

TERATOGENIC EFFECTS-PREGNANCY CATEGORY C

Animal reproduction studies have not been conducted with pralidoxime. It is also not known whether pralidoxime can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Pralidoxime should be given to a pregnant woman only if clearly needed.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when pralidoxime is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Clinical studies of PROTOPAM did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant or other drug therapy.

ADVERSE REACTIONS

Forty to 60 minutes after intramuscular injection, mild to moderate pain may be experienced at the site of injection.

Pralidoxime may cause blurred vision, diplopia and impaired accommodation, dizziness, headache, drowsiness, nausea, tachycardia, increased systolic and diastolic blood pressure, hyperventilation, and muscular weakness when given parenterally to normal volunteers who have not been exposed to anticholinesterase poisons. In patients, it is very difficult to differentiate the toxic effects produced by atropine or the organophosphate compounds from those of the drug.

Elevations in SGOT and/or SGPT enzyme levels were observed in 1 of 6 normal volunteers given 1200 mg of pralidoxime chloride intramuscularly, and in 4 of 6 volunteers given 1800 mg intramuscularly. Levels returned to normal in about 2 weeks. Transient elevations in creatine phosphokinase were observed in all normal volunteers given the drug. A single intramuscular injection of 330 mg in 1 mL in rabbits caused myonecrosis, inflammation, and hemorrhage.

When atropine and pralidoxime are used together, the signs of atropinization may occur earlier than might be expected when atropine is used alone. This is especially true if the total dose of atropine has been large and the administration of pralidoxime has been delayed.[2-4] Excitement and manic behavior immediately following recovery of consciousness have been reported in several cases. However, similar behavior has occurred in cases of organophosphate poisoning that were not treated with pralidoxime.[3,5,6]

DRUG ABUSE AND DEPENDENCE

Pralidoxime chloride is not subject to abuse and possesses no known potential for dependence.

OVERDOSAGE

Manifestations of Overdosage

Observed in normal subjects only: dizziness, blurred vision, diplopia, headache, impaired accommodation, nausea, slight tachycardia. In therapy it has been difficult to differentiate side effects due to the drug from those due to the effects of the poison.

Treatment of Overdosage

Artificial respiration and other supportive therapy should be administered as needed.

Acute Toxicity

IV – man TDLo: 14 mg/kg (toxic effects: CNS)
IV – rat LD_{50}: 96 mg/kg
IM – rat LD_{50}: 150 mg/kg
ORAL – mouse LD_{50}: 4100 mg/kg
IP – mouse LD_{50}: 155 mg/kg
IV – mouse LD_{50}: 90 mg/kg
IM – mouse LD_{50}: 180 mg/kg
IV – rabbit LD_{50}: 95 mg/kg
IM – guinea pig LD_{50}: 168 mg/kg

DOSAGE AND ADMINISTRATION

Organophosphate Poisoning

*Pralidoxime is most effective if administered immediately after poisoning. Generally, little is accomplished if the drug is given more than 36 hours after termination of exposure. When the poison has been ingested, however, exposure may continue for some time due to slow absorption from the lower bowel, and fatal relapses have been reported after initial improvement. Continued administration for several days may be useful in such patients. Close supervision of the patient is indicated for at least 48 to 72 hours. If dermal exposure has occurred, clothing should be removed and the hair and skin washed thoroughly with sodium bicarbonate or alcohol as soon as possible. Diazepam may be given cautiously if convulsions are not controlled by atropine.[7]

Severe poisoning (coma, cyanosis, respiratory depression) requires intensive management. This includes the removal of secretions, airway management, the correction of acidosis, and hypoxemia. Atropine should be given as soon as possible after hypoxemia is improved. Atropine should not be given in the presence of significant hypoxia due to the risk of atropine-induced ventricular fibrillation. In adults, atropine may be given intravenously in doses of 2 to 4 mg. This should be repeated at 5 to 10-minute intervals until full atropinization (secretions are inhibited) or signs of atropine toxicity appear (delirium, hyperthermia, muscle twitching).

Some degree of atropinization should be maintained for at least 48 hours, and until any depressed blood cholinesterase activity is reversed.

Morphine, theophylline, aminophylline, and succinylcholine are contraindicated. Tranquilizers of the reserpine or phenothiazine type are to be avoided.

After the effects of atropine become apparent, PROTOPAM (pralidoxime chloride) may be administered.

PROTOPAM Chloride Injection

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Discard unused solution after a dose has been withdrawn.

In adults, inject an initial dose of 1 to 2 g of PROTOPAM, preferably as an infusion in 100 mL of saline, over a 15- to 30-minute period. If this is not practical or if pulmonary edema is present, the dose should be given slowly by intravenous injection as a 5 percent solution in water over not less than five minutes. After about an hour, a second dose of 1 to 2 g will be indicated if muscle weakness has not been relieved. Additional doses may be given cautiously if muscle weakness persists.

Too-rapid administration may result in temporary worsening of cholinergic manifestations. Injection rate should not exceed 200 mg/minute. If intravenous administration is not feasible, intramuscular or subcutaneous injection should be used.

In severe cases, especially after ingestion of the poison, it may be desirable to monitor the effect of therapy electrocardiographically because of the possibility of heart block due to the anticholinesterase. Where the poison has been ingested, it is particularly important to take into account the likelihood of continuing absorption from the lower bowel since this constitutes new exposure. In such cases, additional doses of PROTOPAM (pralidoxime) may be needed every three to eight hours. In effect, the patient should be "titrated" with PROTOPAM as long as signs of poisoning recur. As in all cases of organophosphate poisoning, care should be taken to keep the patient under observation for at least 24 hours.

If convulsions interfere with respiration, they may be controlled by the slow intravenous injection of diazepam, up to 20 mg in adults.

Anticholinesterase Overdosage

As an antagonist to such anticholinesterases as neostigmine, pyridostigmine, and ambenonium, which are used in the treatment of myasthenia gravis, PROTOPAM may be given in a dosage of 1 to 2 g intravenously followed by increments of 250 mg every five minutes.

HOW SUPPLIED

NDC 60977-141-01-*Hospital Package:* This contains six 20 mL vials of 1 g each of sterile PROTOPAM Chloride (pralidoxime chloride) white to off-white porous cake*, without diluent or syringe. Solution may be prepared by adding 20 mL of Sterile Water for Injection, USP. These are single-dose vials for intravenous injection or for intravenous infusion after further dilution with physiologic saline. Intramuscular or subcutaneous injection may be used when intravenous injection is not feasible.

*When necessary, sodium hydroxide is added during processing to adjust the pH.

Storage

Store at 20°-25°C (68°-77°F), excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature].

ANIMAL PHARMACOLOGY AND TOXICOLOGY

The following table lists chemical and trade or generic names of pesticides, chemicals, and drugs against which PROTOPAM (usually administered in conjunction with atropine) has been found to have antidotal activity on the basis of animal experiments. All compounds listed are organophosphates having anticholinesterase activity. A great many additional substances are in industrial use but have been omitted because of lack of specific information.

AAT–see PARATHION
AFLIX®–see FORMOTHION
ALKRON®–see PARATHION
AMERICAN CYANAMID 3422–see PARATHION
AMITON–diethyl-S-(2-diethylaminoethyl)phosphorothiolate
ANTHIO®–see FORMOTHION
APHAMITE–see PARATHION
ARMIN–ethyl-4-nitrophenylethylphosphonate
AZINPHOS-METHYL–dimethyl-S-[(4-oxo-1,2,3,-benzotriazin-3(4 H)-yl)methyl] phosphorodithioate
MORPHOTHION–dimethyl-S-2-keto-2-(N-morpholyl)ethylphosphorodithioate
NEGUVON®–see TRICHLOROFON
NIRAN®–see PARATHION
NITROSTIGMINE–see PARATHION
O,O-DIETHYL-O-p-NITROPHENYL PHOSPHOROTHIOATE–see PARATHION
O,O-DIETHYL-O-p-NITROPHENYLTHIO PHOSPHATE–see PARATHION
OR 1191–see PHOSPHAMIDON
OS 1836–see VINYLPHOS
OXYDEMETONMETHYL–dimethyl-S-2-(ethylsulfinyl) ethyl phosphorothiolate
PARAOXON–diethyl (4-nitrophenyl) phosphate
PARATHION–diethyl (4-nitrophenyl) phosphorothionate
PENPHOS–see PARATHION
PHENCAPTON–diethyl-S-(2,5-dichlorophenylmercaptomethyl) phosphorodithioate
PHOSDRIN®–see MEVINPHOS
PHOS-KIL–see PARATHION
PHOSPHAMIDON–1-chloro-1-diethylcarbamoyl-1-propen-2-yl-dimethylphosphate
PHOSPHOLINE IODIDE®–see echothiophate iodide
PHOSPHOROTHIOIC ACID, O,O-DIETHYL-O-p-NITROPHENYL ESTER–see PARATHION
PLANTHION–see PARATHION
QUELETOX–see FENTHION
RHODIATOX®–see PARATHION
RUELENE®–4-tert-butyl-2-chlorophenylmethyl-N-methylphosphoroamidate
SARIN–isopropyl-methylphosphonofluoridate
SHELL OS 1836–see VINYLPHOS
SHELL 2046–see MEVINPHOS
SNP–see PARATHION
SOMAN–pinacolyl-methylphosphonofluoridate
SYSTOX®–diethyl-(2-ethylmercaptoethyl) phosphorothionate
TEP–see TEPP
TEPP–tetraethylpyro phosphate
THIOPHOS®–see PARATHION
TIGUVON–see FENTHION
TRICHLOROFON–dimethyl-1-hydroxy-2,2,2-trichloroethylphosphonate
VAPONA®–see DICHLORVOS
VAPOPHOS–see PARATHION
VINYLPHOS–diethyl-2-chloro-vinylphosphate

PROTOPAM (pralidoxime chloride) appears to be ineffective, or marginally effective, against poisoning by:

CIODRIN® (alpha-methylbenzyl-3-[dimethoxyphosphinyloxy]-ciscrotonate)

DIMEFOX (tetramethylphosphorodiamidic fluoride)

DIMETHOATE (dimethyl-S-[N-methylcarbamoylmethyl]phosphorodithioate)

METHYL DIAZINON (dimethyl-[2-isopropyl-4-methylpyrimidyl]-phosphorothionate)

METHYL PHENCAPTON (dimethyl-S-[2,5-dichlorophenylmercaptomethyl]phosphorodithioate)

PHORATE (diethyl-S-ethylmercaptomethylphosphorodithioate)

SCHRADAN (octamethylpyrophosphoramide)

WEPSYN® (5-amino-1-[bis-(dimethylamino) phosphinyl]-3-phenyl-1,2,4-triazole).

The use of PROTOPAM should, nevertheless, be considered in any life-threatening situation resulting from poisoning by these compounds, since the limited and arbitrary conditions of pharmacologic screening do not always accurately reflect the usefulness of PROTOPAM in the clinical situation.

CLINICAL STUDIES

The use of PROTOPAM (pralidoxime) has been reported in the treatment of human cases of poisoning by the following substances:

Azodrin	Methylparathion
Diazinon	Mevinphos
Dichlorvos (DDVP) with chlordane	Parathion
Disulfoton	Parathion and Mevinphos
EPN	Phosphamidon
Isoflurophate	Sarin
Malathion	Systox®
Metasystox I® and Fenthion	TEPP
Methyldemeton	

Of these cases, over 100 were due to parathion, about a dozen each to malathion, diazinon, and mevinphos, and a few to each of the other compounds.

REFERENCES

1. LANDAUER, W.: Cholinomimetic teratogens. V. The effect of oximes and related cholinesterase reactivators, *Teratology 15:33* (Feb) 1977.
2. MOLLER, K.O., JENSEN-HOLM, J., and LAUSEN, H.H.: *Ugeskr. Laeg. 123*:501, 1961.
3. NAMBA, T., NOLTE, C.T., JACKREL, J. and GROB, D.: Poisoning due to organophosphate insecticides. Acute and chronic manifestations, *Amer. J. Med. 50*:475 (Apr), 1971.
4. ARENA, J.M.: Poisoning, Toxicology Symptoms, Treatments, ed. 4, Springfield, IL, Charles C. Thomas, 1979, p. 133.
5. BRACHFELD, J., and ZAVON, M.R.: Organic phosphate (Phosdrin®) intoxication. Report of a case and the results of treatment with 2-PAM, *Arch. Environ. Health 11*:859, 1965.
6. HAYES, W.J., Jr.: Toxicology of Pesticides, Baltimore, The Williams & Wilkins Company, 1975, p. 416.
7. AMA Department of Drugs: AMA Drug Evaluations, ed. 4, Chicago, American Medical Association, 1980, p. 1455.

esi

Manufactured for
Baxter Healthcare Corporation
Deerfield, IL 60015 USA
By: Baxter Pharmaceutical Solutions LLC
Bloomington, IN 47403
For Product Inquiry 1 800 ANA DRUG (1-800-262-3784)

MLT-18/3.0

scandinavian update 2005

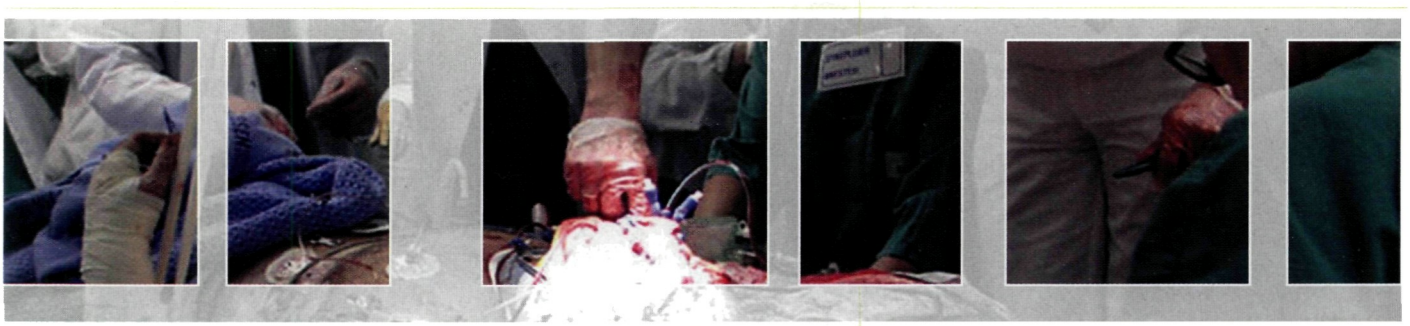
on trauma, resuscitation and emergency medicine

meet, have fun, share ideas and look into the future of trauma, resuscitation and emergency medicine.

stavanger norway

september 8-10th, 2005

multi-disiplinary meeting
interactive learning
international expert faculty
heated pro-con debates - panel discussions
hot topics - scientific breakthroughs
consensus process and Utstein meeting
simulation and workshops
meet-the-experts

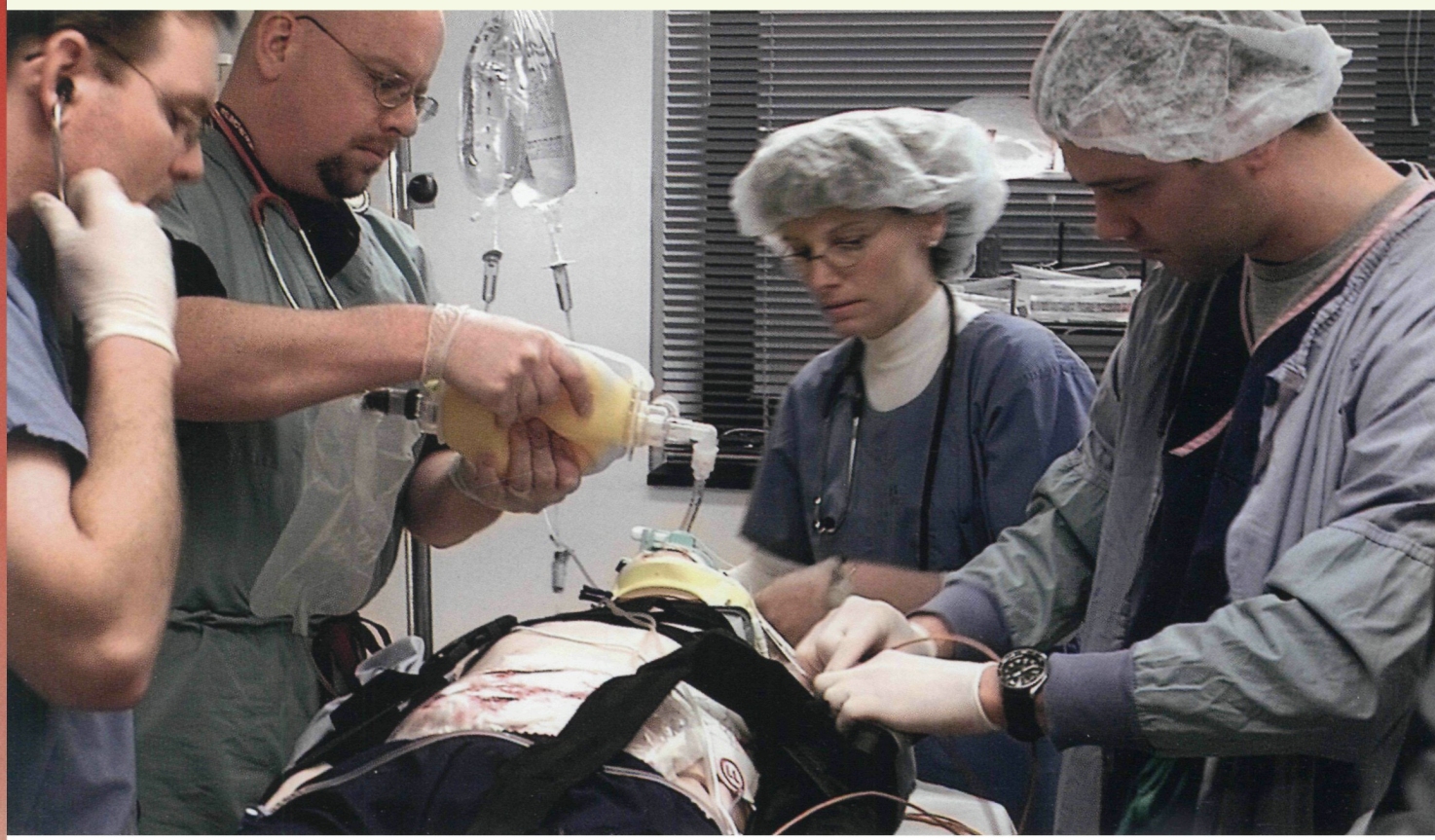


www.scandinavian-update.org

www.akuttjournalen.com

https://doi.org/10.1017/S1049023X00002338 Published online by Cambridge University Press

Bringing Simulation to Life

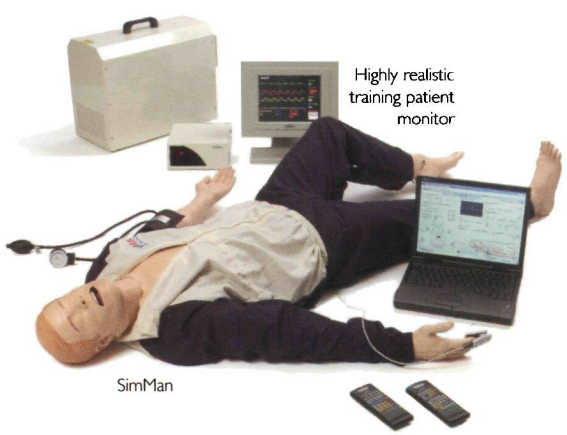


SimMan®

There is a growing awareness that health care is behind other high risk operations in its attention to ensuring basic safety and that there is a need to grasp the scale of the problem [1,2].

Use of patient simulation is considered an important part of the solution as many scenarios can be presented including uncommon but critical situations where a rapid response is needed. Errors can be allowed to occur and reach their conclusion without any risk to a patient. Team member interactions and leadership can also be explored and developed.

Two manikin-based simulators from Laerdal, SimMan® and AirMan®, represent a new generation of affordable and portable solutions to meet these needs.



SimMan

References:
1) BMJ Volume 320, 18 March 2000
2) To Err Is Human: Building a Safer Health System/Linda T. Kohn, Janet M. Corrigan, and Molla S. Donaldson, Editors., © 2000 by the National Academy of Sciences.

For more information visit www.laerdal.com/simman

LAERDAL MEDICAL AS, P.O. Box 377, N-4002 Stavanger, Norway
Tel. 47-51 51 17 00, Fax 47-51 52 35 57, E-mail laerdal.norway@laerdal.no

Laerdal
helping save lives

https://doi.org/10.1017/S1049023X00002338 Published online by Cambridge University Press

SMART TAG®

for triage that works

RECORD VITAL INFORMATION ABOUT TREATMENTS

ENHANCED PATIENT TRACKING WITH BARCODED TRANSPORT STRIP

GLOWING LIGHT STICK FOR MAXIMUM VISIBILTY IN ALL CONDITIONS, NIGHT AND DAY

STAYS WITH CASUALTY THROUGHOUT DECONTAMINATION

HIGHLIGHTS INFECTED AND CONTAMINATED CASUALTIES

CLEAR IDENTIFICATION OF PRIORITY

WMD Tag™

The ultimate resource for improving casualty management at scenes suspected to involve **nuclear, chemical** or **biological agents.** Completely waterproof, the **Smart WMD Tag™** goes with The **Smart Tag®** through casualty Decontamination. Included as a standard in the **Smart Triage Pac™**.

FOR MORE DETAILS AND *FREE* TRAINING GO TO smartmci.com NOW!

SMART TAG®
SMART INCIDENT COMMAND SYSTEM
www.smartmci.com

https://doi.org/10.1017/S1049023X00002338 Published online by Cambridge University Press

https://doi.org/10.1017/S1049023X00002338 Published online by Cambridge University Press