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TOXICOLOGY PROFILES FOR CHEMICALS IDENTIFIED AT NCBC GULFPORT MS

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TOXICOLOGY PROFILES FOR CHEMICALS IDENTIFIED AT NAVAL CONSTRUCTION BATTALION CENTER GULFPORT

GULFPORT, MISSISSIPPI

OCTOBER 1994

SOUTHERN DIVISION
NAVAL FACILITIES ENGINEERING COMMAND
NORTH CHARLESTON, SOUTH CAROLINA
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INTRODUCTION

This document was developed to provide the officials at the Naval Construction Battalion Center (NCBC) Gulfport, MS a quick reference guide on the toxicology associated with both acute and chronic exposure to 17 of the chemicals identified at this site.

This document was derived from the TOMES (R) Medical Management Database (c) 1992 and the Hazardous Substances Data Bank, 1994. The profiles were edited by a board certified, human health toxicologist. In the interest of brevity and readability, this document was not designed to give the officials all of the information available concerning the toxicology of these chemicals. Rather, it gives them the most relevant information concerning the toxicology of these chemicals as well as the full literature citations supporting the information. Parties interested in more complete information concerning the toxicology of these and other chemicals identified may wish to consult other documents such as the Toxicology Profiles developed by the Agency for Toxic Substances and Disease Registry (ATSDR).

The chemicals covered in this document are listed in alphabetical order. The organization of each chemical summary is the same. The first part of each chemical profile is a summary of the toxicology by organ system, e.g. cardiovascular or genitourinary system. The next part gives information concerning the carcinogenicity, teratogenicity, effects on pregnancy, and genotoxicity or chromosomal aberration potential of the chemical. The third section deals with clinical parameters which may be altered by exposure to the chemical. The fourth section covers decontamination and listed treatment protocols for each chemical by route of exposure, e.g. inhalation or dermal exposure. The fifth section gives additional information concerning the toxicology of the chemical and case reports of persons exposure to the chemical. A full listing of references cited in each profile are given in the final section.

This document is written for health care professionals. It uses abbreviations and terminology which are commonly used in the medical field. For further information you may want to consult a reference such as Dorland's Illustrated Medical Dictionary.

The following chemicals are covered in this document:

Benzene
bis (2-Ethylhexyl)phthalate
Cadmium
Chromium
DDT
1,2-Dichloroethane
Dioxin
Ethyl Benzene
Lead

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List of chemicals continued:

Methyl Ethyl Ketone
Naphthalene
Polychlorinated Biphenyls (PCBs)
Pyrene
Toluene
1,1,1-Trichloroethane
Trichloroethylene
Xylenes

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BENZENE

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of benzene in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to benzene.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to benzene. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of benzene and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to benzene.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

Acute benzene toxicity from inhalation results in CNS effects. Ingestion has been reported, associated with toxicity. Chronic exposure has resulted in aplastic anemia, acute myeloblastileukemia, erythroleukemia, and death. The possibility of chronic poisoning in employees of gasoline filling stations and bulk gasoline loading facilities exists due to the high concentration of benzene in gasoline.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

EYES: Splash contact causes a moderate burning sensation, with slight transient epithelial cell injury, and rapid recovery (Grant, 1986).

1.1 CARDIOVASCULAR

Ventricular fibrillation can occur due to myocardial sensitization (Nahum & Hoff, 1934).

1.2 RESPIRATORY

Bronchial and laryngeal irritation may occur after inhalation. Ingestion may cause substernal pain, cough, and hoarseness. Death can occur due to respiratory failure. Pulmonary edema may occur.

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1.3 NEUROLOGIC

Initially euphoria is seen followed by headache, giddiness, vertigo, and ataxia (Harrington, 1917). High doses can result in confusion, convulsions, and coma. Chronic exposure can produce headache (Harrington, 1917), fatigue, dizziness, and loss of appetite. Transverse myelitis has been reported (Herregods et al. 1984).

1.4 GASTROINTESTINAL

Burning develops in mucous membranes of the mouth, pharynx, and esophagus shortly after ingestion. Stomach pain, nausea, and vomiting occur early in intoxication.

1.5 HEPATIC

Toxicity is more common chronically but may occur after a large exposure.

1.6 GENITOURINARY

No information is available.

1.7 HEMATOLOGIC

Exposures producing acute myelotoxicity can result in delayed hematopoietic changes (Gosselin et al. 1984). Chronic exposure can produce suppression of hematopoiesis resulting in spontaneous bleeding, anemia, and leukopenia. Large single-dose exposure has been postulated to produce acute myelotoxicity or leukemia (Gerarde, 1960).

Aplastic anemia and leukemia can occur (Aksoy, 1985a; Aksoy, 1985b). Work exposure to 100 ppm resulted in 140 excess deaths from leukemia per 1000 exposed; 10 ppm resulted in 14 excess deaths (Landrigan & Rinsky, 1984). Bone marrow toxicity in exposed individuals may be triggered by individual susceptibility - women more than men, pregnancy, infection, and alcoholism. All elements of the marrow are affected.

Blood diseases that have been associated with benzene exposure include pancytopenia, leukopenia, bone marrow hypoplasia or aplasia, thrombocytopenia, granulocytopenia, and lymphocytopenia (NTP, 1986).

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1.8 DERMATOLOGIC

Skin contact may cause erythema, blistering, and dermatitis due to the defatting action of benzene.

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

Benzene is classified by the EPA as a group A carcinogen and by IARC as a group 1 carcinogen. Both of these designations mean that benzene is a confirmed human carcinogen.

Although benzene consistently tests negative in most tests for short-term mutagenicity, OSHA assessment has revealed that a 40-year exposure to 1 ppm in the workplace doubles the risk of dying from acute myelogenous leukemia (Goldstein, 1989).

Aplastic anemia and leukemia can occur (Aksoy, 1985a; Aksoy, 1985b). Work exposure to 100 ppm resulted in 140 excess deaths from leukemia per 1000 exposed; 10 ppm resulted in 14 excess deaths (Landrigan & Rinsky, 1984). Risk assessment studies have reported estimated lifetime excess deaths due to leukemia of 14 to 104 per 1000 workers exposed to 10 ppm (Austin et al. 1988).

Bone marrow toxicity in exposed individuals may be triggered by individual susceptibility - women more than men, pregnancy, infection, and alcoholism. All elements of the marrow are affected.

Acute myeloblastic leukemia has been the most common malignancy associated with benzene exposure (Goldstein,1989).

2.1 PREGNANCY

No information is available.

2.2 TERATOGENICITY

Studies in animals have generally been negative. More animal and epidemiological studies are needed before more definitive conclusions can be made (NTP, 1986).

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2.3 CHROMOSOME ABERRATIONS

There are reports of short-lived chromosome abnormalities, chromatid gaps with occasional breaks of chromatids and chromosomes, and some sister chromatid exchanges. At least 23 studies have shown significantly increased chromosomal aberrations, some persisting for years after exposure has ceased (NTP, 1986).

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

Obtain a baseline CBC (complete blood count) on anyone with acute exposure to benzene. Periodic hematologic examination may be necessary until the clinical signs and symptoms of acute exposure have resolved.

3.1 URINE

Inoue et al (1986) found a good correlation between urine phenol levels and benzene concentrations in the breathing zone. Monitoring urine phenol levels are useful in monitoring respiratory exposure. Some OTC medications containing phenol may give false positives and/or increased urine phenols. Examples are Pepto Bismol(R) and Chloraseptic(R) (Baselt & Cravey, 1989).

Urine phenol levels in non-exposed individuals are less than 10 mg/L. Urine phenol levels after chronic exposure to 0.5 to 4 ppm are less than 30 mg/L. Urine phenol levels after exposure to 25 ppm average 200 mg/L (Baselt & Cravey, 1989).

3.3 OTHER

Monitor EKG for cardiac arrhythmias.

IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

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4.0.2 TREATMENT

Monitor patient for respiratory depression. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, and pneumonia. Toxic effects of benzene are produced chiefly by inhalation of the vapor. Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

4.1.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.2.2 TREATMENT

Treatment is symptomatic since benzene is an eye irritant.

4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Emesis may be indicated in recent substantial ingestion unless the patient is or could rapidly become obtunded, comatose or convulsing. Is most effective if initiated within 30 minutes.

ACTIVATED CHARCOAL/CATHARTIC: Activated charcoal has been demonstrated to decrease absorption of benzene in animals (Laass, 1980). Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol.

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4.3.2 TREATMENT

Monitor EKG for cardiac arrhythmias. Avoid epinephrine because of the possibility of myocardial sensitization.

V. OTHER INFORMATION

No further information is available.

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BIS (2-ETHYLHEXYL) PHTHALATE

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of bis (2-ethylhexyl) phthalate in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to bis (2-ethylhexyl) phthalate.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to bis (2-ethylhexyl) phthalate. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of bis (2-ethylhexyl) phthalate and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to bis (2-ethylhexyl) phthalate.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

Bis (2-Ethylhexyl) phthalate is generally considered to be of slight to moderate toxicity. Mucous membrane and eye irritation may be seen. Central nervous system depression may occur. Dermal irritation is seldom seen. Skin sensitization does not occur in humans. The low vapor pressure usually precludes inhalation of any significant amount.

1.0 HEAD, EYES, EARS, NOSE, and THROAT

Irritation of the eyes, nose, and throat may occur.

1.1 CARDIOVASCULAR

No information is available.

1.2 RESPIRATORY

Respiratory tract irritation is not common, but could occur.

1.3 NEUROLOGIC

Central nervous system depression may be seen with ingestion of large amounts.

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1.4 GASTROINTESTINAL

Gastrointestinal tract or esophageal irritation may occur

1.5 HEPATIC

Mild hepatotoxicity has been seen in experimental animals only.

1.6 GENITOURINARY

No information is available.

1.7 HEMATOLOGIC

No information is available.

1.8 DERMATOLOGIC

Dermal irritation may sometimes develop.

1.9 OTHERS

TESTICULAR ATROPHY: Testicular atrophy was seen in rats in chronic feeding experiments with some phthalates (Gosselin et al. 1984). This effect has not been reported in exposed humans.

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

At the time of this review, no data were available to assess the carcinogenic or mutagenic potential of this agent.

2.1 PREGNANCY

At the time of this review, no data were available to assess the potential effects of exposure to this agent during pregnancy or lactation.

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2.2 TERATOGENICITY

Administration of 15 percent of the LD50 dose to pregnant rats on days 5, 10, and 15 of gestation produced resorptions in 27 percent and gross fetal abnormalities in 22 percent (Proctor & Hughes, 1978; Singh et al. 1972).

Some phthalates are teratogenic in mice (Proctor & Hughes, 1978).

2.3 CHROMOSOMAL ABERRATION

No information is available.

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

Monitor liver function tests and blood glucose. A number of chemicals produce abnormalities of the hematopoietic system, liver, and kidneys. Monitoring complete blood count and liver and kidney function tests is suggested for patients with significant exposure.

If respiratory tract irritation is present, monitor arterial blood gases and chest x-ray.

3.1 URINE

A number of chemicals produce abnormalities of the hematopoietic system, liver, and kidneys. Monitoring urinalysis is suggested for patients with significant exposure.

3.2 RADIOLOGICAL

If respiratory tract irritation is present, monitor chest x-ray.

3.3 OTHERS

No information is available.

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IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

Carefully observe patients with inhalation exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary.

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

4.1.2 TREATMENT

Treat dermal irritation or burns with standard topical therapy. Patients developing dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.

4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

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4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Due to potential esophageal or gastrointestinal tract irritation, **EMESIS SHOULD BE AVOIDED.**

DILUTION: Following ingestion and/or prior to gastric evacuation, immediately dilute with 4 to 8 ounces (120 to 240 milliliters) of milk or water (not to exceed 15 milliliters per kilogram in a child).

GASTRIC LAVAGE: Gastric lavage with a large-bore orogastric tube may be indicated if performed soon after ingestion, or in patients who are comatose or at risk of convulsing.

ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol. Administer one dose of a saline cathartic or sorbitol, mixed with charcoal or administered separately.

4.3.2 TREATMENT

No specific treatments have been identified. Treatment is symptomatic.

4.3.3 ENHANCED ELIMINATION

No studies have addressed the utilization of extracorporeal elimination techniques in poisoning with this agent.

4.3.4 MONITORING PARAMETERS

Monitor liver function tests and blood glucose.

Observe patients with ingestion carefully for the possible development of esophageal or gastrointestinal tract irritation or burns. If signs or symptoms of esophageal irritation or burns are present, esophagoscopy may be considered to determine the extent of injury.

Carefully observe patients with ingestion exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary.

Carefully monitor level of consciousness in patients ingesting large amounts. If central nervous system depression occurs, ensure that adequate respirations and oxygenation are maintained.

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V. OTHER INFORMATION

No further information is available.

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CADMIUM

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of cadmium in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to cadmium.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to cadmium. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of cadmium and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to cadmium.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

Acute toxicity most notably occurs after cadmium ingestion or inhalation of cadmium fumes. Poisoning from inhalation is relatively rare but dangerous. Initial signs/symptoms of cadmium poisoning resemble initial symptoms of the flu (Patwardhan & Finckh, 1976).

Long term exposure to cadmium can produce proteinuria, kidney damage, and chronic obstructive lung disease. Toxicity is usually a product of chronic industrial exposure, although acute and subchronic exposure insults these organs as well.

1.0 HEAD, EYES, EARS, NOSE, and THROAT

EYES: Eye irritation follows cadmium oxide fume exposure.

NOSE: Loss of sense of smell occurs after years of exposure.

THROAT: Both salivation and dry mouth have been reported as well as a metallic taste.

EDEMA: Facial, pharyngeal and neck edema developed rapidly after a large dose oral ingestion that proved fatal (Buckler et al. 1986).

TEETH: Yellow rings may be seen in the teeth when chronic exposure occurs.

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1.1 CARDIOVASCULAR

No information is available.

1.2 RESPIRATORY

Following acute inhalation, the lung is the target organ, although symptoms may not begin for up to 12 hours (Beton et al. 1966). Chest pain, cough, dyspnea, bronchitis and pneumonitis have all been noted in acute poisonings (Tibbits & Milroy, 1980).

Respiratory toxicity may progress, over 1 to 4 days, to pulmonary edema which may persist for months. Respiratory pneumonitis with persistent restrictive ventilatory defect may result (Barnhart & Rosenstock, 1984).

Chronic workplace cadmium exposure was associated with radiographic emphysema and decreased carbon monoxide transfer, which correlated with cumulative cadmium exposure. None had a history of acute cadmium pneumonitis (Davison et al. 1988).

1.3 NEUROLOGIC

Headache, vertigo, and shivering occur from cadmium fume fever.

1.4 GASTROINTESTINAL

Following acute oral ingestion, the target organ is the gastrointestinal tract. Acute poisoning produces severe nausea, vomiting, diarrhea, abdominal pain and cramping, substernal pain and gastroenteritis (Taylor et al. 1984).

1.5 HEPATIC

Liver damage can occur in acute or chronic cadmium poisoning because the liver contains high levels of metallothionein. Involvement of the liver does not occur as often as with the kidney (Gosselin et al. 1984).

1.6 GENITOURINARY

Spermatid and spermatocyte damage has been suggested in humans. Although no adverse effects have been reported on human female reproductive function, female rat reproductive function might be suppressed by 10 mg/kg cadmium chloride daily (AMA, 1985).

Testicular necrosis resulting in creatinuria has been seen in cadmium poisoned rats (Gray et al. 1986).

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Renal tubulopathy was reported on autopsy in 4 patients with chronic cadmium intoxication (Takebayashi et al. 1987).

The predominant effect of chronic exposure is proximal renal tubule damage evidenced by enzymuria and proteinuria. Effect is irreversible and may worsen despite termination of exposure (Elinder et al. 1985; Roels et al. 1989).

Renal stones are common when osteomalacia is present.

1.7 HEMATOLOGIC

Hypochromic anemia resistant to iron therapy results from chronic exposure.

1.8 DERMATOLOGIC

No information is available.

1.9 OTHER SYSTEMS

Glycosuria, $Beta_2$ microglobulinuria and aminoaciduria can result from chronic poisoning (Shaikh & Smith, 1984; Takebayashi et al. 1987). In severe cases, higher molecular weight proteins, such as albumin may be present.

Cadmium toxicity affects calcium metabolism, and patients with severe cadmium nephropathy may have renal calculi and excess excretion of calcium, probably related to increased urinary loss, but with chronic exposure, urine calcium may be less than normal. Associated skeletal changes are probably related to calcium loss and include bone pain, osteomalacia, and/or osteoporosis (Klaassen et al. 1986).

Chronic exposure to cadmium has been associated with microfractures, osteomalacia, radiologic decreases in bone density, and disturbances in calcium metabolism (ACGIH, 1986; Gosselin et al. 1984).

In Japan, a painful osteomalacia with skeletal deformities called "itai-itai byo" (ouch-ouch disease) has been linked with ingestion of cadmium-contaminated shellfish (Gosselin et al. 1984; Takebayashi et al. 1987). It has occurred primarily in postmenopausal multi-parous women (Proctor & Hughes, 1978).

Cadmium may act directly on the bone collagen in rats, causing acceleration of collagen catabolism and demineralization (Gosselin et al. 1984).

II. CARCINOGENICITY/TERATOGENICITY

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2.0 CARCINOGENICITY

The EPA considers cadmium to be a B1 carcinogen while IARC considers cadmium a 2A carcinogen. These designations indicate that cadmium is a probable human carcinogen. The EPA believes there is adequate evidence of carcinogenicity in animals and some evidence of carcinogenicity in humans but the evidence is not conclusive. IACR considers cadmium to be a human carcinogen. Based upon these designations, cadmium should be considered to be a human carcinogen.

Cadmium workers exposed to 0.3 mg cadmium/m^3 may be at increased risk for lung and prostatic cancer (Elinder, 1986). However, other studies have failed to demonstrate an increase risk of prostatic cancer (Armstrong & Kazantzis, 1985; Armstrong & Karantzis, 1983; Sorahan & Waterhouse, 1985).

2.1 PREGNANCY

Offspring of women receiving industrial exposure to 0.16 to 35 mg soluble cadmium salts/m^3 weighed less than controls (AMA, 1985). These effects may be secondary to cadmium placental toxicity (Reproductive Toxicology, 1986).

Smoking during pregnancy has been reported to cause fetal cadmium accumulation and decreased birth weight (Sikorski et al. 1988).

Human breast milk cadmium averaged less than 0.1 ng/g, although previously reported values were higher (Dabeka et al. 1986). Although breast milk averaged less than 0.1 mcg/kg the range of cadmium in milk and commercial infant formula was up to 1.2 mcg/L.

2.2 TERATOGENICITY

No information is available.

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2.3 CHROMOSOME ABERRATIONS

Increased sister chromatid exchange was not seen in cultured lymphocytes from people exposed to cadmium nor in lymphocytes of non-exposed humans after addition of cadmium sulfate (1.6 to 6.2 x 10^{-6} M) to the culture (Nogana et al. 1986; Bassendow Karska & Zawadzkakos, 1987).

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

Cadmium levels in normal adults, not exposed to environmental cadmium and who do not smoke average 0.4 to 1.0 mcg/L. Smokers average 1.4 to 4.5 mcg/L. These values are for whole blood, as cadmium is bound to red blood cells (Friberg et al. 1985).

Blood cadmium correlates well with urinary cadmium following chronic exposure (Verschoor et al. 1987).

3.1 URINE

Urinary cadmium is normally below or around 1 mcg/L. Care must be taken to accurately measure urinary cadmium (Friberg et al. 1985). A 24 hour urine sample is preferable. Urinary cadmium levels reflect cadmium body burden. Irreversible renal damage may occur at urinary cadmium concentrations above 5 mcg/g urinary creatinine (Verschoor et al. 1987).

Proteinuria, evidenced by increased urinary low molecular weight proteins (eg, $Beta_2$-microglobulin in pH >5.6 urine) results from nephrotoxicity (Ellis et al. 1983; Shaik & Smith, 1984). This is the first evidence of cadmium-induced renal tubular dysfunction. It correlates with duration of exposure, cumulative exposure, and urinary cadmium (Elinder et al. 1985). The renal damage appears to be largely irreversible (Elinder et al. 1985). Decreased glomerular filtration rate occurs in severe cases.

Metallothionein also correlates with cumulative cadmium exposure and may be more specific than other proteins (Shaikh et al. 1990). Elevated urinary metallothionein suggests exposure to cadmium or other metals (eg, Cu or Zn).

Urinary N-acetyl-B-D-glucosaminidase (NAG) also correlates to renal tubular damage from heavy metals; both proteinuria and enzymuria are non-specific indicators of renal injury (Kosnett, 1990).

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3.2 RADIOLOGICAL

In chronic poisoning x-ray findings are characteristic of osteomalacia and may show multiple fractures.

Chest x-ray findings after acute inhalation exposures may indicate diffuse pulmonary edema. Later they are those of bronchopneumonia (proliferative interstitial pneumonitis) (Gosselin et al. 1984).

3.3 OTHERS

Urine, blood, and hair cadmium are all elevated after prolonged exposure, but individual variability is large enough to make these useful only as indices of significant prolonged exposure in individuals.

Direct in vivo measurement, using neutron activation analysis or x-ray fluorescence of liver and kidney cadmium are the best indicators of cadmium body burden and cumulative exposure (Morgan, 1979; Christoffersson et al. 1987). A renal cortical cadmium concentration of 200 mcg/g wet weight is often associated with renal dysfunction (Friberg et al. 1985).

IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

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4.1 EYE EXPOSURE

4.1.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.1.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.2 EYE EXPOSURE

No information is available.

4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Emesis may be indicated in substantial recent ingestion unless the patient is obtunded, comatose or convulsing or is at risk of doing so based on ingestant. Emesis is most effective if initiated within 30 minutes of ingestion.

ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline.

4.3.2 TREATMENT

No specific treatment has been suggested for cadmium poisoning. Treatment is symptomatic.

CHELATION: May be used after acute exposure but has not been shown to be of definite benefit. The effectiveness of chelation therapy decreases markedly with time after exposure. Chelation cannot be recommended to treat chronic cadmium poisoning.

All complexing agents may increase the risk of cadmium-induced renal damage. BAL, EDTA, and penicillamine should not be used with cadmium since the complex formed is nephrotoxic (Friberg, 1956; Klaassen et al. 1984).

Chronic cadmium poisoning appears to respond to large doses of vitamin D in the presence of adequate dietary calcium and phosphorus (Braunwald et al. 1987). Calcitriol has

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been used pragmatically to treat chronic cadmium toxicity; vitamin D deficiency has been postulated as a predisposing factor for the development of chronic cadmium toxicity and its associated osteoporosis (Angle et al. 1989).

4.3.3 ENHANCED ELIMINATION

Charcoal hemoperfusion is ineffective due to high cadmium plasma protein and red blood cell binding.

V. OTHER INFORMATION

5.0 CASE REPORTS

Ingestion of 150 g of cadmium chloride in a 17 year-old-girl resulted in acute vomiting, facial edema, hypotension, acidosis, respiratory arrest, followed by pulmonary edema and oliguria over 24 hours, and death 30 hours post-ingestion (Buckler et al. 1986).

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CHROMIUM

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of chromium in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to chromium.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to chromium. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of chromium and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to chromium.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

Acute toxicity occurs in two phases; an initial multisystem shock due primarily to gastrointestinal corrosion, and a late occurring involvement of renal, hepatic, and hematopoietic systems.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

EYES: Severe corneal injury may result from ocular contact with solid or concentrated solutions of chromic acid and other hexavalent salts (Grant, 1986). Astigmatism and anesthesia of affected surfaces may persist after acute exposure.

Chronic keratitis, conjunctival inflammation and brown bands of discoloration in the corneal surface may occur with chronic exposure (Grant, 1986).

NOSE: Ulceration and perforation of the nasal septum and larynx may result from chronic inhalation of fumes (Dixon, 1929). A purulent discharge with crust formation and breathing difficulty are primary symptoms.

Rhinorrhea and nasal hyperemia may result from acute exposure (Fregert, 1982).

THROAT: Oral burns may be noted.

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1.1 CARDIOVASCULAR

Circulatory collapse and shock due to multisystem trauma may occur within a few hours of acute oral ingestion.

1.2 RESPIRATORY

Acute exposure to massive concentrations of chromic acid mist can severely damage deep lung structure (Meyers, 1950). Pulmonary edema may be delayed for up to 72 hours following acute exposure.

Chronic industrial exposure may result in bronchitis or pulmonary carcinoma (Ballal, 1986; Burrows, 1983).

Spotty, moderately severe non-nodular pneumoconiosis has been described (Taylor & Davis, 1977).

Bronchial asthma generally occurs within 4 to 8 hours after exposure (Committee on Biologic Effects of Atmospheric Pollutants, 1978).

Respiratory distress syndrome may be noted with significant oral ingestion (Iserson et al. 1983).

Metal fume fever has been reported after exposure to chromium oxide in a ferro-chrome alloy plant (Stoke, 1977).

1.3 NEUROLOGIC

Toxic or hepatic encephalopathy has been reported; usually occurring as a late manifestation, but has occurred within 15 minutes of oral ingestion (Ellis et al. 1982).

Cerebral edema and meningoencephalitis can occur.

1.4 GASTROINTESTINAL

Violent gastroenteritis with rice-water stools, yellow-green or coffee-ground emesis and hemorrhage occur immediately upon oral ingestion of chromates (Iserson et al. 1983).

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1.5 HEPATIC

Acute hepatitis may occur as a late manifestation, but is less common than renal injury. Centrilobular necrosis and Kupffer cell proliferation have been noted at autopsy (Pascale et al. 1952).

1.6 GENITOURINARY

Renal proximal tubular damage with marked interstitial edema is frequently observed as a late manifestation during the first or second day. Hematuria and oliguria may be noted (Iserson et al. 1983).

Acute renal failure occurred after ingestion of chromic acid (Bader, 1986; Saryan & Reedy, 1988), and dichromate (Kaufman et al. 1970).

Eosinophilic cystitis surrounding chromated catgut suture material has been reported in a patient who had a positive patch test to chromate and to intradermal chromic catgut (Engler et al. 1986).

1.7 HEMATOLOGIC

Hemorrhagic diathesis, thrombocytopenia, and anemia have been observed, usually occurring after 3 to 7 days. Intravascular hemolysis occurs rarely (Sharma et al. 1978).

Chromates are capable of oxidizing free hemoglobin in vitro to methemoglobin, and clinically significant methemoglobinemia has been seen in overdose (Iserson et al. 1983).

1.8 DERMATOLOGIC

Chromates are highly corrosive to skin and mucous membranes. Deep perforating ulcers (chrome holes) may be noted (Burrows, 1983).

The trivalent form of chromium is an active allergen, however it does not penetrate the stratum corneum; thus patch tests are negative and intradermal tests positive. The majority of occupational dermatitis occurs secondary to exposure to hexavalent chromium. It is believed that the hexavalent salt penetrates the skin, where it is reduced to trivalent chromium and reacts with skin proteins to form antigens (Milner, 1980).

Occupational allergic contact dermatitis has been reported secondary to chromate in cement (Goh, 1986; Goh et al. 1986; Olumide, 1987a; Farm, 1986); in yellow chromated components of automobile engine parts (Hjerpe, 1986); in metal sprays (Handfield-Jones et al. 1987); and in chrome plating processes (Lee & Goh, 1988).

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Oral ingestion of chromium in amounts within the range of normal daily intake may result in exacerbation of chronic dermatitis (Kaaber & Veien, 1978; Kaaber & Veien, 1977).

Contact dermatitis in a chromate-sensitive patient occurred after exposure to chromium-containing acupuncture needles (Castelain et al. 1987).

Contact dermatitis of the neck due to chromates in military uniforms has also been reported; whereas, contact dermatitis of the feet may occur due to dichromate used in leather tanning (Olumide, 1987b; Olumide, 1987c).

Burns initially resemble first and second degree burns, but extend to subcutaneous tissue within a couple of days (Kelly et al. 1982; Schiffe et al. 1982).

1.9 OTHER

Muscle cramps may be noted (Wang et al. 1985).

An anaphylactoid reaction, with urticaria, dyspnea, and chest tightness, occurred in a male welder after occupational exposure to chromium vapors. A challenge with sodium chromate aerosol produced delayed urticaria, angioedema and decreased FEV1 and an increase in plasma histamine (Moller et al. 1976).

II. CARCINOGENICITY/TERATOGENICITY

2.1 CARCINOGENICITY

Chromium is found in two major forms, trivalent and hexavalent. The trivalent form of chromium is not a carcinogen. The hexavalent form of chromium is designated as a class A carcinogen by the EPA and a group 1 carcinogen by IARC. These designations indicate that hexavalent chromium is a confirmed human carcinogen.

Occupational exposure to hexavalent chromium has been associated with an increased incidence of lung cancer in many groups (Norseth, 1986): welders (Sjogren et al. 1987; Becker et al. 1985); chrome-platers (Franchini et al. 1983; Sorahan et al. 1987); chromium chemical producers (Braver et al. 1985); chromite ore refiners (Enterline, 1974); chromium pigment producers (Sheffet et al. 1982; Langard & Vigander, 1983). However, a retrospective mortality study of workers in chrome leather tanneries revealed no occupationally related increased risk of cancer (Stern et al. 1987).

Chromium-induced carcinogenicity appears to be related to exposure to hexavalent compounds and not to trivalent compounds because only chromium (VI) is readily transported into cells. Furthermore, the solubility of chromium compounds has some influence on

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carcinogenicity (Lee et al. 1988; Levy et al. 1987; Petrille & de Flora, 1987; US Dept of Health Education & Welfare, 1975).

2.2 TERATOGENICITY

A review of the literature found no reports of reproductive or developmental effects of chromium in humans (Clarkson et al. 1985).

2.3 CHROMOSOMAL ABERRATIONS

No information is available

2.4 MUTAGENICITY

Hexavalent chromium potentiates the mutagenicity of sodium azide, possibly by affecting the repair of DNA (LaVelle, 1986).

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

Chromium (VI) and complexes of chromium (III) can be rapidly determined in plasma and other biological specimens via a high performance anion-exchange liquid chromatograph coupled to visible range (370 nm) and UV (280 nm) detectors and an atomic-absorption spectrometer. The detection limits for chromium (III) for each method were 2 and 5 ng, respectively (Suzuki, 1987).

3.1 URINE

Beta (2)-microglobulins were significantly higher in chrome-platers exposed to hexavalent chromium than in non-exposed controls (Lindberg & Vesterberg, 1983a).

Potassium dichromate-induced renal tubular damage in rats results in a bimodal increase in excretion of Tamm-Horsfall mucoprotein, which is located in the epithelial cells of the ascending limb and distal convoluted tubule. The first peak at 12 hours occurs prior to structural changes in the tubular epithelia. The second peak at 24 to 72 hours coincides with tubular necrosis and cast formation. Excretion of this mucoprotein may be useful in evaluating early renal damage (Schwartz et al. 1972).

IV. TREATMENT BY EXPOSURE ROUTE

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4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

OBSERVATION: If concentrated solutions of chromic acid are inhaled, hospitalize and observe for 72 hours for delayed onset of severe pulmonary edema.

Obtain baseline chest x-ray and vital signs. Evaluate for nasopharyngeal burns. Treatment should include recommendations listed in the Oral Exposure section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

4.1.2 TREATMENT

Treat burns prophylactically for infection. EDTA ointment 10 percent may facilitate removal of chromate scabs (Finkel, 1982). Excision of affected skin is recommended in severe exposures. Chronic chrome ulcers generally heal in several weeks with no specific treatment. Treatment should include recommendations listed in the Oral Exposure section when appropriate.

Contact dermatitis reportedly has been prevented by repeated application of a 10% ascorbic acid solution during exposure to reduce the active hexavalent chromium to an inactive trivalent form (Milner, 1980). Favorable results have also been obtained in 64% of patients who used a barrier cream containing 2% glycine and 1% tartaric acid. Tartaric acid reportedly reduces hexavalent to trivalent chromium which is then chelated by glycine and tartaric acid (Romaguera et al. 1985).

4.2 EYE EXPOSURE

4.1.2 DECONTAMINATION

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Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

ASCORBIC ACID: Administration of 1 gram per 0.135 gram of elemental chromium was effective in preventing toxicity in rats if given before stomach emptying occurred (within 2 hours) (Samitz et al. 1962). Ascorbic acid reacts with hexavalent chromium to form a less toxic trivalent complex (Korallus et al. 1984).

EMESIS: **DO NOT INDUCE VOMITING.** Spontaneous emesis will normally occur if a toxic dose has been ingested.

DILUTION: Immediately dilute with 4 to 8 ounces (120 to 240 milliliters) of milk or water (not to exceed 15 milliliters per kilogram in a child).

DEMULCENTS: Follow dilution with appropriate demulcents, milk, cornstarch, antacids and water.

GASTRIC LAVAGE: Gastric lavage with antacids, such as magnesium hydroxide using a soft nasogastric or orogastric tube should be initiated.

ACTIVATED CHARCOAL: Activated charcoal has not been evaluated in chromate poisoning.

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4.3.2 TREATMENT

Exchange transfusion is recommended in all substantial ingestion. Exchange transfusion of 10.9 L of blood over a 5 hour period produced a reduction of 67% in blood chromium concentrations from 5.9 to 1.9 mcg/mL in one case (Kelly et al. 1982).

Monitor volume status hematocrit and platelet count. GI hemorrhage may result following ingestion of chromium salts and transfusions may be necessary.

Monitor and correct hyperkalemia when potassium chromates are ingested.

After initial hydration, forced diuresis may be beneficial. Alkaline diuresis should be performed if there is any evidence of hemolysis to prevent renal deposition of red blood cell breakdown product.

Hemodialysis should be implemented in case of renal failure, but is not more effective than forced diuresis in removing chromium from the body (Behari & Tandon, 1980). Hemodialysis and charcoal hemoperfusion were ineffective in a massive overdose (Iserson et al. 1983).

Determination of the methemoglobin concentration may be necessary. Treat patients who are cyanotic and symptomatic or if methemoglobin concentration is greater than 30 percent in an asymptomatic patient. Administer oxygen to cyanotic patients while preparing for methylene blue therapy.

Peritoneal dialysis is no more effective than forced diuresis.

Chelation may be used but has not been shown to be of definite benefit. BAL did not change renal or dialyzer clearance of hexavalent chromium in dogs (Ellis et al. 1982). EDTA does not chelate hexavalent chromium salts.

4.3.3 ENHANCED ELIMINATION

EXCHANGE TRANSFUSION: Exchange transfusion is recommended in all substantial ingestion. Exchange transfusion of 10.9 L of blood over a 5 hour period produced a reduction of 67% in blood chromium concentrations from 5.9 to 1.9 mcg/mL in one case (Kelly et al. 1982).

HEMODIALYSIS: Chromium clearances of 4 to 16 milligrams/8 hours of hemodialysis have been reported (Kaufman et al. 1970). However, hemodialysis clearance rates have not been shown to be greater than inherent renal clearance (Behari & Tandon, 1980).

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In a fatal oral ingestion of 5 grams of potassium dichromate, neither hemodialysis nor charcoal hemoperfusion were effective. Only approximately 265 mg of chromium was removed by 4 hours of hemodialysis (Iserson et al. 1983).

In a fatal case of sodium dichromate ingestion, hemodialysis resulted in an average clearance of 12.4 +/- 2.4 mL/min. During 8 hours of dialysis, approximately 62 mg of chromate were removed (Ellis et al. 1982).

PERITONEAL DIALYSIS: Similar in efficacy to hemodialysis. A clearance rate of 22.4 milligrams/24 hours was reported (Kaufman et al. 1970). A study of the efficacy of peritoneal dialysis versus hemodialysis in patients with renal failure was done following intravenous injection of 500 u Ci(51) CrCl(3). The peritoneal dialysis and 2.5 +/- 0.8 mL/min during hemodialysis. The difference was statistically significant (Schiffl et al. 1982).

V. OTHER INFORMATION

5.0 CASE REPORTS

A 49-year-old male was sprayed with hot chromic acid involving approximately 40% body surface area. He was irrigated at the scene and admitted to the hospital 1 hour after injury. The first urine sample contained hemoglobin. Treatment included IV crystalloids, mannitol, glucose, glucuronic acid, and whole blood. Nine hours after injury approximately half of the burned skin was excised, and grafts were placed. During the post-operative period, he became confused and began vomiting bile-stained fluid. Thrombocytopenia developed on the second day after injury, and he became unconscious. Treatment included antibiotics, chelating agents and diuretics. By the 4th day, the patient had developed hallucinations, muscle spasms, guaiac positive stools and emesis. Respiratory arrest occurred, and the patient died on the 6th day (Wang et al. 1985).

A 17-year-old male ingested approximately 5 grams of potassium dichromate 2 hours prior to admission in a suicide attempt. Vital signs were BP-130/58, P-120, R-48. Initial treatment included IV saline, oxygen by mask, and morphine sulfate for pain. After 15 minutes, vital signs were BP-80 mm Hg/palpation, P-130, R-24/minute, CVP-0. Treatment included IV saline and dimercaprol (5 mg/kg IM). The initial chromium level was >6000 mcg/dL. Because the patient had bloody stools, endoscopy was done which revealed caustic burns in the stomach and duodenum. Hemodialysis decreased the hyperkalemia but did not decrease the chromium level significantly. Despite transfusions and dopamine to support the blood pressure, the patient died of hypovolemic shock 14 hours post-ingestion (Clochesy, 1984; Iserson et al. 1983).

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Draft

DDT (DICHLORODIPHENYLTRICHLORETHANE)

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of DDT (dichlorodiphenyltrichloroethane) in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to DDT.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the Hazardous Substance Data Bank, 1994, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to DDT. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of DDT and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to DDT.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

While DDT may exert toxic effects from all routes of exposure, acute effects from ingestion are the most dramatic and frequently experienced, ranging from vomiting and diarrhea to coarse tremors, convulsions, and death. Effects from dermal contact (eg, dermatitis) and inhalation (eg, irritation of the nose and throat) have been noted, but are rare.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

NOSE: Almost continuous daily exposure to aerosols sufficient to leave white deposit of DDT on nasal vibrissae of volunteers, produced moderate irritation of nose, throat, and eyes. Except for this irritation during exposure, there were no symptoms (Hayes, 1982).

EYES: Ocular toxicity has been reported from systemic exposure in animals.

1.1 CARDIOVASCULAR

Palpitations, tachycardia, and "irregular heart action" have been noted in some but not all cases of acute DDT poisoning (Hayes, 1982). It is not clear whether DDT, the solvent, or the convulsions are responsible for occasional disorders in the cardiac mechanism. (Gosselin, 1984).

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1.2 RESPIRATORY

Aspiration of insecticide containing petroleum distillate may result in pneumonitis. Respiratory depression may occur concurrently with CNS seizures.

1.3 NEUROLOGIC

DDT may disrupt the central nervous system resulting in CNS excitation and seizures. Respiratory depression may occur concurrently with seizures. Other effects may include convulsions, tremor, ataxia, agitation, nervousness, and amnesia.

Dose of 16 mg/kg have resulted in convulsions (Hayes, 1982).

1.4 GASTROINTESTINAL

Nausea, vomiting, and diarrhea may follow ingestion of DDT.

1.5 HEPATIC

Involvement of liver has been mentioned in only small portion of cases of accidental poisoning by DDT. In 3 men who ingested pancakes contaminated with 5,000 to 6,000 mg DDT, slight jaundice appeared after 4 to 5 days, and lasted 3 to 4 days. (Hayes, 1982).

There was no evidence of liver disease or abnormalities in function tests in 31 chemical workers who in the course of their work had ingested the equivalent of 3.6 to 18 mg of DDT daily for 16 to 25 years. Serum concentration of DDT and its metabolites in 10 of the workers were 20 times greater than in the normal population (Marindale, 1982).

1.6 GENITOURINARY

No information is available.

1.7 HEMATOLOGIC

Blood dyscrasias, anemia, and leukemia have been associated with organochlorine exposure. In acute DDT poisonings a slight decrease in hemoglobin and moderate leukocytosis, without any constant deviation in differential white count, have been observed in volunteers (Hayes, 1982).

1.8 DERMATOLOGIC

Extensive contact results in dermal irritation.

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II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

There is inadequate evidence in humans for the carcinogenicity of DDT. There is sufficient evidence in experimental animals for the carcinogenicity of DDT. IARC has determined that DDT is possibly carcinogenic to humans (2B) (IARC, 1991).

USEPA classifies DDT as a B2 or probable human carcinogen. This classification is based on seven studies in which tumors (generally of the liver)were observed various mouse strains. Three studies in rats yielded similar results. Additionally, DDT is structurally similar to other probable carcinogens, such as DDD and DDE. There is inadequate human carcinogenicity data.

2.1 PREGNANCY

2.2 TERATOGENICITY

2.3 CHROMOSOMAL ABERRATIONS

No increase in chromosomal aberrations were observed in human lymphocyte cultures.

No increase in chromosomal aberration were observed in occupationally exposed workers with compared to an unexposed cohort. In one small group of severely exposed workers, a small increase in chromatid aberrations was found. In general, a positive correlation was observed between DDT levels in the plasma and time of exposure. However, there was no relationship between the plasma level of DDT and the frequency of chromosomal aberrations (Rabello, 1979).

III. LABORATORY STUDIES

Blood chlorinated hydrocarbon levels are not clinically useful following acute exposure. For most compounds they reflect cumulative exposure over a period of months or years rather than recent exposure.

The most meaningful measurements for monitoring exposure to DDT are of DDT itself in serum or adipose tissue, or of bis(p-chlorophenyl)-acetic acid in urine. Each of these levels has been shown to be proportional to the extent of DDT exposure.

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3.0 SERUM/BLOOD

A 10 mg daily dose of DDT results, after an equilibrium period of 6-12 months, in steady-state levels of 0.15 to 0.20 mg/l DDT in serum (Baselt, 1988).

3.1 URINE

A 10 mg daily dose of DDT results, after an equilibrium period of 6-12 months, in steady-state levels of 0.5 to 2.0 mg/l bis(p-chlorophenyl)-acetic acid in urine (Baselt, 1988).

3.2 RADIOLOGICAL

3.3 OTHERS

A 10 mg daily dose of DDT results, after an equilibrium period of 6-12 months, in steady-state levels of 100 mg/kg DDT in biopsy fat (Baselt, 1988).

Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and/or other tests that might become useful or mandatory (IARC, 1979).

VI. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

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4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

If clothing is contaminated remove and wash skin and hair three times; do an initial soap washing followed by an alcohol washing followed by a soap washing.

4.1.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Emesis may be indicated in substantial recent ingestion unless the patient is or could rapidly become obtunded, comatose or convulsing. It is most effective if initiated within 30 minutes of ingestion.

ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as slurry. Charcoal slurry may be aqueous or a mixture of charcoal with saline cathartics or sorbitol.

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4.3.2 TREATMENT

Seizures may be treated with a diazepam IV bolus. If seizures are uncontrollable or recur, administer phenytoin.

Do not give oils by mouth.

Do not administer adrenergic amines, which may further increase myocardial irritability and produce refractory ventricular arrhythmias.

Oral administration of chloestyramine may enhance the excretion of kepone and chlordane which are trapped in the enterohepatic circulation.

V. OTHER INFORMATION

5.0 CASE REPORTS

Studies of DDT in volunteers have been designed to search for possible effects of doses considered to be safe. In the first of these studies, men received three dose levels, 0.0021 to 0.0034, 0.038 to 0.063, and 0.36 to 0.61 mg/kg/day (the exact value was dependent on the weight of each individual). Volunteers were dosed for 12 to 18 months. No volunteer complained of any symptom. The same results were obtained in the second study, in which the same dosages were administered for 21 months and volunteers were observed for minimum of 27 additional months (Hayes, 1982).

Evidence that significant poisoning or disturbance of eyes or vision is unlikely from prolonged occupational exposure has been provided by study of 35 men exposed for 11-19 yr to large amounts of DDT in its manufacture. Worker body fat concentrations of DDT, its isomers and metabolites ranged from 38-647 ppm, contrasting with avg of 8 ppm for general population. Among these men and in other employees of manufacturing plant, no instances of clinical poisoning were recognized, and none of 35 patients in the study had eye complaints (Grant, 1986).

An 13-yr-old Mexican was admitted to hospital with anemia, bleeding, high fever, and unconsciousness. His home had been sprayed with dicophane every other day for 4 months preceding admission and repeatedly for the past 2 years. Laboratory investigation showed low hemoglobin, low reticulocytes, low white cell count, and diminished platelets. He started to recover after transfusions of packed red blood cells, and administration of prednisone and tetracycline. But spraying of the hospital room with a 10% solution of dicophane provoked an allergic reaction; he slowly became more ill and died about 30 hours later. Post-mortem

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examination showed hypocellularity of the bone marrow and massive bleeding in the lung (Martindale, 1982).

Symptomatology 2-3 hours after ingestion: 1) Very large doses are followed promptly by vomiting, due to local gastric irritation. Delayed emesis and/or diarrhea may occur (the mechanism is not understood). 2) Numbness and paresthesias usually starting with lips, tongue, and face. 3) Malaise, headache, sore throat, fatigue, weakness. 4) Coarse tremors (neck, head, and particularly of eyelids), apprehension, ataxia, and confusion. 5) Convulsions, both clonic and tonic, may alternate with periods of coma and paresis. 6) In absence of convulsions, vital signs are essentially normal, but in severe poisonings the pulse may be irregular and be abnormally slow. Whether DDT, the solvent, or the convulsions are responsible for occasional disorders in the cardiac mechanism is not clear. If pulmonary edema supervenes, it is probably an expression of solvent intoxication. 9). Death is usually due to respiratory failure from medullary paralysis. 10) In acute exposures, recovery is usually complete within 1-3 days, but sometimes weakness, or paralysis and ataxia may persist for weeks (Gosselin, 1984).

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ETHYLENE DICHLORIDE
(1,2 Dichloroethane)

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of ethylene dichloride in humans. In addition it provides information on the symptomology, by organ system, which may be encountered in a person exposed to ethylene dichloride.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to ethylene dichloride. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of ethylene dichloride and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to ethylene dichloride.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

Initial effects seen after ethylene dichloride ingestion are gastrointestinal; vomiting is common. Cyanosis, dyspnea, and coma may be delayed in onset. Pulmonary edema may develop. Death may be due to cardiovascular, respiratory, or hepato-renal failure. Liver and kidney injury may occur in significant exposures. Neurologic effects have been reported including headache, weakness, tremor, and dizziness.

1.0 HEAD, EYES, EARS, NOSE, and THROAT

EYES: Twenty cases of corneal burns were reported from splash contact in the workplace, with rapid recovery (McLaughlin, 1946).

THROAT: A 2-year-old had some burning of the mouth and throat after he swallowed some toy airplane glue containing ethylene dichloride (Jacobziner & Raybin, 1961). Metallic taste has been described after inhalation exposure (HSDB, 1990).

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1.1 CARDIOVASCULAR

Inhalation of high concentrations of ethylene dichloride may result in death from ventricular fibrillation (Procter et al. 1988; Nouchi et al. 1984).

1.2 RESPIRATORY

Ethylene dichloride may cause irritation to the upper respiratory tract and burning in the nose.

Respiratory toxicity may progress to pulmonary edema, characterized by cough, then production of frothy sputum. Pulmonary edema may appear immediately, or it may be delayed (Yodaiken & Babcock, 1973; Marraccini et al.1983).

Respiratory depression, dyspnea,and cyanosis may occur (Jacobziner & Raybin, 1961).

1.3 NEUROLOGIC

Seizures as well as excitability may be seen (Jacobziner& Raybin, 1961). CNS depression, dizziness, ataxia, confusion, malaise,lethargy, stupor, coma, and dizziness have been reported(Jacobziner & Raybin, 1961). Ingestion of ethylene dichloride is very likely to cause shock,then death by multiple mechanisms (Jacobziner & Raybin, 1961). Headache has been reported.

1.4 GASTROINTESTINAL

Nausea and vomiting may occur (Proctor et al. 1988; Watrous, 1942; Jacobziner & Raybin, 1961; Yodaiken & Babcock, 1973; Letz et al. 1984). Diarrhea may occur following ingestion of ethylene dichloride (Hubbs & Prusmack, 1955). Cramping and abdominal pain were reported following inhalation and dermal exposure to ethylene dichloride (Wirtschafter & Schwartz, 1939).

1.5 HEPATIC

A later toxic effect is liver necrosis. The necrosis is midzonal, rather than centrilobular, and is accompanied by fatty degeneration (Yodaiken & Babcock,1973).

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1.6 GENITOURINARY

Acute tubular necrosis may occur following ethylene dichloride ingestion (Jacobziner & Raybin, 1961;Yodaiken & Babcock, 1973).

1.7 HEMATOLOGIC

Hypoprothrombinemia has been reported in severe cases, secondary to liver necrosis (Yodaiken & Babcock, 1973).

1.8 DERMATOLOGIC

Ethylene dichloride produced raw, red, scalded appearing hands of workers after 4 hours of intermittent immersion. The hands appeared dry, shiny with a "cigarette-paper" appearance 2 weeks after exposure despite application of emollient ointment (Wirtschafter & Schwartz, 1939). Heavy dermal exposure results in a bluish purple skin discoloration (NIOSH, 1978).

1.9 OTHER SYSTEMS

Hypercalcemia was reported 4 days post ingestion in one severe case, possibly secondary to parathyroid damage(Yodaiken & Babcock, 1973).

Hypoglycemia was reported in one severe case; onset was the second day post ingestion; etiology was secondary to massive liver necrosis (Yodaiken & Babcock, 1973).

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

Ethylene dichloride is designated by the EPA as a B2 carcinogen. IARC designates ethylene dichloride as a 2B carcinogen. Both of these designations indicate that ethylene dichloride is a probable human carcinogen. This means that there is adequate evidence of carcinogenicity in animals but that human evidence of carcinogenicity is either lacking or inadequate.

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Colacci et al (1985) reported 1,1-dichloroethane is capable of inducing tumors in rats and mice. Ethylene dichloride is metabolically bioactivated and once activated will bind with macromolecules in vivo & in vitro (Arfellini et al.1984).

The addition of disulfiram to the diet of rats exposed to 50 ppm ethylene dichloride for 2 years resulted in a significant increase in the incidence of bile duct cholangiomas, subcutaneous fibromas, neoplastic nodules,interstitial cell testicle tumors, and mammary adenocarcinomas (Cheever et al. 1990).

Disulfiram also increases the hepatotoxic potential of ethylene dichloride, presumably due to inhibition of microsomal mixed-function oxidase-mediated metabolism of ethylene dichloride, and a compensatory increase in metabolism to reactive metabolites formed by glutathione-e-ethylene dichloride conjugation (Igwe et al. 1986).

2.1 PREGNANCY

An average concentration of 0.074 +/- 0.046 mg/kg was reported in breast milk of workers exposed to ethylene dichloride at the workplace (Mukhametova & Vozovaya, 1972). This compound was still detectable in breast milk at 17 hours after exposure was discontinued.

2.2 TERATOGENICITY

There are no human or convincing animal data to suggest that ethylene dichloride is a reproductive hazard (AMA, 1985; Barlow & Sullivan, 1982).

2.3 CHROMOSOME ABERRATIONS

POSITIVE for sex chromosome loss and nondisjunction in Drosophila melanogaster via inhalation at 2 ppm/96 hours (RTECS, 1989).

2.4 GENOTOXICITY/MUTAGENICITY

2.4.1 GENOTOXICITY

POSITIVE for DNA damage in Salmonella typhimurium at 7060 mcmol/L (RTECS, 1989).

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POSITIVE for DNA repair in E. coli at 10 mg/plate (RTECS, 1989).

POSITIVE for DNA inhibition in human lymphocytes at 5 mL/L (RTECS, 1989).

2.4.2 MUTAGENICITY

Ethylene dichloride was a 'direct-acting' mutagen in human lymphoblastoid cell lines (AHH-1 and TK6) (Crespi et al. 1985).

POSITIVE for mutation in human somatic cells (lymphocytes) at 100 mg/L (RTECS, 1989).

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

Monitor prothrombin time, serum glucose, electrolytes, liver function, and renal function in severe cases.

A number of chemicals produce abnormalities of the hematopoietic system, liver, and kidneys. Monitoring complete blood count and liver and kidney function tests is suggested for patients with significant exposure.

If respiratory tract irritation is present, monitor arterial blood gases and chest x-ray.

3.1 URINE

No information is available.

3.2 RADIOLOGICAL

If respiratory tract irritation is present, monitor chest x-ray.

3.3 OTHER

If respiratory tract irritation is present, it may be useful to monitor pulmonary function tests.

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IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

4.1.2 TREATMENT

Treatment should include recommendations listed in the ORAL/PARENTERAL EXPOSURE section when appropriate.

Burns should be treated as appropriate for any chemical burn.

4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

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4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Oral ingestion of ethylene dichloride may result in burns of the oropharynx. **EMESIS IS NOT RECOMMENDED.**

DILUTION: Following ingestion and/or prior to gastric evacuation, immediately dilute with 4 to 8 ounces (120 to 240 mL) of milk or water (not to exceed 15 mL/kg in a child).

GASTRIC LAVAGE: Careful gastric lavage with a soft nasogastric tube should be considered following dilution in all but trivial ingestions (a taste or less) in patients presenting within one hour post ingestion.

Gastric lavage with a large-bore orogastric tube may be indicated if performed soon after ingestion, or in patients who are comatose or at risk of convulsing.

ACTIVATED CHARCOAL: Activated charcoal has been shown to adsorb ethylene dichloride in animals (Laass, 1975). Activated charcoal may be given following gastric lavage, and as sole decontamination in patients with trivial ingestions or delayed presentations. Administer as aqueous slurry.

CATHARTIC: Cathartics may not be necessary since diarrhea may occur following oral ingestion.

4.3.2 TREATMENT

No information is available.

4.3.3 ENHANCED ELIMINATION

No information is available.

4.3.4 MONITORING PARAMETERS

Respiratory and cardiovascular function should be followed carefully. Onset of symptoms may be delayed and sudden in onset.

Monitor EKG for potential cardiac arrhythmias.

Monitor seizure activity with EEG.

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Monitor liver and kidney function following significant exposure.

4.3.5 SPECIFIC ANTIDOTES

N-acetylcysteine has been suggested as a potential antidote for ethylene dichloride poisoning, but its efficacy has not been documented in the English literature (Kurashov et al. 1989). It had no apparent clinical effect in another study (Luzhnikov et al. 1985). Other agents, such as Vitamin E, have been tried based on the presumption that toxicity is secondary to generation of free chlorine radicals (Luzhnikov et al. 1989).

V. OTHER INFORMATION

5.0 CASE REPORTS

A 14-year-old boy drank 15 mL of ethylene dichloride for recreational purposes. Onset of symptoms was within 2 hours, including severe headache, staggering, lethargy, and vomiting. Oliguria was noted initially and persisted. Hypoglycemia was noted on the second day. On the third day dyspnea and somnolence were noted. Liver function tests were slightly abnormal on admission and steadily worsened.

Hypoprothrombinemia occurred on the third day, secondary to depletion of liver-dependent clotting factors. Aspiration occurred secondary to endotracheal intubation attempt. Pulmonary edema was then documented, which resolved over the next 36 hours. The serum calcium level began to rise on the fourth day to 14.5 mg/dL. Sinus tachycardia and ST-T wave changes were reported. Refractory hypotension developed on the fifth day, followed by death on the sixth day (Yodaiken & Babcock, 1973).

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Draft

DIOXIN (2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN)

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin) in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to dioxin.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the Hazardous Substance Data Bank, 1994, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to dioxin. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of dioxin and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to Dioxin.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

Most exposures to dioxins (TCDD) occur during chemical reactions. Acute early symptoms include chemical burns of the skin, mucous membranes and eyes, nausea and vomiting, and severe muscle pains. After a latency of several weeks, chloracne, porphyria cutanea tarda, hirsutism, and/or hyperpigmentation may occur. Polyneuropathies and liver damage are frequently noted. Elevated blood lipids are common and may persist.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

Conjunctivitis may be noted acutely.

1.1 CARDIOVASCULAR

Hyperlipidemia has been described following exposure, and may persist for 10 years or longer. Other cardiovascular disorders, such as atherosclerosis and myocardial infarction have not been conclusively shown to be related to TCDD exposure.

1.2 RESPIRATORY

Dyspnea may be noted.

1.3 NEUROLOGIC

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Polyneuropathies with sensory impairment and lower extremity weakness is common following moderate industrial exposures to TCDD. Mild exposures may result in asymptomatic EMG alteration

1.4 GASTROINTESTINAL

Nausea and vomiting may be an early symptom of TCDD exposure. Pancreatitis has been reported following an industrial exposure.

1.5 HEPATIC

Enzyme induction is prominent in acute and chronic TCDD exposure. Moderate and acute exposure to TCDD may manifest with elevated liver function tests, mild fibrosis, fatty liver changes and hepatomegaly.

1.6 GENITOURINARY

Self-limiting hemorrhagic cystitis has been reported.

1.7 HEMATOLOGIC

Prothrombin time prolongation has been noted rarely, in conjunction with liver damage.

1.8 DERMATOLOGIC

Chloracne is considered a sensitive indicator of dioxin exposure, however, some patients appear to be resistant. Chloracne appears within 2 to 4 weeks after initial exposure in most cases, consisting of comedones, milia or epidermal straw colored cysts on the malar, temple or periorbital area. Skin fragility, hirsutism, and photosensitivity may occur. Chloracne may persist for several months in mild cases, while severe cases may persist for 30 years or longer. Porphyria cutanea tarda may occur in moderate or severe exposures.

Dermal exposure to soil concentrations of greater than 100 ppm are likely to produce chloracne.

1.9 MUSCULOSKELETAL

Myalgia is common in acute occupational exposure.

II. CARCINOGENICITY/TERATOGENICITY

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2.0 CARCINOGENICITY

The Human Health Assessment Group in EPA's Office of Health and Environmental Assessment has evaluated 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) for carcinogenicity. According to their analysis, the weight-of-evidence for 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is group B2, which is based on inadequate evidence in humans and sufficient evidence in animals. As a group B2 chemical, 2,3,7,8-Tetrachlorodibenzo-p-dioxin is considered to be a probable human carcinogen (USEPA, 1988).

A review of employment records and tissue specimens of seven workers, reported previously as having occupational dioxin exposure and soft-tissue sarcomas, confirms that four workers had employment of 2 to 19 years in the production of 2,4,5-trichlorophenoxyacetic acid or trichlorophenol, products contaminated with 2,3,7,8-tetrachlorodibenzodioxin. Of these individuals, two have confirmed soft-tissue sarcomas (Fingerhut et al., 1984).

A retrospective cohort mortality study was conducted in a cohort of 5,172 chemical workers from 12 facilities located in the United States. Workers had histories of exposure to phenoxy herbicides and chlorophenols contaminated with TCDD. A review of process descriptions and job duties was used along with measurement of serum TCDD levels to document occupational exposure. In this cohort the mortality from several rare cancers previously associated with TCDD contamination was not notable. In a subcohort of 1,520 workers with more than one year of exposure and more than 20 years of latency, soft tissue sarcoma mortality was significantly elevated (standard mortality ratio 922). Respiratory system cancer was also significantly elevated (standard mortality ratio 142) in this subcohort. Mortality due to all cancers combined was significantly elevated both in the cohort (standard mortality ratio 115) and the subcohort (standard mortality ratio 146). Mortality due to all accidents was also significantly elevated in the cohort (standard mortality ratio 128). It was concluded that the excess cancer mortality, especially in the subcohort, is consistent with TCDD being a carcinogen (Fingerhut et al., 1990).

2.1 PREGNANCY

To determine whether paternal exposure to TCDD or other polychlorinated dioxins might be associated with adverse pregnancy, a survey was conducted among wives of Dow Michigan Division employees in Midland, MI area who had been potentially exposed to dioxins. The control group consisted of wives of employees who had no dioxin exposure and whose hire dates were comparable to those of men in exposed group. Overall, no statistically significant association was found between any exposure and pregnancy outcome, either before or after stratification by pertinent sets of up to 9 covariables (Townsend, et al., 1982).

2.2 TERATOGENICITY

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The effects of TCDD on human embryonic palatal shelves were studied in vitro and compared with results from previous studies on mouse and rat organ cultures. Results indicate that TCDD alters human embryonic palatal shelf proliferation and differentiation similar to that noted in mice but at a decreased sensitivity level (Abbott and Birnbaum, 1991).

2.3 CHROMOSOMAL ABERRATIONS

III. LABORATORY STUDIES

It is difficult and expensive to detect dioxins in human tissue specimens. Current analytical techniques involve gas chromatography and mass spectrometry.

Liver function tests, CBC, prothrombin time, serum lipids, and uroporphyrins should be obtained in acute exposure. EMG may be useful in detecting subclinical neuropathy.

3.0 SERUM/BLOOD

3.1 URINE

3.2 RADIOLOGICAL

3.3 OTHERS

Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and/or other tests that might become useful or mandatory (IARC, 1979).

VI. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

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Treatment should included recommendations listed in the ORAL EXPOSURE Section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Immediately wash exposed area extremely thoroughly with soap and water.

4.1.2 TREATMENT

Chloracne may respond to topical retinoic acid, and oral tetracyclines to treat secondary pustular follicles. Resistant cases may require acne surgery or dermabrasion. Isotretinoin may be tried.

4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain , swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.3 ORAL EXPOSURE

Cumulative oral doses of 100 mcg/kg are estimated as the minimum toxic dose.

4.3.1 PREVENTION OF ABSORPTION

EMESIS: May be indicated in recent substantial ingestion unless the patient is or could rapidly become obtunded, comatose or convulsing. Is most effective if initiated within 30 minutes..

ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as a slurry. The charcoal slurry may be aqueous or a mixture of charcoal with saline cathartics or sorbitol.

4.3.2 TREATMENT

ACUTE EXPOSURE: Treatment is supportive.

Monitor liver function serially in confirmed exposures.

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V. OTHER INFORMATION

5.0 CASE REPORTS

Seventy-six cases of chloracne in workers were reported following exposure to TCDD between 1965-1968 in factory producing 2,4,5-T and pentachlorphenol in Czechoslovakia ... Fifty-five patients followed for over 5 years; symptoms included porphyria cutanea tarda, uroporphyrinuria, abnormal liver tests and liver enlargement. The majority suffered severe neurasthenia and depressive syndrome. In 17 subjects, signs of peripheral neuropathy, especially in lower extremities, were confirmed. More than half of the patients showed raised levels of blood cholesterol and total lipids (IARC, 1977).

Three scientists were poisoned during preparation of TCDD by heating potassium trichlorophenate. Two of the scientists developed typical chloracne 6 and 8 weeks after exposure. Delayed symptoms, most likely due to TCDD, developed about 2 yr/later in 2 scientists, these included personality changes, mainly loss of energy and drive, impairments of vision, taste and muscular coordination, sleep disturbances, GO symptoms and hirsutism. Hypercholesterolemia (in excess of 300 mg/100 ml) occurred in all 3 patients (IARC, 1977).

Chloracne was found in 52% of 226 workers in a 1979 cross-sectional survey at a plant where 2,4,5-T had been manufactured from 1948 to 1969. A significant increased prevalence of abnormal gamma-glutamyl transpeptidase and higher mean gamma-glutamyl transpeptidase were found in those with chloracne, compared to those without. Although mean triglyceride values were higher in those with chloracne, the difference was not statistically significant. Neurological exam showed statistically significantly higher prevalence of abnormal sensory findings in those with chloracne. Increased prevalence of reported sexual dysfunction and decreased libido in those with chloracne compared to those without was statistically significant after age adjustment. (Moses, et al., 1984)

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ETHYL BENZENE

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of ethyl benzene in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to ethyl benzene.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to ethyl benzene. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of ethyl benzene and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to ethyl benzene.

I. SYMPTOMOLOGY BY ORGAN SYSTEM

Toxicity occurs most frequently following repeated intentional inhalation of paints or solvents containing ethyl benzene. Industrial exposure to vapors in confined areas has resulted in collapse, coma, and death. Acute ingestion of ethyl benzene solvents probably causes transient CNS depression.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

EYES: Eye exposure results in ocular irritation, pain and possible corneal burns if the liquid is directly splashed in the eye. Lacrimation may also occur.

1.1 CARDIOVASCULAR

Death, if it occurs, is from respiratory failure or cardiac arrhythmia due to myocardial sensitization.

1.2 RESPIRATORY

Inhalation may result in bronchial laryngeal irritation, acute bronchitis, bronchospasm, and pulmonary edema. Death can occur from respiratory failure. Ethyl benzene may exacerbate the symptoms of obstructive airway disease due to its irritant properties.

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1.3 NEUROLOGIC

Inhalation may result in a transient euphoria, headache, giddiness, vertigo and ataxia, especially after glue sniffing. Early excitatory effects are soon followed by depression. At higher doses confusion and coma may occur.

1.4 GASTROINTESTINAL

Ingestion may cause a burning sensation in the mouth and stomach, nausea, salivation and vomiting. Substernal pain, coughing and hoarseness can occur.

1.5 HEPATIC

No information is available.

1.6 GENITOURINARY

No information is available.

1.7 HEMATOLOGIC

It is not currently believed that ethyl benzene is myelotoxic.

1.8 DERMATOLOGIC

Continued or repeated skin contact causes dermatitis.

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

Ethyl benzene is not considered to be carcinogenic by either the EPA or IARC.

2.1 PREGNANCY

Ethyl benzene is not considered a reproductive hazard .

2.2 TERATOGENICITY

Ethyl benzene is not teratogenic or mutagenic.

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2.3 CHROMOSOME ABERRATIONS

Ethyl benzene is negative in mutagenicity and chromosomal aberration tests.

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

Obtain a baseline CBC and monitor renal and hepatic function.

3.1 URINE

Excretion of less than 2.1 grams in a 24 hour urine sample indicates exposure to less than 200 ppm.

IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

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4.1.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Probably not indicated following small amounts due to possibility of aspiration and the lack of substantial evidence of systemic toxicity from oral ingestion.

GASTRIC LAVAGE: Gastric lavage may be indicated when: the patient has ingested a large quantity of ethyl benzene (greater than 5 milliliters of pure substance), or there is a large amount of benzene contamination, and emesis is contraindicated (obtunded, comatose, convulsing). A cuffed endotracheal tube must be in place. The potential toxicity of the amount ingested must be weighed against the substantial risk of aspiration.

ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol.

4.1.2 TREATMENT

If the patient is already coughing upon arrival at the medical facility, aspiration has probably already occurred. Monitor arterial blood gases in cases of severe aspiration pneumonitis to assure adequate ventilation.

If aspiration is suspected (history of coughing/choking), obtain baseline chest x-ray and vital signs. Admit patient if symptomatic and/or chest roentgenogram is positive for signs of aspiration pneumonia.

If the baseline chest x-ray and vitals are normal, observe patient for 6 hours (obtaining hourly vital signs, when possible) and repeat the roentgenogram in 6 hours or sooner, if the patient becomes symptomatic.

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If the serial vital signs indicate tachypnea, hyperpnea, fever or other signs/symptoms of aspiration pneumonia and/or the repeat chest x-ray is positive, admission should be considered. Asymptomatic patients with a negative repeat chest x-ray require no further observation.

Chronic toxicity should include evaluation of the hepatic and renal status.

Hematologic evaluation is indicated if benzene contamination is suspected in cases of chronic inhalation.

Cardiac function should be monitored, and avoid epinephrine because of the possibility of myocardial sensitization.

V. OTHER INFORMATION

5.0 CASE REPORTS

No further information is available.

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LEAD

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of lead in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to lead.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to lead. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of lead and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to lead.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

Signs and symptoms of lead poisoning are referable to the nervous, hematologic, renal, gastrointestinal, and cardiac systems (Cullen et al, 1983). There may be no unique signs or symptoms to suggest lead poisoning as the diagnosis. Serious injury can occur when neither signs nor symptoms have been present. Case detection is best done by screening populations at risk, which include, for example, operatives in lead industries, their children,and children living in homes built before 1950 where lead-containing paint is the source.

Most lead poisoning is slow in onset and results from gradual accumulation of lead from sources of low solubility such as lead paint or industrial dusts. The ingestion of rapidly absorbed salts causes an acute syndrome which includes hepatic injury and hemolysis as well as the effects found with more chronic exposure.

1.0 HEAD, EYES, EARS, NOSE, and THROAT

EARS: Mild hearing loss has been associated with increased blood lead levels in children (Schwartz & Otto, 1986).

1.1 CARDIOVASCULAR

Chronic exposure in the adult leads to renal hypertension and secondary cardiac effects.

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1.2 RESPIRATORY

No information is available.

1.3 NEUROLOGIC

The most serious long term effects of lead poisoning, as well as death, results from acute encephalopathy. Intracranial pressure is increased. The encephalopathic syndrome includes depressed sensorium, vomiting, irritability, coma, and convulsions. Lateralizing signs occurred in 35% (Whitfield et al.1972). Differential diagnosis may include CNS tumor(Harrington et al. 1986)

More obscure symptoms of acute lead poisoning include:malaise, fatigue, headache, irritability, anorexia, and constipation.

The principal target system for lead toxicity in children is considered to be the developing central nervous system (Mushak et al. 1989). Increasing blood lead levels in children have also been correlated with hearing impairment, developmental delay (Schwartz & Otto, 1987), and growth retardation (Angle & Kuntzelman, 1989). Several studies have agreed that asymptomatic children with either normal (less than 25 mg/dL) or elevated blood lead levels may have significant decrements in IQ when compared to unexposed children (Landrigan & Graef, 1987; Pocock et al. 1987; Faust & Brown, 1987). This finding has been hotly debated, however (Ernhart & Needleman, 1987). In a meta-analysis of 12 lead studies evaluating the relationship between blood and tooth lead levels and IQ in children, Needleman & Gatsonis (1990) concluded that a strong link exists between low-dose lead exposures and intelligence deficits in children.

The relationship between low blood levels and neonatal (Ernhart et al. 1986) and early cognitive development (Bellinger et al. 1987) has been controversial and somewhat inconclusive. A longitudinal study of 305 women and their babies found a direct relationship between prenatal and neonatal blood lead levels and decreased performance on the Bayley Mental Developmental Index at 3 and 6 months of age. At least part of this may be attributable to lead-related reductions in birth weight and gestation. Male infants and infants from low socioeconomic families were found to be more sensitive (Dietrich et al. 1987). This finding is consistent with relative risk of perinatal mortality and morbidity from several epidemiologic studies (Abramowicz & Barnett, 1970; Naeye et al. 1971).

Mushak et al (1989), in reviewing 4 separate longitudinal studies (conducted in Boston, Cincinnati, Cleveland and Port Pirie, Australia), conclude that a link does exist between low-level lead exposure (10 to 15 mcg/dL) and deficits in early development and later neurobehavioral performance as measured by the Bayley Mental Development Index of the Bayley Scales of Infant Development. The critical exposure period appears to be prenatal.

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Peripheral neuropathy does not seem to correlated with blood lead levels or length of exposure (Ehle, 1986). Weakness, focal palsy (eg, wrist drop or other). Sensory deficit has been reported less commonly. Nerve, as well as spinal cord, conduction rates are slowed (Araki et al.1986). Blood lead level in children has a significant negative association with maximal motor nerve conduction velocity (Schwartz et al. 1988). Measurement of maximal motor nerve conduction is an insensitive screen for low-level lead toxicity (Schwartz et al. 1988).

Neurobehavioral tests in lead workers show deficits in cognitive function including decrease in memory, attention, concentration, and psychomotor performance (Arnvig et al. 1980; Valciukas et al. 1986; Williamson & Teo, 1986).

1.4 GASTROINTESTINAL

Thirty-four workers with elevated blood lead levels were studied to determine the incidence and type of abdominal pain associated with their exposure. Twenty-seven of thirty-nine (79%) reported crampy, intermittent periumbilical pain which was worst in the morning. Constipation and anorexia frequently preceded the pain by several weeks. As the pain increased, nausea, vomiting, and a metallic taste in the mouth (similar to sucking on a penny) were noted in some. Five patients developed diarrhea instead of constipation (Dahlgren,1978).

A 35-month-old child presented with unremitting paralytic intestinal ileus associated with acute lead poisoning (Zwiener et al. 1990).

1.5 HEPATIC

Hepatic injury has not been reported following chronic lead poisoning.

Liver injury has been reported following acute ingestion of 7 g of lead acetate (Karpatkin, 1961;Sixel-Dietrich, 1985).

Hepatic injury and hemolysis has been reported following acute ingestion of red lead (lead oxide) in a 21 year old male (Nortier et al. 1980).

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1.6 GENITOURINARY

ACUTE: Tubular injury noted by proteinuria, glycosuria,and aminoaciduria is seen (a Fanconi-like syndrome). Acute renal failure has been reported in a child (Khan et al. 1983).

CHRONIC: Long term exposure leads to azotemia and hypertension. Gout results from the diminished clearance of urate (Colleoni & D'Amico, 1986).

Deposits of lead in the kidneys may produce glycosuria and aminoaciduria. Reversible acute renal failure has been reported in a 26 month old female(with glucose-6-phosphate dehydrogenase deficiency)following chronic lead poisoning and prolonged chelation therapy with EDTA and BAL (Khan et al. 1983).

Lead nephropathy after chronic lead exposure has been well described. Interstitial nephritis, reduced glomerular filtration rate, and nonspecific proximal tubular dysfunction are typical (Wedeen et al. 1986; Verschoor et al. 1986).

Sperm count suppression was seen in lead exposed workers in a battery plant; endocrine function was normal (Assenato et al. 1987). Decreased sperm count and infertility were seen in a lead poisoned firearms instructor whose sperm count rose and who became fertile again after chelation therapy (Fisher-Fischbein et al.1987).

1.7 HEMATOLOGIC

A case of severe lead intoxication accompanied by hemolytic anemia was reported by Miwa et al(1981). Hemolysis has been reported following acute ingestion of red lead (lead oxide) (Nortier et al. 1980).

Heme synthesis is affected at several enzymatic steps. This leads to the buildup of the diagnostically important substrates o-aminolevulinic acid, coproporphyrin (measured in the urine) and zinc protoporphyrin (measured in the red cell as erythrocyte protoporphyrin or EP). The result of these enzymatic inhibitions is microcytic, hypochromic anemia. There is no permanent effect of lead on blood production. Blockade of erythrocyte pyrimidine nucleotidase (Cook et al. 1986)leads to stippling. Stippling is useful in suggesting the diagnosis of lead poisoning but not in assessing severity or monitoring the course or therapy.

Even when hemoglobin and hematocrit values are within the normal range, there is a decrease as the blood lead increases over 10 mcg/dL (Poulos et al. 1986).

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1.8 DERMATOLOGIC

Dermal application of lead acetate solution on eczematous skin has resulted in intoxication (Triebig, 1984). Other lead compounds have not been reported to cross the skin.

1.9 OTHER SYSTEMS

Hyperuricemia and gout may be seen in patients with lead nephropathy (Wedeen et al. 1986).

Rajkumar et al (1987) reported children with high blood lead concentrations were more likely to have biochemical iron deficiency (49/170) than anemia (26/170). Anemia, iron deficiency, or iron deficiency anemia was reported in 75/170 children (age range, 1.12 yr to 8.75 yr) with high blood lead concentrations.

Lead status alone was reported to account for 42% of the explained variance in FEP. Screening for iron deficiency in children with elevated blood lead should not be based solely on degree of elevation in FEP but also on dietary and socioeconomic risk factors (Carraccio et al. 1987).3. In a study of 26 children from upper-middle class families, exposed to lead during home renovation (blood lead levels of greater than 25 mcg/dL), only 1 had iron indices below normal. This suggests that iron deficiency may be more closely related to socioeconomic status than to lead intoxication (Linakis & Shannon, 1989).

Myalgia and arthralgia are presenting symptoms. Lead is deposited in the metaphyses of growing bones and slows linear growth (Schwartz & Otto, 1986).

Ninety percent of the lead body burden may be found in bone. The mean initial bone lead level in a group of smelter workers was 97 mcg/gram (range 61 to 131) with an average half-life of 6.7 years (range 3.4 to 15) after exposure was terminated (Christofferson et al.1986).

Neuroendocrine dysfunction has been implicated as a contributing factor in the decreased stature of children with high blood lead levels. In one study, 12 pediatric patients with blood lead levels of greater than 40 mcg/dL were assessed for thyroid stimulating hormone and prolactin responses to thyroid releasing hormone, growth hormone and cortisol response to insulin, and growth hormone response to L-Dopa and basal T4, T3, free T4 and somatomedin C before and after EDTA-BAL chelation therapy. The study demonstrated an inverse correlation between growth rate, somatomedin C concentration and peak growth hormone concentration and blood lead levels (Angle et al.1989).

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Children exposed to lead levels previously thought to be low and non-toxic lead have been found to have behavior and intelligence deficits (Needleman et al. 1979; Needleman et al. 1990; Needleman & Gatsonis, 1990), decreased heme biosynthesis (Piomelli et al. 1982), decreased nucleotide metabolism (Angle & McIntire, 1978), and decreased concentrations of 1,25-dihydroxyvitamin D (Rosen et al. 1980).

In an urban environment that may still be heavily contaminated with lead, one study showed children seen in the emergency department for non-lead ingestions were 3 times more likely to have elevated blood lead and erythrocyte protoporphyrin levels than matched children in a similar environment. The authors suggest that children seen in the emergency department for ingestion, that maybe at risk for chronic lead poisoning due to environmental conditions, should be screened for elevated blood lead and erythrocyte protoporphyrin levels when routine bloods are drawn (Hammer et al. 1985).

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

Lead has been found to be carcinogenic in animals but there is inconclusive evidence of carcinogenicity of lead in humans. The EPA considered lead to be a B2 carcinogen. IARC considers organic lead to be a class 3 carcinogen, inorganic lead to be a class 2B carcinogen. This designation means that there is adequate evidence of carcinogenicity in animals but that evidence of carcinogenicity in humans is either lacking or inadequate.

2.1 PREGNANCY

Cord blood lead is 80% of the maternal lead level. The development of children born with levels above 10 mcg/dL has been found to lag behind controls with lower levels (Bellinger et al. 1986; Bellinger et al. 1987). Beattie et al (1975) reported an increased prevalence of mental retardation in populations with high water lead.

Reduced gestational age and reduced birth weight have been linked with maternal blood lead levels. The risk of preterm deliveries with a maternal blood lead level of 14 mcg/dL was 8.7 times that of 8 mcg/dL (Mushak et al. 1989).

EFFECTS DURING BREAST-FEEDING

An insignificant amount of lead crosses into breast milk.

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2.2 TERATOGENICITY

Lead crosses the placenta (Korpela et al. 1986). Minor congenital anomalies (most commonly hemangiomas and lymphangiomas, hydrocele, skin tags) were associated with higher cord lead levels in a prospective study of 5183 deliveries (Needleman et al. 1984).

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

A blood lead level is currently the most commonly used test to determine an individual's relative lead burden (Carton et al. 1987; Mushak et al. 1989). All decisions in lead poisoning must be made on the basis of lead assay on venous blood. Blood lead levels (BLL) obtained from capillary pricks is valuable only if normal, as elevated contamination from skin lead is likely. Blood for erythrocyte protoporphyrin (EP) may be capillary blood. Blood lead levels indicate recent exposure or exposure over a period of up to 3 to 5 weeks (Mushak et al. 1989).

Blood levels of employees exposed to lead above the action level of 30 mcg/m(3) must be maintained at levels at or below 40 mcg/100 g, determined by monitoring every 6 months. For those (both male and female) who intend to have children, blood lead levels should be maintained at or below 30 mcg/100 g to minimize adverse reproductive health effects to the parents and to the developing fetus (CFR, 1988).

If an employee's blood lead level exceeds 40 mcg/100 g, monitoring frequency must be increased to at least every 2 months until two consecutive blood lead levels are below 40 mcg/100 g. Employees whose blood lead level is equal to or greater than 50 mcg/100 g shall be temporarily removed from exposure until their blood lead level is at or below 40 mcg/100 g. Employees may also be removed from exposure for medical reasons even if their blood lead levels are within 40 mcg/100 g. The use of erythrocyte protoporphyrin levels for adult monitoring has been proposed (Wang et al. 1985), but this monitoring tool has not been incorporated into OSHA requirements or ACGIH recommendations.

CHILD: Zinc or erythrocyte protoporphyrin level is probably the best screening test for both lead poisoning and iron deficiency (Anon, 1987). If greater than 35 mcg/dL, a blood lead is indicated. The Centers for Disease Control has defined childhood lead poisoning as blood lead of 25 mcg/dL or greater in association with an erythrocyte protoporphyrin level of 35 mcg/dL or greater. It should be kept in mind that lead has no biologic value. An ideal blood lead level is zero. Therefore, physiologic changes may be seen with blood lead levels far below 25 mcg/dL (Anon, 1987).

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It is widely expected that the CDC will revise its guidelines for lead poisoning, possibly to a threshold of 10 mcg/dL (Parsons et al. 1991). Measurement of erythrocyte protoporphyrin may not be the screening test of choice at this lower threshold.

The sensitivity of erythrocyte protoporphyrin may decrease at a threshold of 10 mcg/dL making it ineffective or cost prohibitive as a screening test (Parsons et al. 1991).

Lead status alone was reported to account for 42% of the explained variance in FEP. Screening for iron deficiency in children with elevated blood lead should not be based solely on degree of elevation in FEP but also on dietary and socioeconomic risk factors (Carraccio et al. 1987).

Screening of children at risk because of dwelling age or site, is done at 6, 9, 12, and 18 months and 2, 3, 4, and 5 years of age. Screening is by EP and, if elevated, a BLL is obtained (CDC, 1985). The following table may be used for decision making when a hematofluorometer is used for EP analysis (adapted from CDC, 1985).

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Risk Classification of Asymptomatic Children for Priority Medical Evaluation

BLOOD LEAD (mcg/dL)	ZINC ERYTHROCYTE PROTOPORPHYRIN (EP) (mcg/dL)			
	<35	35-74	75-174	>175
Not done	I	*	*	*
<24	I	Ia	Ia	EPP+
25-49	Ib	II	III	III
50-69	**	III	III	IV
>70	**	**	IV	IV

* = Blood lead test needed to estimate risk.
EPP+ = Erythropoietic protoporphyria. Iron deficiency may cause elevated EP levels up to 300 mcg/dL, but this is rare.
** = In practice, this combination of resultsis not generally observed; if it isobserved, immediately retest with wholeblood.
Grade I: Normal
Grade Ia: Iron deficiency anemia
Grade Ib: Early exposure or contaminated specimen
Grade II: Moderate toxicity. Limit of exposure required.
Grade III: Severe toxicity. Early assessment required.
Grade IV: Urgent toxicity. Hospitalization required.

Zinc protoporphyrin levels may not be a sensitive indicator of the blood lead level in children with adequate iron status. In 11 children with mean blood lead levels of 86 mcg/dL and normal iron status, the mean ZEP was 240 mcg/dL, compared to over 500 mcg/dL for 26 children with similar blood lead levels and inadequate iron status (Clark et al. 1988).

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LEAD

A non-linear, dose-response relationship between blood lead concentration and depression of hematocrit was observed in a study of 579 one- to five-year-old children living near a primary lead smelter (Schwartz et al. 1990). Background blood lead level was defined as 20 mcg/dL.

Risk of Hematocrit below 35% (% above background)	Blood Lead Level (mcg/dL)
0	<20
2	20 to 39
18	40 to 59
40	60 or greater

Age influences this relationship, but not sex (Schwartz et al. 1990).

	Approximate Probability of Hematocrit Below 35% for Blood Lead Level (mcg/dL)		
AGE (yr)	50	100	150
1	0.18	0.46	0.76
2	0.14	0.39	0.72
3	0.1	0.3	0.65
4	0.08	0.24	0.56
5	0.06	0.17	0.47

‘ NOTE: This relationship was developed with a small sample size.

Erythrocyte pyrimidine-5'-nucleotidase (P5N) activity can be measured by high performance liquid chromatography and may serve as a useful screen for lead toxicity (Sakai & Ushio, 1986).

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Blood lead level limitations include understatement of the potentially toxic fraction, representation of recent exposure only with an undefined input from past lead stores and possible inaccuracies as an indicator at levels lower than 25 mcg/dL (Mushak et al. 1989).

Lead is assayed in whole blood as most is in the RBC. Either atomic absorption spectrometry or anodic stripping voltametry may be used successfully for both blood and urine. Erythrocyte protoporphyrin (EP) (formerly called FEP and sometimes referred to as ZPP or ZnPP) is measured in a wet drop of blood in a special fluorometer (Hematofluorometer).

Measurement of coproporphyrin or o-aminolevulinic acid concentrations or red cell o-aminolevulinic acid dehydrase activity are no longer necessary clinical procedures.

Nieburg et al (1974) demonstrated a high correlation between red cell delta-amino-levulinic acid dehydratase (ALAD) with chelatable lead.

Morris et al (1988) found that ALAD in combination with blood lead was a marginally better predictor of urinary lead excretion than was EP at either time point in a study of 20 pediatric patients.

Measurement of maximal motor nerve conduction velocity is an insensitive screen for low-level lead toxicity (Schwartz et al. 1988).G. Lille et al (1988) reported decreased peripheral conduction velocities in 13 workers occupationally exposed to inorganic lead.

3.1 URINE

A urine mobilization test will be more definitive as to total body burden. Obtain 24 hour quantitative urine lead output, with and without D-penicillamine or EDTA mobilization.

Beta-aminoisobutyric acid may be elevated in urine of lead exposed workers (Farkas et al. 1987).

In renal failure patients without undue lead exposure and with blood leads of less than 40 mcg/dL, decreases in blood lead after EDTA injection correlated with creatinine decrease and urine protein but not with urine lead excretion (Osterloh & Becker, 1986).

Sokas et al (1988) found that a 6-hour urine lead result will account for 88% of the variability of full 24-hour diagnostic chelation in patients with serum creatinine levels less than 2 mg/dL and no known current lead exposure in a study of 35 adult male volunteers.

Provocation chelation was performed by administering 1 g CaNa2-EDTA in 250 mL of D5W intravenously over 1 hour. Two doses were given 12 hours apart. Urinary lead excretion was determined at 3-hours, 6-hours, and 24-hours after the first dose of EDTA. 2. Data were analyzed by linear regression, exponential curve fitting, and power curve fitting.

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Three-hour and 6-hour urine lead results were found to correlate linearly with the two-dose 24-hour urine results.

The following equations describe the relationship observed:

24-hour predicted = 157.3 + 4.03 (3-hour lead) lead
correlation coefficient = 0.89 ($P<0.001$)

24-hour predicted = 113.19 + 2.31 (6-hour lead) lead
correlation coefficient = 0.94 ($P<0.001$)

This method may be of value for screening purposes, however, additional studies are needed in larger populations if it is to be considered an appropriate epidemiologic tool or if therapeutic chelation trials should be deemed warranted.

Young children (age 1 to 3.5 years) given the EDTA mobilization test producing a single urine lead concentration of 1 mcg/mL or greater were associated with positive mobilization ratios in a retrospective study of 58 patients (Shannon et al. 1989). This method ($r=.63$) may be useful in cases where inadequate 6 to 8 hour urine samples are obtained, and a mobilization ratio cannot be determined. Additional studies are needed to confirm the observations of this study in larger populations.

Berger et al (1990) reported that a lead excretion ratio of greater than 1 micromoles of urinary lead excretion to millimoles calcium disodium EDTA administered corresponded to a cutoff value for 24-hour unstimulated urinary lead excretion of 10.4 micrograms. Additional studies are needed to verify these results.3.2.3 OTHER

3.2 RADIOLOGICAL

X-ray of the wrists and knees is useful in the diagnosis of heavy metal poisoning. Normally, in the small bone (ulna or fibula), there is no increased opacity in the metaphyseal area whereas the adjacent radius and tibia normally show increased metaphyseal density. Increased density in the small bones is indication of lead exposure of several months duration (Blickman et al. 1986).

Other bones where densities can be seen include bones of arm and hand, thigh and foot, ribs, and clavicles. Lead content of bones can be quantitated by x-ray fluorescence (Wielopolski et al. 1986).

Abdominal films reveal lead-containing paint or objects as radio-opacities.
L-line x-ray fluorescence (LXRF) technique for measuring cortical bone lead non-invasively has been developed (Wielopolski et al. 1989). Rosen et al (1989) reported 90% of lead-toxic children were correctly classified as being CaNa2EDTA-positive or -negative from blood lead and LXRF alone.

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Bone lead content was monitored for efficacy of the chelation treatment by simultaneous iliac crest bone lead measurement (bone biopsy measured by flameless atomic absorption spectrophotometry) and in vivo tibial x-ray fluorescence (XRF) in a 54-year-old male exposed to lead fumes and dust for approximately 30 years. Iliac lead, tibial lead, blood lead, zinc protoporphyrin, and 30 gram EDTA test were 64 mcg/g wet weight, 46 mcg/g wet weight, 40 mcg/dL, and 3,206 mcg/3 days, respectively, and 14mcg/g wet weight, 8 mcg/g wet weight, 23 mcg/dL, 42 mcg/dL, and 726 mcg/3 days, respectively, 7 months later (Batuman et al. 1989). The authors concluded that XRF measurement of bone lead content is a practical method for establishing the diagnosis and monitoring the efficacy of therapy.

CT: Computerized tomography may detect cerebral edema in patients with lead encephalopathy. A 23-month-old female who died from lead encephalopathy had a negative CT scan for cerebral edema prior to death. Cerebral edema was noted at autopsy (Hugelmeyer et al. 1988).

IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.2 EYE EXPOSURE

No information is available.

4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Emesis may be indicated in substantial recent ingestions unless the patient is obtunded, comatose or convulsing or is at risk of doing so based on ingestant. Emesis is most effective if initiated within 30 minutes of ingestion.

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ACTIVATED CHARCOAL/CATHARTIC: There are no data on adsorption of inorganic lead to activated charcoal, however salts of some other heavy metals are adsorbed.

Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol.

4.3.2 TREATMENT

Hospitalize any patient with significant CNS or protracted gastrointestinal symptoms, or with a blood lead level of 50 micrograms/100 milliliters or greater even if no symptoms are present. Chelation therapy should be instituted in all patients with blood lead level of 45 to 60 micrograms/100 milliliters (2.4 to 2.9 micromoles/liter) or greater, and in patients with a positive calcium EDTA provocation test. Patients treated as outpatients must be discharged to a lead-free environment.

4.3.3 ENHANCED ELIMINATION

No information other than chelation therapy is available.

4.3.4 MONITORING PARAMETERS

DIAGNOSIS: In addition to blood lead and EP level, the following tests can be useful in assessing lead absorption status:

a. CBC, serum iron, and iron binding capacity to rule out iron deficiency, which often accompanies lead toxicity.

b. Flat plate of the abdomen may be useful if lead has been ingested in the preceding 24 to 36 hours.

c. X-ray of long bones may help determine duration of exposure. Lead lines become visible after at least 4 to 8 weeks of exposure.

d. Calcium Disodium EDTA Provocative Test: May be useful in determining necessity for therapeutic chelation in children with blood lead levels of 25 to 55 micrograms/deciliter. This may be performed as an outpatient if the patient remains in the clinic (Piomelli et al. 1984).

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Obtain baseline blood lead level, have patient empty bladder. Administer CaNa2EDTA 500 milligrams/square meter intravenously, or intramuscularly with procaine. Some authors recommend 1 gram as a maximum daily dose. Collect all urine in lead-free containers for 8 hours. The lead excretion ratio is calculated using the following equation:

The lead excretion ratio is calculated using the following equation:

$$\frac{\text{Total urine lead excreted (mcg)}}{\text{Total amount of Ca EDTA given (mg)}}$$

Weinberger et al (1987) suggested that a test is positive if the lead excretion ratio is equal to or greater than 0.5 based on an analysis of 248 initial mobilization tests performed on an ambulatory basis.

In a study of twelve pediatric patients (blood lead levels of 26 to 60 mcg/dL) given the CaNa2EDTA mobilization test as outpatients, the mean percentage of EDTA excreted in the first four hours was 67%. EDTA was below the level of detection for seven patients in the 6 to 24 hour collection. The authors conclude that a four hour, as opposed to 24 hour, outpatient mobilization test for lead may be indicated (Aronow et al. 1989).

V. OTHER INFORMATION

5.0 CASE REPORTS

Shannon et al (1987) reported the case of a 4-year-old child with a previous history of lead poisoning, who developed elevated lead levels requiring multiple courses of chelation therapy following immobilization with acute paraplegia from transverse myelitis. Blood lead levels as high as 70 micrograms per deciliter were noted, with no exogenous sources of lead identified. Osteoporosis was seen on skeletal x-rays, suggesting that the lead was being released from bone stores.

Bradley et al (1987) reported 6 cases of ingestion of lead oxide-containing ceramic glazes by residents of nursing homes. These glazes contained from 30 to 71 percent lead oxide, and ingested amounts ranged from a "taste" to 240 milliliters. Blood lead levels were obtained in 4 cases,and were elevated in 3 patients (64, 93.6, and 148 micrograms per deciliter). These three patients received chelation therapy. None of the 6 patients became symptomatic.

Ingestion of 15 mL of a ceramic paint glaze containing 30%lead oxide in a 13 month old girl resulted in radio-dense material on abdominal radiographs. Stomach lavage with saline and activated charcoal were given. A serum lead level was 2 mcg/dL 45 minutes post

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ingestion, which peaked at 28 mcg/mL 18 hours post-ingestion. No adverse effects were noted (Sturm, 1988).

ACUTE EXPOSURE: A 32-year-old male drank 8 ounces of a 55% lead naphthenate solution. He became lethargic and ataxic. He was confused and had sensory hallucinations. BLL on admission was 130 mcg%; EP was 20 mcg%. Chelation with EDTA and BAL lowered BLL to 20 mcg% within 8 days (Alequas et al. 1986).

A 23-month-old female died from lead encephalopathy caused by the ingestion of a lead curtain weight approximately 1 month prior to onset of flu-like illness. An x-ray of her abdomen was performed to rule out obstruction as a cause of abdominal pain and vomiting. A radio-opaque object was detected but there was no evidence of obstruction or perforation. The significance of this finding was not appreciated. The child subsequently had a grand mal tonic clonic seizure and was found unresponsive, in respiratory arrest. She continued to deteriorate and died 18 hours after the initial grand mal seizure despite supportive care. Lead poisoning was suspected when the abdominal film was reviewed after death and confirmed by autopsy (Hugelmeyer et al. 1988).

A 43-year-old woman developed inorganic lead poisoning from chewing sheets of metallic lead that enclose European wine bottle necks. She presented with signs/symptoms of abdominal pain and anemia. Metallic densities within the lumen of the large bowel were observed on plain abdominal x-ray films. Her blood lead concentration was 110 micrograms/deciliter, free red cell protoporphyrin concentration was 398 micrograms/deciliter, and 24-hour urine lead content was 738 micrograms. She was chelated with intravenous calcium disodium EDTA over two 5-day treatment periods. Blood and urine lead concentrations were normal at 3 month follow-up (Rovira et al. 1989).

Montalvan et al (1989) reported the case of a 17-year-old Haitian male whose symptoms of a two week febrile illness were finally attributed to severe lead poisoning from long term exposure to lead in the production of lead figurines by his grandfather. He had a lengthy history of marked developmental delays and poor academic performance. His blood lead level upon admittance was 90 mcg/dL. Treatment included BAL/EDTA for 48 hours followed by oral chelation therapy with DMSA and resulted in a marked gain in strength and resolution of fasciculations and hypesthesias.

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METHYL ETHYL KETONE

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of methyl ethyl ketone in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to methyl ethyl ketone.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to methyl ethyl ketone. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of methyl ethyl ketone and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to methyl ethyl ketone.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

The various ketones are absorbed by ingestion, inhalation, and dermal exposure. Exposure to ketone solvents (methyl ethyl ketone, methyl isobutyl ketone, etc) must be distinguished from exposure to the peroxides of these same ketones. Exposure to ketone solvents should be managed as hydrocarbons. Ketone peroxides (such as MEKP-methyl ethyl ketone peroxide used as a plastic catalyst) are extremely caustic and exposure may result in burns of the epidermis and mucous membrane surfaces. The minimal toxic or lethal dose of the various ketones are not well established in the clinical findings.

1.0 HEAD, EYES, EARS, NOSE, and THROAT

EYES: Eye exposure may result in ocular pain and corneal damage. Direct contact of the liquid with eyes may cause corneal damage. Lacrimation and ocular irritation may be noted following exposure to high vapor concentrations (Parmeggiani, 1983).

NOSE: Ketones are generally strong irritants of mucous membranes, especially of the nose. Sneezing may occur.

THROAT: The ketones are generally strong irritants of mucous membranes, especially of the mouth, and can cause sore throat, coughing, and salivation.

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1.1 CARDIOVASCULAR

Tachycardia may be noted.

A 47-year-old inebriated male developed cardiac arrest following an accidental ingestion of 50 to 100 mL of methyl ethyl ketone peroxide in dimethyl phthalate (Karhunen et al. 1990).

1.2 RESPIRATORY

Direct aspiration of liquid ketones into the lungs can result in chemical pneumonia.

Exposure can produce an anesthetic type of respiratory depression, dyspnea, and gasping.

1.3 NEUROLOGIC

Inhalation of high concentrations of ketones produce CNS depressant effects. Effects include headache, dizziness, fainting, tremor, incoordination, lowered body temperature, depressed respirations and heart rate, dyspnea, gasping, coma, and death.

Ingestion of 50 to 100 mL methyl ethyl ketone peroxide in dimethyl phthalate resulted in loss of consciousness approximately 30 minutes later in an inebriated 47-year-old male (Karhunen et al. 1990).

Peripheral neuropathy has been reported in workers exposed to methyl-n-butyl ketone (Mendell et al. 1974) 2,5-hexanedione (Couri & Milks, 1985), and methyl ethyl ketone (Parmeggiani, 1983).

Skin exposure to vapor or liquid may result in paraesthesia of affected areas.

Trimethylnonanone is a possible exception in causing narcosis.

1.4 GASTROINTESTINAL

Inhalation may cause nausea and vomiting (Browning, 1965; Parmeggiani, 1983).

Severe burning of the mouth and vomiting may be noted (Karhunen et al. 1990).

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1.5 HEPATIC

Ketones have been shown to potentiate the hepatotoxic effects of halogenated hydrocarbons (eg, chloroform and carbon tetrachloride) (Plaa & Vezina, 1987).

Co-exposure to methyl ethyl ketone and xylene in man has resulted in inhibition of xylene metabolism (Liira et al. 1988).

A 47-year-old male died from hepatic coma associated with blood coagulation disorders 4 days following an accidental ingestion of 50 to 100 mL methyl ethyl ketone peroxide in dimethyl phthalate (Karhunen et al. 1990).

1.6 GENITOURINARY

No information is available.

1.7 HEMATOLOGIC

No information is available.

1.8 DERMATOLOGIC

Skin exposure to vapor or liquid may result in dermatoses and paraesthesia of affected area.

Contact urticaria has been reported after chronic exposure to methyl ethyl ketone (Varigos & Nurse, 1986).

1.9 OTHER SYSTEMS

Metabolic acidosis has been reported in a 47-year-old woman with chicken-pox who mistakenly ingested butanone (methyl ethyl ketone) for rum. The patient's plasma butanone concentration was 13.2 millimoles/L (95 mg/100 mL), and the patient's plasma lactate concentration at admission was increased to 14.3 millimoles/L (129 mg/100 mL) (Kopelman & Kalfayan, 1983).

Metabolic acidosis (pH 6.86, base excess 28 mmol/L) was reported in a 47-year-old inebriated male following an accidental ingestion of 50 to 100 mL of methyl ethyl ketone peroxide in dimethyl phthalate (Karhunen et al. 1990).

Hypothermia may also be noted.

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II. CARCINOGENICITY/TERATOGENICITY

No information is available.

III. LABORATORY STUDIES

3.0 URINE

The urine can be tested for an increase in conjugated glucuronic acid. In animals injected with acetophenone, the urine contained red cells, hemoglobin and albumin.

IV. TREATMENT BY EXPOSURE ROUTE

4.0 DERMAL EXPOSURE

4.0.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 EYE EXPOSURE

4.1.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.2 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

DILUTION: Immediately dilute with 4 to 8 ounces (120 to 240 milliliters) of milk or water (not to exceed 15 milliliters per kilogram in a child).

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KETONE PEROXIDES: Distinguish between ketone solvent ingestion and ketone peroxides, which are caustic and cause burns.

4.3.2 TREATMENT

Correct acidosis with kilogram intravenous sodium bicarbonate. About 1 to 2 milliequivalents/kilogram is a useful starting dose. Monitor blood gases to guide bicarbonate therapy.

KETONE SOLVENTS: Ingestion of ketone solvents should be managed as in hydrocarbons.

KETONE PEROXIDES: Care must be taken to distinguish between ketone solvent ingestion and ingestion of the peroxides of such ketones as cyclohexanone or methyl ethyl ketone peroxide.

Ketone peroxides are extremely caustic and cause burns and erosions of mouth, esophagus, respiratory tract and gastric mucosa. The following treatment procedures should be followed:

a. Dilution of ingested substance with milk or water in the non-respiratory compromised patient.

b. Patients should be hospitalized for observation of possible esophageal or tracheal burns and may require IV hydration.

c. Steroids remain controversial, but, if elected, must be initiated immediately.

d. Monitor cardiac function closely.

V. OTHER INFORMATION

5.0 CASE REPORTS

Ingestion of a plastic catalyst containing 60% methyl ethyl ketone peroxide and 40% dimethyl phthalate resulted in dyspnea, vomiting, hemorrhagic esophagitis, gastritis, bronchopneumonia, and, 3 days later, myocarditis (Browning, 1965).

A 47-year-old woman accidentally ingested methyl ethyl ketone, mistaking it for a bottle of rum. On presentation, she was comatose and hyperventilating. She had a severe metabolic acidosis (pH 7.19), and her blood glucose was 293 mg/dL. A sodium bicarbonate infusion was started, which resulted in obvious clinical improvement. She regained consciousness within 12 hours, and made a complete and uneventful recovery (Kopelman & Kalfayan, 1983).

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NAPHTHALENE

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of naphthalene in humans. In addition it provides information on the symptomology, by organ system, which may be encountered in a person exposed to naphthalene.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to this chemical. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of this chemical and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to naphthalene.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

1.0 HEAD, EYES, EARS, NOSE, and THROAT

HEAD: Flushing of the face have been described following an acute exposure (Gidron & Leurer, 1956).

EYES: Vapors of naphthalene probably do not produce corneal damage in humans but a sensaton of eye irritation from the vapor is said to occur at concentrations of 15 ppm in air (Robbins, 1951; Grant, 1986). Chorioretinitis has been reported in workers who had cataracts and no other symptoms (van der Hoeve, 1906). Bilateral optic neuritis was described by Koelsch (1926) in a patient who worked with naphthalene for a long time. Lena opacities were observed in 8 of 21 employees who were exposed for 5 years to fumes in a plant producing a dye-intermediate from naphthalene (Ghetti, 1956). However, other industrial surveys revealed no eye abnormalities among workers exposed to naphthalene for years (Axenfeld, 1915; Pike, 1944).

Serious toxic effects on the eye have been well established in poisoned animals but injury of human eyes from systemic naphthalene is scantily documented (Grant, 1986). The first reported case of naphthalene-induced cataracts occurred in 1900 when a pharmacist was given 5 grams of unpurified naphthalene over 13 hours. On awakening 8 to 9 hours later, he was nearly blind; a year later, he had a non-progressive zonular cataract (Lezenius, 1902).

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1.1 CARDIOVASCULAR

Tachycardia and flow murmurs secondary to anemia have been reported following acute naphthalene ingestion (Zuelzer & Apt, 1949).

1.2 RESPIRATORY

No information is available.

1.3 NEUROLOGIC

Syncope, lethargy, restlessness, delirium, ataxia, and irritability, may develop (Abelson & Henderson, 1951; Gidron & Leurer, 1956; Mackell et al. 1951; and Zuelzer & Apt, 1949). Convulsions may occur (Siegal & Wason, 1986). Coma as been reported (Siegal & Wason, 1986). Headache has been described following acute oral and inhalation exposure (Gidron & Leurer, 1956; ACGIH, 1986).

1.4 GASTROINTESTINAL

Nausea, vomiting, and anorexia can occur up to 48 hours following an acute ingestion (Gidron & Leurer, 1956; Zuelzer & Apt, 1949). Nausea has also been reported after inhalation (ACGIH, 1986). Diarrhea may occur up to 48 hours following an acute ingestion (Gidron & Leurer, 1956; Zeulzer & Apt, 1949). Abdominal pain may occur up to 48 hours following an acute ingestion (Gidron & Leurer, 1956; Zeulzer & Apt, 1949). Anorexia has been reported after inhalation (ACGIH, 1986).

1.5 HEPATIC

Although rare, hepatomegaly and jaundice have been reported following acute exposure (Abelson & Henderson, 1951; MacGregor, 1954; Dawson et al. 1958; Zuelzer & Apt, 1949). Hyperbilirubinemia has been described especially in newborns exposed to naphthalene (Cock, 1957; Schafer, 1951; Valaes et al. 1963).

Centrilobular necrosis was seen in a 10 year old Indian boy who sniffed mothballs for 2 months (Siegal & Wason, 1986).

1.6 GENITOURINARY

Dark, benzidine-positive urine containing no red blood cells when hemolytic anemia has occurred. Renal damage is usually caused by tubular damage secondary to hemolysis (Chugh et al. 1977; Schafer, 1951).

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Signs and symptoms of renal dysfunction include urgency, dysuria, and the passage of a brown or black urine with or without albumin and casts. Usually these effects disappear within a few days and they should be distinguished from a hemolytic reaction (Gosselin et al. 1984).

1.7 HEMATOLOGIC

Severe hemolytic anemia has been reported following acute ingestion, inhalation or skin absorption. When present, anemia usually is not evident until 2 to 5 days following initial exposure but has been reported as early as 1 day after ingestion (Newns, 1949; Mackell et al. 1951; Zuelzer & Apt, 1949).

Hemolysis occurred 24 to 72 hours following ingestion of naphthalene in three children reported by Shannon and Buchanan (1982). Hemolytic anemia is most severe in individuals with glucose-6-phosphate dehydrogenase deficiency and can occur following exposure to very small amounts of naphthalene (Dawson et al. 1958; Gross et al. 1958; Valaes et al. 1963; Sherer, 1965).

Significant hemolysis has been reported in newborns having normal G-6-PD levels (Valaes et al. 1963), but documentation of naphthalene in urine or blood was not reported. The classic features of the self-limiting naphthalene-induced hemolysis include anisocytosis, poikilocytosis, reticulocytosis, severe anemia, leukocytosis, and icterus (Anziulewicz et al. 1959). More severe reactions include Heinz body formation (Zuelzer & Apt, 1949; Valaes et al. 1963; Hanssler, 1964; Irle, 1964) and hemoglobinuria (Abelson & Henderson, 1951; Gidron & Leurer, 1956; Valaes et al. 1963).

Aplastic anemia has been reported in one patient exposed to both naphthalene and para-dichlorobenzene (Hardin & Baetjer, 1978).

Methemoglobinemia has been reported (Valaes et al. 1963).

1.8 DERMATOLOGIC

Pallor secondary to hemolytic anemia has been reported (Siegal & Wason, 1986).

Erythema and dermatitis have been described and attributed to hypersensitivity (Key et al. 1977; Gosselin et al. 1984).

Exfoliative contact dermatitis has been reported (Fanberg, 1940).

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1.9 OTHER SYSTEMS

FLUID-ELECTROLYTE

Fatal hyperkalemia has been described with marked intravascular hemolysis due to severe intoxication (Gidron & Leurer, 1956; Am Ind Hyg Assoc, 1967).

TEMPERATURE REGULATION

Fever may occur following acute oral ingestion (Zuelzer & Apt, 1949).

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

Of 15 workers exposed to vapors of naphthalene and coal tar over a period of up to 32 years, 4 smokers contracted laryngeal carcinoma and 2 developed neoplasms of the pylorus and cecum (Wolf, 1976).

2.1 PREGNANCY

No information is available.

2.2 TERATOGENICITY

Hemolytic anemia has been reported in a newborn following maternal ingestion of naphthalene during pregnancy (Zinkham & Childs, 1958).

Naphthalene, when used as an antiseptic, was said to induce cataract in rats (Zhikov & Atanasov, 1985).

IMMUNOLOGIC

A chronic ingestion study done on mice showed no immunotoxicity (Shopp et al. 1984).

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III. LABORATORY STUDIES

Techniques used in forensic medicine for the detection and quantitation of naphthalene and its metabolites include (Snyder, 1987): thin-layer chromatography; high-pressure liquid chromatography; gas chromatography with mass spectrometry; high resolution proton magnetic resonance

3.0 SERUM/BLOOD

Obtain a baseline CBC, glucose-6-phosphate dehydrogenase level, liver and renal function tests and urinalysis (check for hemoglobinuria). Monitor methemoglobin levels in cyanotic patients.

Blood smears in toxic patients may show anisocytosis, poikilocytosis and red cell fragmentation (Siegal & Wason, 1986).

3.1 URINE

Identification of urinary metabolites, especially 1-naphthol and mercapturic acids, may confirm a diagnosis (Summer, 1979; Gosselin et al. 1984).

IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

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4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing. Discard contaminated clothing since washing will not remove the naphthalene. Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Emesis may be indicated in substantial recent ingestion unless the patient is obtunded, comatose or convulsing or is at risk of doing so based on ingestant. Emesis is most effective if initiated within 30 minutes of ingestion.

ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol.
Administer one dose of a saline cathartic or sorbitol, mixed with charcoal or administered separately. There are no specific data to support charcoal efficacy (Siegal & Wason, 1986).

4.3.2 TREATMENT

DIURESIS: Alkaline diuresis should be performed if there is any evidence of hemolysis to prevent renal deposition of red blood cell break down product (Gosselin et al. 1984). Monitor fluid and electrolyte balance carefully.

CORTICOSTEROIDS: Utilization of corticosteroids is suggested to possibly reduce the hemolysis caused by naphthalene (Gosselin et al. 1984).

METHEMOGLOBINEMIA: Determination of the methemoglobin concentration may be necessary. Treat patients who are cyanotic and symptomatic or if methemoglobin concentration is greater than 30 percent in an asymptomatic patient. Administer oxygen to cyanotic patients while preparing for methylene blue therapy. The dose of methylene blue in adults and children

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is 1 to 2 milligrams per kilogram per dose (0.1 to 0.2 milliliters per kilogram per dose) intravenous over a few minutes as needed every 4 hours. Improvement is noted shortly after administration if diagnosis is correct. Additional doses may be required. Doses of greater than 15 milligrams per kilogram may cause hemolysis.

BLOOD SMEARS: The physician may wish to screen blood smears for abnormalities for at least one week after exposure. This may be especially important in patients with G6PD deficiency (Siegal & Wason, 1986).

BLOOD TRANSFUSIONS: Severe anemia due to hemolysis may require small repeated blood transfusions, preferably with red cells from a non-sensitive individual (Gosselin et al. 1984).

4.3.3 ENHANCED ELIMINATION

Hemodialysis has been used for supportive care but is not routinely recommended. Exchange transfusions have been used for supportive care but are not routinely recommended.

V. OTHER INFORMATION

5.0 CASE REPORTS

ACUTE: A 6-day-old female who was dermally exposed to diapers and blankets for 3 days which had been stored in naphthalene developed a heart murmur, cyanosis, and jaundice. She died after 4 days. Autopsy revealed hematopoiesis in the heart, liver, spleen and adrenal glands as well as hemoglobin deposits in the renal tubules (Schafer, 1951).

Hemolysis following inhalation was reported in 21 Greek infants, 9 of whom did not have G6PD deficiency. Eight developed kernicterus and 2 died. Two children developed methemoglobinemia (Valaes et al. 1963).

Acute ingestion of 50 mL of an anointing oil containing a high concentration of naphthalene in a 30-year-old woman resulted in abdominal pain, fever, and diarrhea within 1 to 2 days, followed by acute hemolytic crisis on the fourth day. G6PD levels were normal (Ostlere et al. 1988).

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CHRONIC: A 2-year-old child ingested naphthalene on and off for a year before he presented with fever, lethargy, and jaundice (Chusid & Fried, 1955).

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POLYCHLORINATED BIPHENYLS

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of polychlorinated biphenyls in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to polychlorinated biphenyls.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to polychlorinated biphenyls. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of polychlorinated biphenyls and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to polychlorinated biphenyls.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

PCBs have low acute toxicity, but because they accumulate in the environment and in animal and human tissues, the potential for chronic or delayed toxicity is significant. PCBs are mildly irritating to eyes and skin. Possible symptoms include facial edema, eye discharge, swollen eyelids, conjunctival hyperemia, and visual and hearing disturbances. Increases in diastolic and systolic blood pressure are possible.

Neurobehavioral and psychomotor impairment have been seen after occupational and in utero exposure. PCBs are potent enzymes inducers, more potent than phenobarbital. Chloracne is consistently associated with PCB exposure.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

HEAD: Facial edema may be noted

EYES: PCBs are mildly irritating to eyes and skin at concentrations of 0.1 mg/m(3), and unbearable at 10 mg/m(3) (Letz, 1983).

Other symptoms observed during the Yusho poisoning included subcutaneous facial edema, cheese-like discharge from the eyes, swelling of the eyelids, transient visual disturbances, hyperemia of the conjunctiva, and hearing difficulties (Kuratsune, 1972).

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1.1 CARDIOVASCULAR

One study demonstrated a slight increase in systolic and a statistically significant increase in diastolic pressure for patients exposed to PCBs (Kreis et al. 1981).

1.2 RESPIRATORY

No information is available.

1.3 NEUROLOGIC

Weakness and numbness of the extremities has been reported (Kuratsune et al. 1972; Dally et al. 1987).

Headache occurred in 26 of 115 (22%) exposed persons following exposure to combustion products of PCB (Dally et al. 1987).

Neurobehavioral dysfunction with cognitive impairment and memory loss has been seen in firemen six months after a single exposure (Kilburn et al. 1989), and in 4-year-old children exposed in utero (Jacobson et al. 1990).

Psychomotor impairment has been seen in 6-and 12-month-old infants exposed in utero (Gladen et al. 1988).

1.4 GASTROINTESTINAL

Gastrointestinal upset and diarrhea were seen with the Yusho group (Kuratsune et al. 1972). Diarrhea may occur.

1.5 HEPATIC

Clinical hepatitis was seen with the acute ingestions involved with the Yusho epidemic. Consistent documentation of elevated hepatic enzymes after chronic exposure has been difficult to demonstrate (Letz, 1983). However, Emmett et al (1988) showed a statistically significant positive correlation between adipose PCBs and serum gamma-glutamyl transpeptidase (GGT). The clinical significance of this remains unknown.

Hepatic porphyria has been reported in animals, but not yet in man (Letz, 1983).

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1.6 GENITOURINARY

A small number of humans accidentally exposed to PCBs in a transformer fire demonstrated small elevations in urinary uroporphyrin levels and decreased coproporphyrin levels (Osterloh et al. 1987).

1.7 HEMATOLOGIC

No information is available.

1.8 DERMATOLOGIC

Chloearacne is a specific skin reaction associated with cyclic halogenated compounds (Letz, 1983). It resembles adolescent acne, but has distinct cystic, skin-colored lesions and comedones, both of which may become inflamed and infected.

It occurs at any age and may be found on trunk, arms, legs, face, neck, or back. The condition is very persistent and resistant to treatment. It may occur from either dermal contact or from systemic absorption (Letz, 1983; Dally et al. 1987).

17 of 115 (14%) exposed persons developed pruritus following exposure to combustion products of PCB (Dally et al. 1987).

1.9 OTHER SYSTEMS

Hyperthyroxinemia was reported in victims of the 1968 Japanese "Yusho incident" 16 years post-exposure. Although serum thyroxine and triiodothyronine levels were elevated, TSH levels were normal. No symptoms of hyperthyroidism were noted (Murai et al. 1987).

PCBs are potent enzyme inducers, more potent than phenobarbital. The effect is long term, existing even after discontinuation of the PCBs. Enzymes affected are the cytochrome P-450 and P-448 systems (Letz, 1983). Highly chlorinated PCB mixtures are more potent enzyme inducers (Wasserman et al. 1979).

PCBs have been shown to decrease thiamine levels in the blood and liver of test animals (Deichmann, 1981).

PCBs appear to elevate serum triglycerides. This was first seen with the Yusho oil group and later confirmed in a study by Chase et al (1982).

Exposed subjects were shown to have elevations in serum gamma-glutamyl transpeptidase (GGT) and decreases in 17-hydroxycorticosteroid excretion, which may reflect subtle metabolic effects of PCB exposure (Emmett et al. 1988).

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Edema of the limbs has been reported (Kuratsune et al. 1972).

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

PCBs are designated B2 carcinogens by the EPA and 2A by IARC. These designations indicate that there is sufficient evidence of carcinogenicity in animals but that evidence of carcinogenicity in humans is either lacking or inadequate.

PCBs are clearly carcinogens in animals, producing liver tumors in rats. Although human studies have not been conclusive, PCBs should be considered potential human carcinogens (Letz, 1983). There has been reported a slight increase in melanoma of the skin in men occupationally exposed to PCBs (Deichmann, 1981).

Renal adenocarcinomas have occurred in workers chronically exposed to PCBs. Of note is that in this report, the neoplasms were strikingly similar cytologically. In addition, all three patients were young males, in which this malignancy is rare (Shalat et al. 1989).

2.1 PREGNANCY

Embryotoxicity including fetal death, fetal resorption, cleft palate, dilated renal pelvis, and hypoplasia of the thymus were observed after maternal administration, with an ED50 of 100 mg/kg (d'Argy et al. 1987).

PCBs are excreted in breast milk. The amount contained ranges from 0 to 390 ppb, depending on the geographic location (Wasserman et al. 1979).

2.2 TERATOGENICITY

The Yusho epidemic produced 15 cases of reproductive and fetotoxic human effects. Two stillbirths, 10 abnormal pigmentations, 9 cases of ocular discharge, and 12 of 13 cases of below natural birth weights were reported in this group. Persistent abnormalities were not seen in this group when followed for years (Hammond, 1972).

Mammalian reproductive effects include changes in the estrus cycle, implantation failure, increased abortions, low birth weight offspring, and decreased postnatal survival (Letz, 1983).

Both animal studies and epidemiologic data from the Yusho epidemic would indicate that males are more susceptible to the teratogenic effects than females (Kuratsune et al. 1972; Hurtz, 1973).

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Rogan et al (1988) examined and evaluated 117 children born to mothers who were previously exposed to cooking oil contaminated by thermally degraded polychlorinated biphenyls in Taiwan in 1979 and 108 unexposed controls. Exposed children were lighter and shorter than controls. They also had a higher frequency of abnormalities of gingiva, skin, nails, teeth, and lungs than controls. The exposed children showed delay of developmental milestones, deficits on formal developmental testing, and abnormalities on behavioral assessment.

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

Gas chromatography-mass spectrometry may be used to determine PCBs in a sample (Hammond, 1972), as may gas chromatography-hydrogen flame ionization detection (Parker et al. 1983). Blood background is approximately 20 ppb (Letz, 1983).

3.1 URINE

A small number of patients accidentally exposed to PCBs in a transformer fire were found to have slightly elevated urinary uroporphyrin levels and slightly decreased coproporphyrin levels (Osterloh et al. 1987).

3.2 OTHER

Adipose tissue background is 1 to 2 ppm (Letz, 1983). Background in human milk is approximately 40 to 100 ppb (Letz, 1983). Schilling et al (1988) studied serum PCB levels in pet dogs living near restricted areas with average soil levels of 9,000 ppm as compared to levels in dogs from other areas. They found that dogs living near contaminated sites had higher serum PCB concentrations than controls, and suggested that dogs may serve as sentinels of human exposure to environmental PCBs.

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IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Post contamination washing cannot be assumed to remove PCBs. In animal studies only 59% of applied PCBs were removed from the skin with immediate washing with water and acetone, and only 1% was removed by washing 24 hours after exposure (Wester et al. 1983). Multiple soap and water washing are necessary.

4.1.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.2 EYE EXPOSURE

4.2.2 TREATMENT

Treatment is symptomatic since PCBs are irritating to the eyes. Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

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4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: In almost all cases, ingestions of PCBs will not be recognized until long after emesis would be of any value. In the unlikely event that an individual would ingest pure substance, the value of using emesis to remove a substance with low acute toxicity but potentially high aspiration risks must be considered.

ACTIVATED CHARCOAL/CATHARTIC: The value of administering activated charcoal for an acute, known ingestion is unknown. Activated charcoal is a fairly benign treatment, and therefore, should be tried. PCBs are absorbed orally, therefore, decreasing the amount of time in the gastrointestinal tract should decrease absorption. Cathartics may be of some use for acute ingestions of pure substance. Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol.

4.3.2 TREATMENT

There is little specific treatment. Patients should be monitored for increased hepatic enzymes, chloracne, and the nonspecific eye, gastrointestinal, and neurologic symptoms seen in the Yusho poisonings.

V. OTHER INFORMATION

5.0 CASE REPORTS

YUSHO POISONING: The most dramatic series of cases of PCB poisoning occurred in Western Japan in 1968. A rice oil contaminated with PCBs (48% chlorine content) poisoned more than 1,600 people. The average amount ingested was 2 g, the minimum 500 mg.

More than 25% of the people developed fatigue, headache, increased sweating of the palms, itching, temporary visual disturbances, numbness of the extremities, joint swelling and pain, cough, intermittent abdominal pain, and menstrual changes (Letz, 1983). These symptoms may not have been due purely to PCB toxicity, since the oil (Yusho) was known to contain dibenzofurans and quarterphenyls, which are known to be toxic (Letz, 1983).

Fourteen firemen who were exposed to PCBs and their pyrolysis products during a transformer fire were evaluated six months post-exposure. All 14 were judged to have neurobehavioral, cognitive, and memory impairment. The patients were "detoxified" with diet, exercise, and sauna baths, and were said to be "significantly improved" when retested six weeks later (Kilburn et al. 1989).

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PYRENE

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of pyrene in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to pyrene.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to pyrene. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of pyrene and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to pyrene.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

Pyrene is irritating to exposed skin and eyes. No other acute toxic effects in humans were mentioned in available literature at the time of this review.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

EYES: Conjunctival irritation may be noted (RTECS, 1989).

NOSE: Although not reported, irritation of the mucosa of the nose and throat may be predicted to occur based on this agent's other irritant properties.

THROAT: Although not reported, irritation of the mucosa of the nose and throat may be predicted to occur based on this agent's other irritant properties.

1.1 CARDIOVASCULAR

No information is available.

1.2 RESPIRATORY

Although not reported, irritation of the respiratory tract may be predicted to occur based on this agent's other irritant properties.

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1.3 NEUROLOGIC

Excitation and muscle spasticity were noted in exposed experimental animals (RTECS, 1989). These effects have not been reported in exposed humans.

1.4 GASTROINTESTINAL

Although not reported, irritation or burns of the esophagus or gastrointestinal tract may be predicted to occur based on this agent's other irritant properties.

1.5 HEPATIC

No information is available.

1.6 GENITOURINARY

No information is available.

1.7 HEMATOLOGIC

No information is available.

1.8 DERMATOLOGIC

Dermal irritation occurs following skin exposure (EPA, 1985; RTECS, 1989).

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

Pyrene is an equivocal tumorigen in mice (RTECS, 1989).

IARC Reviews note no evidence for carcinogenicity in animals. Therefore, IARC considers pyrene as a group 3 carcinogen (RTECS, 1989). The EPA does not consider pyrene to be a carcinogen.

2.1 PREGNANCY

At the time of this review, no data were available to assess the potential effects of exposure to this agent during pregnancy or lactation.

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2.2 TERATOGENICITY

Some unspecified teratogenic effects were noted in workers exposed to between 3 and 5 mg/m(3) (Clayton & Clayton, 1982).

2.4 CHROMOSOMAL ABERRATIONS/GENOTOXICITY

Pyrene has caused mutations in bacterial, non-mammalian and mammalian cell, and human cell assays (RTECS, 1989).

EPA GENETOX Program (1986) found that Pyrene was negative or inconclusive in all assay systems (RTECS, 1989).

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

A number of chemicals produce abnormalities of the hematopoietic system, liver, and kidneys. Monitoring complete blood count and liver and kidney function tests is suggested for patients with significant exposure.

If respiratory tract irritation is present, monitor arterial blood gases and chest x-ray.

3.1 URINE

A number of chemicals produce abnormalities of the hematopoietic system, liver, and kidneys. Monitoring urinalysis is suggested for patients with significant exposure.

3.2 RADIOLOGICAL

If respiratory tract irritation is present, monitor chest x-ray.

3.3 OTHER

If respiratory tract irritation is present, it may be useful to monitor pulmonary function tests.

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IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

IRRITATION: Respiratory tract irritation, if severe, can progress to pulmonary edema which may be delayed in onset up to 24 to 72 hours after exposure in some cases.

BRONCHOSPASM: If bronchospasm and wheezing are present, treatment with inhaled sympathomimetic agents may be required.

OBSERVATION: Carefully observe patients with inhalation exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary.

OTHER: Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

4.1.2 TREATMENT

IRRITATION: Treat dermal irritation or burns with standard topical therapy. Patients developing dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.

PERCUTANEOUS ABSORPTION: Pyrene is absorbed through intact skin (EPA, 1985; Sax& Lewis, 1989). Some chemicals can produce systemic poisoning by absorption through intact skin. Carefully observe patients with dermal exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary.

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4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Because of potential esophageal or GI irritant effects or burns, **DO NOT INDUCE EMESIS.**

GASTRIC LAVAGE: The possible benefit of early removal of some ingested material by cautious gastric lavage must be weighed against potential complications of perforation or bleeding if significant esophageal or gastrointestinal tract irritation or burns are present.

Gastric lavage with a large-bore orogastric tube may be indicated if performed soon after ingestion, or in patients who are comatose or at risk of convulsing.

ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol. Administer one dose of a saline cathartic or sorbitol, mixed with charcoal or administered separately.

4.3.2 TREATMENT

DILUTION: Following ingestion and/or prior to gastric evacuation, immediately dilute with 4 to 8 ounces (120 to 240 milliliters) of milk or water (not to exceed 15 milliliters per kilogram in a child).

IRRITATION: Observe patients with ingestion carefully for the possible development of esophageal or gastrointestinal tract irritation or burns. If signs or symptoms of esophageal irritation or burns are present, esophagoscopy may be considered to determine the extent of injury.

OBSERVATION: Carefully observe patients with ingestion exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary.

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4.3.3 ENHANCED ELIMINATION

No studies have addressed the utilization of extracorporeal elimination techniques in poisoning with this agent.

V. OTHER INFORMATION

No further information is available.

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TOLUENE

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of toluene in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to toluene.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to toluene. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of toluene and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to toluene.

I. SYMPTOMOLOGY BY ORGAN SYSTEM

Toxicity occurs most frequently following repeated intentional inhalation of glues, paints or solvents containing toluene. Industrial exposure to vapors in confined areas has resulted in collapse, coma, and death. Muscular weakness syndromes, GI syndromes, or neuropsychiatric syndromes are common in toluene sniffers. Acute ingestion of toluene/xylene solvents probably causes transient CNS depression.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

EYES: Eye exposure results in ocular irritation, pain and possible corneal burns if the liquid is directly splashed in the eye. Lacrimation may also occur.

EARS: Ototoxicity has been noted after the subcutaneous administration of toluene (Pryor & Howd, 1986).

1.1 CARDIOVASCULAR

Death, if it occurs, is from respiratory failure or cardiac arrhythmia due to myocardial sensitization. Myocardial infarction and ventricular fibrillation have been reported in a 16 year old male after sniffing toluene (Cunningham et al. 1987). Congestive heart failure has also been described in a 15 year old male after toluene sniffing (Wiseman & Banim, 1987).

The animals experiments suggest that in most cases of sudden death in toluene-sniffing, the cause of death is severe hypoxia during toluene narcosis, but in a few cases it is fatal arrhythmia due to the direct effect of toluene to the heart muscle (Ikeda et al. 1990).

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1.2 RESPIRATORY

Inhalation may result in bronchial laryngeal irritation, acute bronchitis, bronchospasm, and pulmonary edema. Death can occur from respiratory failure.

1.3 NEUROLOGIC

Inhalation may result in a transient euphoria, headache, giddiness, vertigo and ataxia, especially after glue sniffing. Early excitatory effects are soon followed by depression. At higher doses confusion and coma may occur. Reports have indicated that toluene preferentially accumulates in the brain and fatty tissues following inhalation exposure, producing profound CNS depression. Changes in cortical and subcortical EEGs have been noted to appear in the early stages of exposure to high concentration of toluene vapor (Takeichi et al. 1986). Xylene is similar but has lower affinity for the central nervous system and less acute toxicity than toluene or benzene.

Pathological and magnetic resonance imaging (MRI) abnormalities have been reported in chronic toluene vapor abusers (Rosenberg et al. 1988). Filley et al (1990) noted that the degree of white matter abnormality disclosed by MRI strongly correlated ($p<0.01$) with neuropsychological impairment in 14 chronic toluene abusers.

Progressive memory loss, fatigue, impaired concentration, irritability, persistent headaches and cerebellar dysfunction, diagnosed as mixed encephalopathy with cognitive difficulty and cerebellar ataxia, was reported in one case 8 months after the initial, acute exposure to toluene in spray paint (Carlton et al. 1989).

The prevalence of organic brain syndrome among long-term toluene-exposed workers who are still working were reported. There was a significantly greater prevalence of mild chronic encephalopathy and organic affective syndrome in the toluene-exposed group (Larsen et al. 1988).

The acute behavioral effects of inhaling toluene after a single exposure are reversible, but although reversible, they may also be an early sign of central nervous system impairment leading to irreversible losses in performance with repeated exposures. The number of headaches and eye irritation also increased in a dose response manner. The greatest effect was found for an increasing number of observations of sleep (Escheverria et al. 1989).

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1.4 GASTROINTESTINAL

Ingestion may cause a burning sensation in the mouth and stomach, nausea, salivation and vomiting. Substernal pain, coughing and hoarseness can occur.

1.5 HEPATIC

Animals studies have suggested that toluene abuse may increase the severity of alcoholic fatty liver and may increase the risk of alcoholics to develop serious liver disease (Howell et al. 1986). A 19-year-old developed acute renal failure and hepatic failure that was associated with inhalation of an industrial glue containing toluene 29% (Taverner et al. 1988).

Pericentral fatty liver with mild reactive hepatitis is the most likely diagnosis in workers exposed to toluene, for whom common causes of mild liver test abnormalities have been excluded. An increased ALT/AST ratio may represent a convenient, previously unrecognized indicator of this condition (Guzelian et al. 1988).

1.6 GENITOURINARY

Chronic toluene may cause renal toxicity (Streicher et al. 1981; Taher et al. 1974; Martinez et al. 1989). Distal renal tubular acidosis (RTA) as a complication of long-term abuse of toluene-containing inhalants is now well documented and includes a single case with both distal RTA and proximal tubular dysfunction consistent with Fanconi's syndrome ie, glucosuria, bicarbonaturia, uricosuria, phosphaturia, and aminoaciduria. High-anion gap metabolic acidosis has also been observed and is likely caused by an accumulation of benzoate or hippurate (toluene metabolites). Severe muscle weakness, a result of profound hypokalemia that is sometimes manifested as quadriparesis, frequently dominates the clinical presentation of patients with toluene-induced RTA.

There has been one case of irreversible renal insufficiency reported (Voights & Kaufman, 1983).

Glomerulonephritis was reported in a 16-year-old female with a history of heavy smoking and deliberate glue sniffing. The glue contained n-hexane, toluene, ethyl acetate, and petrol fraction (Bonzel et al. 1987).

A 60-year-old man with long-term exposure to toluene presented with both myelofibrosis and focal segmental glomerulosclerosis (Bosch et al. 1988).

A 19-year-old developed acute renal failure and hepatic failure that was associated with inhalation of an

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Myoglobinemia, rhabdomyolysis, and acute renal failure were associated with intoxication in a 26-year-old solvent sniffer who accidentally ingested 100 mL of a solvent containing 70% toluene. Confounding factors in this case included the fact that he was tied to a pole with both wrists and ankles behind his back and left for 9 hours in the hot sun as punishment (Mizutani et al. 1989).

Inhalation may result in renal tubular acidosis, especially after glue sniffing. Hyperchloremic high anion gap metabolic acidosis associated with profound hypokalemia, hypobicarbonatemia, and hypophosphatemia are common following repeated inhalation of toluene (Streicher et al. 1981; Moss et al. 1980).

1.7 HEMATOLOGIC

Toluene does not usually have hematopoietic toxicity as does benzene, but it may cause eosinophilia. Bosch et al (1988) reported a case of myelofibrosis and focal segmental glomerulosclerosis in a patient who had been working in direct contact with toluene for 40 years. The hematocrit was 24% and the haemoglobin level was 8 g/dL, with anisocytosis and poikilocytosis. The reticulocyte count was 1.8%, and the platelet count was 115,000/mm(3). The WBC count was 2800/mm(3). Serum creatinine was 4 mg/dL, BUN 68 mg/dL. Bone marrow biopsy from the posterior superior iliac spine showed a collagen fibrosis grade III, with accompanying ostersole-rosis, megakaryocytic hyperplasia, and a decrease in erythroid and myeloid elements.

1.8 DERMATOLOGIC

Continued or repeated skin contact causes dermatitis.

1.9 OTHER

Rhabdomyolysis has been reported after chronic inhalation abuse (King, 1985).

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

Toluene is not considered to be carcinogenic by either the EPA or IARC.

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2.1 PREGNANCY

Gravidas who get high by sniffing glue or paint are quite likely to give birth to a premature infant with severe neonatal acidosis. The neonatal acidosis may be due to maternal renal tubular acidosis generally associated with chronic glue and paint sniffing (Pediatric News, Nov 1982; p 26).

No controlled studies of adverse fetal effects from exposure in humans have been published. In a case report involving toluene addiction via inhalation, Toutant (1979) reported a child with multiple physical deformities and symptoms similar to fetal alcohol syndrome born to a mother who also consumed significant amounts of alcohol in addition to inhaling toluene. The author suggested that toluene may have diminished the mother's ability to detoxify alcohol.

Hersh et al (1985) described 3 children with microcephaly, CNS dysfunction, minor craniofacial and limb anomalies, and variable growth deficiencies whose mothers inhaled large quantities of toluene throughout pregnancy.

Of 5 infants born to mothers who had a history of abusing toluene-containing paint during pregnancy, 3 of 5 were growth-retarded and 2 of 5 had dysmorphic features and anomalies (Goodwin, 1988).

Renal-urinary defects in infants were associated with toluene/xylene exposure of mother during pregnancy (McDonald et al. 1987).

Two infants born to mothers who abused pure toluene during pregnancy, without excessive alcohol consumption, were reported to have developmental delay, attentional deficits, growth retardation, and phenotypic abnormalities (microcephaly, narrow bifrontal diameter, short palpebral fissures, deep set eyes, low set ears, flat nasal bridge, micrognathia, and blunt fingertips) (Hersh, 1989).

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2.2 TERATOGENICITY

Hudak & Ungvary (1978) conducted several studies where different animal species were subjected at high concentrations to vapors of toluene during critical periods during pregnancy. In two studies involving rats and mice, no teratogenic effects were observed. In another study, exposed rats exhibited a statistically significantly higher incidence of skeletal malformations than controls.

Nawrot & Staples (1979) noted a statistically significantly increased incidence of cleft palate in mice fed toluene during critical periods of gestation compared to controls.

2.3 CHROMOSOME ABERRATIONS

Chromosome damage has been described in children who chronically inhale volatile agents. A significant increase in the rate of chromosome abnormalities and in the frequency of sister chromatid exchanges was found in sniffers vs controls (Salamanca-Gomez et al. 1989).

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

Obtain a baseline CBC and monitor renal and hepatic function.

3.1 URINE

Excretion of less than 2.1 grams in a 24 hour urine sample indicates exposure to less than 200 ppm.

Workers exposed to low concentrations of toluene had increased urinary D-glucaric acid excretion at the end of the shift compared with controls (Moretto et al. 1990).

Diets high in fruits and vegetables which contain benzoic acid or benzoid acid precursors such as quinic acid (especially in prunes, cranberries and plums) often lead to increased hippuric acid output. Urinary o-cresol levels have been suggested as a more specific indicator of toluene exposure (Ng et al. 199), however o-cresol correlated better with daily environmental concentrations in one study (DeRosa, et al. 1987).

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IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

4.1.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

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4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Probably not indicated following small amounts due to possibility of aspiration and the lack of substantial evidence of systemic toxicity from oral ingestion.

GASTRIC LAVAGE: Gastric lavage may be indicated when: the patient has ingested a large quantity of toluene (greater than 5 milliliters of pure substance), or there is a large amount of benzene contamination, and emesis is contraindicated (obtunded, comatose, convulsing). A cuffed endotracheal tube must be in place. The potential toxicity of the amount ingested must be weighed against the substantial risk of aspiration.

ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol.

4.1.2 TREATMENT

If the patient is already coughing upon arrival at the medical facility, aspiration has probably already occurred. Monitor arterial blood gases in cases of severe aspiration pneumonitis to assure adequate ventilation.

If aspiration is suspected (history of coughing/choking), obtain baseline chest x-ray and vital signs. Admit patient if symptomatic and/or chest roentgenogram is positive for signs of aspiration pneumonia.

If the baseline chest x-ray and vitals are normal, observe patient for 6 hours (obtaining hourly vital signs, when possible) and repeat the roentgenogram in 6 hours or sooner, if the patient becomes symptomatic.

If the serial vital signs indicate tachypnea, hyperpnea, fever or other signs/symptoms of aspiration pneumonia and/or the repeat chest x-ray is positive, admission should be considered. Asymptomatic patients with a negative repeat chest x-ray require no further observation.

Chronic toxicity should include evaluation of the hepatic and renal status.

Hematologic evaluation is indicated if benzene contamination is suspected in cases of chronic inhalatiON.

Cardiac function should be monitored, and avoid epinephrine because of the possibility of myocardial sensitization.

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V. OTHER INFORMATION

5.0 CASE REPORTS

Ingestion of 60 mL of toluene in a 51-year-old male, suffering from a mental disorder, was fatal in approximately 30 minutes. At autopsy toluene concentrations detected by GC and GC/MS were liver 433.5 mcg/g, pancreas 88.2 mcg/g, brain 85.3 mcg/g, heart 62.6 mcg/g, blood 27.6 mcg/g, fat 12.2 mcg/g, and cerebrospinal fluid 11.1 mcg/g (Ameno et al. 1989).

A 38-year old male, exposed to toluene while spray painting a truck in an enclosed unventilated garage, experienced nausea, headaches, dizziness and respiratory problems. He continued to demonstrate chronic solvent toxicity up to 8 months after exposure, including progressive memory loss, fatigue, impaired concentration, irritability, persistent headaches and cerebellar dysfunction. Mixed encephalopathy with cognitive difficulty and cerebellar ataxia were diagnosed through a neurological evaluation. Carlton et al (1989) believe this to be the first report of chronic neurologic sequelae following acute toluene exposure.

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1,1,1-TRICHLOROETHANE

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of 1,1,1-trichloroethane in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to 1,1,1-trichloroethane.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to 1,1,1-trichloroethane. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of 1,1,1-trichloroethane and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to 1,1,1-trichloroethane.

I. SUMMARY OF SYMPTOMOLOGY BY ORGAN SYSTEM

1,1,1-Trichloroethane is one of the least toxic of the chlorinated hydrocarbons used as a solvent. 1,1,1-Trichlorethane is a CNS and respiratory depressant, and a skin and mucous membrane irritant.

Contact with eyes will result in chemosis and hyperemia. Following an acute exposure, hypotension and cardiac arrhythmias due to myocardial sensitization have occurred. Respiratory depression may be noted following acute exposure. Nausea, vomiting, diarrhea and burns of the esophagus have been noted after large ingestion.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

EYES: Contact with the eyes will result in chemosis and hyperemia.

THROAT: Burns of the esophagus have been noted after large ingestions (Gerace, 1981).

1.1 CARDIOVASCULAR

Following acute exposure, hypotension may be noted.

Cardiovascular collapse has been reported following single, large exposures (Stewart, 1971). Cardiac arrhythmias may result from myocardial sensitization to catecholamines. Premature ventricular contractions, depressed S-T segments, and one case of cardiac arrest were seen at anesthetic levels (Donaldson et al. 1976).

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Ventricular arrhythmias and cardiopulmonary arrest were reported in a 15-year-old male who inhaled typewriter correction fluid (Wodka & Jeong, 1991). Serial electrocardiograms and subsequent stress echocardiogram findings were consistent with recent antero-apical subendocardial infarction. The patient was discharged 4 days after admission.

Sudden death has been reported. It is believed to be related to the onset of cardiac arrhythmias from exposure to 1,1,1 trichloroethane (King et al. 1985; Banathy & Chan, 1983).

1.2 RESPIRATORY

Respiratory depression may be noted following acute exposure (Stewart, 1971).

1.3 NEUROLOGIC

1,1,1-Trichloroethane has a rapid anesthetic action.

Report of a post-mortem evaluation revealed a pattern of cerebral hypoxia similar to but not identical to carbon monoxide poisoning - selective to lenticular nuclei and calcarine cortex with loss of Purkinje cells in cerebellum (Gresham & Treip, 1983).

The symptoms of acute overdosage include dizziness, fainting, unconsciousness and coma. Depression of CNS and disturbances in equilibrium have been reported (Stewart, 1971).

In chronic (5 day) studies at 500 ppm lethargy during sedentary periods was a consistent finding (Stewart et al. 1969). Agitation may be noted (King et al. 1985).

1.4 GASTROINTESTINAL

Nausea and vomiting have been noted within 30 minutes following oral ingestion of 1,1,1-trichloroethane (Gerace, 1981).

Diarrhea has been reported 30 to 60 minutes following 1,1,1- trichloroethane oral ingestion (Gerace, 1981).

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1.5 HEPATIC

1,1,1-Trichloroethane may cause transient increase in liver enzymes (Gerace, 1981).

Hodgson et al (1989) reported 4 cases of fatty liver disease in patients whose work entailed substantial exposure to 1,1,1-trichloroethane. No cause and effect relationship could be established.

1.6 GENITOURINARY

1,1,1-Trichloroethane may cause transient renal impairment.

Positive urinary urobilinogen was found 7 hours after exposure to 2 subjects exposed to 0 to 2,650 ppm over a 15 minute period (Stewart et al. 1961).

There was no indication of liver or kidney damage in subjects exposed 7 hours/day for 5 days to 440 to 4560 ppm (Stewart et al. 1969).

1.7 HEMATOLOGIC

No information is available.

1.8 DERMATOLOGIC

Skin vesications may occur with prolonged contact (Jones & Winter, 1983). An

Erythematous reaction may occur from prolonged contact (Stewart & Dodd, 1964).

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

1,1,1-Trichloroethane is not considered to be a carcinogen by the EPA or IARC.

2.1 PREGNANCY

No information is available.

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2.2 TERATOGENICITY

One report showed an increased incidence of skeletal and soft tissue abnormalities in fetal rats when their mothers were exposed to higher than TLV levels of trichloroethane prior to and during gestation; these abnormalities appeared to resemble developmental delays rather than true teratogenicity (York et al. 1982).

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

1,1,1-Trichloroethane can be detected in blood.

3.1 URINE

1,1,1-Trichloroethane can be detected in urine. Its metabolites, trichloroacetic acid and trichloroethanol can also be detected in the urine.

Excessive single exposures to 1,1,1-trichloroethane produce liver stress.The most sensitive test of liver stress has been reported as urinary urobilinogen (Gerace, 1981).

3.2 RADIOLOGICAL

1,1,1-Trichloroethane was shown to be radio-opaque in rats (Dally et al. 1987).

3.3 OTHERS

1,1,1-Trichloroethane can be found in expired air. Breath analysis of air collected in a plastic bag and analysis by IR or GC is becoming more widely used (Stewart et al. 1969). Serial breath analyses may allow for an estimation of the amount absorbed.

VI. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

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4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

4.1.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Emesis may be indicated in substantial recent ingestions unless the patient is obtunded, comatose or convulsing or is at risk of doing so based on ingestant. Emesis is most effective if initiated within 30 minutes of ingestion.

ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol.

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4.3.2 TREATMENT

There is no specific treatment for trichloroethane poisoning. Supportive measures should be instituted promptly to combat the effects of CNS depression, respiration should be assisted if necessary. Although trichloroethane is eliminated via the lung, there is no evidence that administration of an oxygen carbon dioxide mix, to stimulate respiration, has any effect (Stewart, 1971).

Monitor cardiac function closely.

Obtain baseline hepatic and kidney function test, since dysfunction may occur transiently after recovery from CNS depression, and hypotension (Stewart, 1971).

V. OTHER INFORMATION

5.0 CASE REPORTS

Troutman (1987) reported 3 deaths from the intentional inhalation abuse of a typewriter correction fluid containing both 1,1,1-trichloroethane and trichloroethylene. One patient was found collapsed in a field with a bottle of this material in his hand, one was found locked in a bathroom with a bag containing the material over his head, and the third collapsed during an altercation after abusing the material throughout the day. None of the three patients could be resuscitated. Although mustard oil has been added to this product to discourage abuse, it did not deter these three victims.

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TRICHLORETHYLENE

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of trichloroethylene in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to trichloroethylene.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to trichloroethylene. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of trichloroethylene and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to trichloroethylene.

I. SYMPTOMOLOGY BY ORGAN SYSTEM

Trichloroethylene is toxic by ingestion, inhalation or dermal exposure. Vasodilation and malaise ("Degreasers Flush") occur in workers who drink ethanol after exposure to trichloroethylene. Inhalation abuse of typewriter correction fluid has been reported.

Optic neuritis and blindness has been reported following ingestion. Eye exposure causes pain and irritation but permanent injury is unlikely. Cardiac arrhythmias (ventricular fibrillation), hypotension, conduction defects, and myocardial injury
have been noted.

Respiratory depression and cyanosis; pulmonary hemorrhages and edema have been reported following ingestion and inhalation, respectively. CNS depression, light headedness, dizziness, and euphoria, most notably after inhalation, have been noted. Trigeminal nerve impairment has been noted in individuals chronically poisoned by trichloroethylene.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

HEAD: Weakness and numbness of the face, as well as trigeminal neuralgias may be seen (NIOSH, 1973).

EYES: Optic neuritis and blindness have been reported following inhalation as have double vision and blurred vision (Mitchell & Parsons-Smith, 1969; Baxton & Hayward, 1967; NIOSH, 1973; Grant, 1986). The majority of these reports appear to be associated with trichloroethylene and its decomposition products from exposure to heat and alkali.

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Contact with the eye produces irritation but, permanent injury is unlikely. However, first and second degree burns have been attributed to the vapors (NIOSH, 1973; Browning, 1965; Grant, 1986).

EARS: Bilateral, symmetrical, eighth cranial nerve deafness, slight for low frequencies but complete for tones over 1000 cycles/sec has been reported with trichloroethylene (NIOSH, 1973).

THROAT: Difficulty in swallowing and salivation occurred in 3 coal miners accidentally poisoned by trichloroethylene subjected to decomposition in closed circuit oxygen respirators (Grant, 1986).

TASTE: Loss of taste has been noted (Mitchell & Parsons-Smith, 1969).

Dysphagia has been reported in workers exposed to trichloroethylene (Lawrence & Partyka, 1981; Grant, 1986).

1.1 CARDIOVASCULAR

Ventricular fibrillation may occur as a result of cardiac sensitization to endogenous catecholamines and is thought to be the cause of death in fatal exposure (Anon,1974).

Hypotension and first degree heart block have been reported following ingestion of trichloroethylene (Wells,1982).

Bradycardia, occasional premature contractions, and in a few cases, a rapid irregular pulse have been reported during trichloroethylene anesthesia (Barnes & Ives, 1944; Gutch et al. 1965).

Prolongation of PR interval (0.26 seconds) occurred following an ingestion of nearly 5 ounces of trichloroethylene in a 22 year old (Stentiford & Logan, 1956).

1.2 RESPIRATORY

Respiratory depression resulting in cyanosis is common (Derobert, 1952).

Pulmonary hemorrhages and edema have been reported (Koch, 1931; Patel et al. 1973).

Bronchial irritation and shortness of breath from trichloroethylene inhalation exposure have been noted (Anderssen, 1957; McCarthy & Jones, 1983).

1.3 NEUROLOGIC

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Ingestion and inhalation will produce central nervous system depression, coma, visual disturbances, mental confusion, ataxia, dizziness, loss of coordination, and fatigue (McCunney,1988; Stentiford & Logan, 1956; McCarthy & Jones, 1983). Residual encephalopathy was present 16 years after a single acute exposure to trichloroethylene (Feldman et al.1985).

Multiple nerve palsies and peripheral neuropathy have been observed following trichloroethylene intoxication (NIOSH, 1973; Joron et al. 1955).

Inhalation may result in euphoria and addiction (Reynolds, 1988).

Clinical hypesthesia of the trigeminal nerve has been noted in some individuals suffering from chronic poisoning (Mitchell & Parsons-Smith, 1969; Baxton & Hayward, 1967); tests of somatosensory evoked potentials seem to be useful in assessing chronic intoxication caused by trichloroethylene (Barret et al. 1982; Arezzo et al. 1985). There is some evidence that suggests that trichloroethylene decomposition products or impurities may be responsible for cranial nerve injuries (Grant, 1986).

Headache has been reported (Derobert, 1952).

Resting tremor may occur (McCunney, 1988).

Anorexia has been reported (McCunney, 1988).

A 46-year-old worker developed carpal spasm of six weeks duration following cleaning of a vapor degreaser. He wore an air purifying respirator during the cleaning procedure that took about one hour to complete(McCunney, 1988).

Organic dementia has been described in workers exposed to trichloroethylene (Mitchell & Parsons-Smith, 1969; Bardodej & Vyskocil, 1956; Grandjean et al. 1955; Trense, 1965).

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1.4 GASTROINTESTINAL

There are reports associating primary Pneumatosis Cystoides Intestinalis with exposure to trichloroethylene prior to onset of the disease. No cause and effect relationship could be established (Yamaguchi et al. 1985; Sato et al. 1987).

Gastric pain and vomiting were reported following inhalation exposure to trichloroethylene (Derobert, 1952; McCarthy & Jones, 1983).

1.5 HEPATIC

Acute hepatic damage has been reported infrequently and usually only after massive exposure (Joron et al. 1955; James, 1963; AMA, 1985).

A 28-year-old man developed hepatitis that was associated with the use of trichlorethylene in a small, unventilated, basement room. Other causes of hepatitis were ruled out. His 24 hour urinary trichloroacetic acid level, 6 months after the hepatitis, was 9 mg/L (McCunney, 1988).

Hepatitis has also been reported following trichloroethylene anesthesia (Herdman, 1945).

1.6 GENITOURINARY

Acute tubular necrosis and renal failure may follow oral or respiratory exposure (Gutch et al.1965; Reynolds, 1988).

A 42-year-old man developed gynecomastia and impotence following prolonged exposure to trichloroethylene (Barlow & Sullivan, 1982).

1.7 HEMATOLOGIC

No information is available.

1.8 DERMATOLOGIC

Trichloroethylene is mildly irritating to the skin and prolonged contact may give rise to eczema and dermatitis (Anon,1974).

Chronic exposure may produce rough, chapped skin (Clayton & Clayton, 1982).

Exfoliative dermatitis occurred on two separate occasions following inhalational exposure to trichloroethylene in a 29-year old male (Goh & Ng, 1988). A 21-year-old male developed exfoliative dermatitis with mucous membrane involvement, fever, and liver dysfunction

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associated with occupational exposure to trichloroethylene. A positive patch-test reaction was observed to trichloroethylene and trichloroethanol (Nakayama et al. 1988).

Progressive systemic sclerosis was associated with dermal exposure to trichloroethylene of 2.5 hours duration in a 47 year old previously healthy woman (Lockey et al. 1987).

1.9 OTHER

Menstrual irregularities occurred in a 20-year-old woman following an exposure in the workplace to a high concentration of trichloroethylene vapor. Basal body temperature indicated lack of ovulation (Barlow &Sullivan, 1982).

A condition called "Degreaser's Flush" has been reported in workers who drink ethanol after exposure to trichloroethylene. It consists of vasodilation and feeling of malaise. The cutaneous flushing fades with the reduction of blood alcohol level (Waters et al. 1977).

II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

Trichloroethylene is designated a B2 carcinogen by the EPA and but a class 3 carcinogen by IARC. This indicates that the EPA considers trichloroethylene to be a probable human carcinogen while IARC does not consider it to be carcinogenic.

Trichloroethylene is not considered to be carcinogenic in man (AMA, 1985; Kimbrough et al. 1985). Hepatocellular carcinoma was reported in B6C3F1 mice only after chronic administration of high, cytotoxic dose levels (AMA, 1985).

2.1 PREGNANCY

Trichloroethylene has been used as an anesthetic in obstetrics. It may aggravate the normal acidosis and hypoxia of second stage of labor (Phillips & Macdonald, 1971).

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2.3 TERATOGENICITY

Animal studies have not found trichloroethylene to be particularly teratogenic or fetotoxic (Schwetz et al. 1975; Dorfmueller et al. 1979; Land et al. 1981).

III. LABORATORY STUDIES

3.0 SERUM/BLOOD

Blood concentration of trichloroethylene in anesthesia are 5 to 10 mg/dL (Polson & Tattersall, 1969).

3.1 URINE

No information is available.

3.2 RADIOLOGICAL

Trichloroethylene was radiopaque in vitro (Dally et al.1987).

3.3 OTHER

Breath analysis for trichloroethylene analyzed by gas chromatography appeared to be an accurate indicator of the time-weighted vapor exposure to a worker (Stewart et al. 1974).

IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

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4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

4.1.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.3 ORAL EXPOSURE

4.3.1 PREVENTION OF ABSORPTION

EMESIS: Emesis may be indicated in substantial recent ingestion unless the patient is obtunded,comatose or convulsing or is at risk of doing so based on ingestant. Emesis is most effective if initiated within 30 minutes of ingestion.

GASTRIC LAVAGE: Gastric lavage with a large-bore orogastric tube may be indicated if performed soon after ingestion, or inpatients who are comatose or at risk of convulsing.
ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol.

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4.3.2 TREATMENT

Monitor cardiac function closely. Epinephrine or other stimulants should not be used because of the danger of cardiac sensitization, especially by beta-adrenergic agents.

Pulmonary edema, renal failure and liver damage should be treated symptomatically.

Propranolol 40 to 80 milligrams orally in adults MAY be useful to reverse "degreaser's flush."

4.3.3 ENHANCED ELIMINATION

Koppel et al (1988) estimated 70% of the absorbed dose was eliminated in expired air when hyperventilation therapy was used in a 32-year-old male following a suicidal ingestion of 150 grams of trichloroethylene and ethanol. Previous reports indicated 75% of the absorbed dose is metabolized in the liver when hyperventilation treatment was not utilized (Baselt,1982). No liver or renal dysfunction were noted and level of consciousness improved with hyperventilation therapy.

V. OTHER INFORMATION

5.0 CASE REPORTS

Troutman (1988) reported 3 deaths from the intentional inhalation abuse of a typewriter correction fluid containing both 1,1,1-trichloroethane and trichloroethylene. One patient was found collapsed in a field with a bottle of this material in his hand, one was found locked in a bathroom with a bag containing the material over his head, and the third collapsed during an altercation after abusing the material throughout the day. None of the three patients could be resuscitated. Although mustard oil has been added to this product to discourage abuse, it did not deter these three victims.

Bernad et al (1987) reported a cohort of 22 persons exposed to trichloroethylene at low levels (8 to 14 parts per million) in well water for a 5 to 20 year period. Hyperesthesia was present on current perception threshold measurement in 21 of 22 patients. Ten of 10 adults complained of fatigue, somnolence, lack of energy, and numbness and tingling, while 8 of 10 had headache and dizziness, and 4 of 10 had tremor. Three of the 10 had also been evaluated for cardiac arrhythmias. Of the 12 children, 9 had behavioral difficulties (poor learning, aggressive behavior, poor attention span), and one had multiple congenital anomalies.

Ventricular fibrillation and cardiac arrest were reported in a 15-year-old male who inhaled typewriter correction fluid (Wodka & Jeong, 1991). Serial electrocardiograms and

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subsequent stress echocardiogram findings were consistent with recent antero-apical subendocardial infarction. The patient was discharged 4 days after admission.

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XYLENES

INTRODUCTION

This document provides information to the health professional concerning the known toxic effects of xylene in humans. In addition it provides information on the symptomology which may be encountered in a person exposed to xylene.

This document also provides the health professional suggestions concerning medical surveillance and laboratory tests which may be of use in the medical management of the exposed patient. This information is derived from the TOMES(R) Medical Management Database, (c)1987-1992, from Micromedix, Inc. This document is not a comprehensive guide to the medical management of the patients exposed to xylene. Rather, it is designed to give the health care professional up-to-date information on the toxic effects of xylene and provide information on the management of these patients that the health care professional may find useful. The health care professional may wish to consult additional sources of information concerning the management of patients exposed to xylene.

I. SYMPTOMOLOGY BY ORGAN SYSTEM

Toxicity occurs most frequently following repeated intentional inhalation of glues, paints or solvents containing xylene. Industrial exposure to vapors in confined areas has resulted in collapse, coma, and death. Muscular weakness syndromes, GI syndromes, or neuropsychiatric syndromes are common in toluene/xylene sniffers. Acute ingestion of toluene/xylene solvents probably causes transient CNS depression.

1.0 HEAD, EYES, EARS, NOSE AND THROAT

EYES: Eye exposure results in ocular irritation, pain and possible corneal burns if the liquid is directly splashed in the eye. Lacrimation may also occur.

1.1 CARDIOVASCULAR

No specific information concerning xylene is available.

1.2 RESPIRATORY

Inhalation may result in bronchial laryngeal irritation, acute bronchitis, bronchospasm, and pulmonary edema. Death can occur from respiratory failure.

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1.3 NEUROLOGIC

Inhalation may result in a transient euphoria, headache, giddiness, vertigo and ataxia, especially after glue sniffing. Early excitatory effects are soon followed by depression. At higher doses confusion and coma may occur. Reports have indicated that toluene preferentially accumulates in the brain and fatty tissues following inhalation exposure, producing profound CNS depression. Changes in cortical and subcortical EEGs have been noted to appear in the early stages of exposure to high concentration of toluene vapor (Takeichi et al. 1986). Xylene is similar but has lower affinity for the central nervous system and less acute toxicity than toluene or benzene.

1.4 GASTROINTESTINAL

Ingestion may cause a burning sensation in the mouth and stomach, nausea, salivation and vomiting. Substernal pain, coughing and hoarseness can occur.

1.5 HEPATIC

Hepatic toxicity has been reported following ingestion of xylene, inhalation abuse, and workplace exposure.

1.6 GENITOURINARY

Inhalation may result in renal tubular acidosis, especially after glue sniffing. Hyperchloremic high anion gap metabolic acidosis associated with profound hypokalemia, hypobicarbonatemia, and hypophosphatemia are common following repeated inhalation of xylene (Martinez et al. 1989).

1.7 HEMATOLOGIC

No specific information concerning xylene is available.

1.8 DERMATOLOGIC

Continued or repeated skin contact causes dermatitis.

1.9 OTHER

Rhabdomyolysis has been reported after chronic inhalation abuse (King, 1985).

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II. CARCINOGENICITY/TERATOGENICITY

2.0 CARCINOGENICITY

Xylene is not considered to be carcinogenic by either the EPA or IARC.

2.1 PREGNANCY

Gravidas who get high by sniffing glue or paint are quite likely to give birth to a premature infant with severe neonatal acidosis. The neonatal acidosis may be due to maternal renal tubular acidosis generally associated with chronic glue and paint sniffing (Pediatric News, Nov 1982; p 26).

No controlled studies of adverse fetal effects from exposure in humans have been published. In a single case report, a 25 year old mother exposed to xylene via abuse during the third to sixteenth week of pregnancy delivered a stillborn baby with multiple deformities (Kucera, 1968).

Renal-urinary defects in infants were associated with toluene/xylene exposure of mother during pregnancy (McDonald et al. 1987).

Renal-urinary defects in infants were associated with toluene/xylene exposure of mother during pregnancy (McDonald et al. 1987).

2.2 TERATOGENICITY

Kucera (1968) and Mirkova (1983) conducted studies on the effects of xylene inhalation in various animals species during critical periods of gestation and found a variety of congenital abnormalities ranging from external deformities and internal anomalies to increased fetal deaths. One study, performed with rats and similar in design to the above mentioned studies, failed to demonstrate a teratogenic effect (Tatrai, 1980).

2.3 CHROMOSOME ABERRATIONS

Chromosome damage has been described in children who chronically inhale volatile agents. A significant increase in the rate of chromosome abnormalities and in the frequency of sister chromatid exchanges was found in sniffers vs controls (Salamanca-Gomez et al. 1989).

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III. LABORATORY STUDIES

3.0 SERUM/BLOOD

Obtain a baseline CBC and monitor renal and hepatic function. Xylene can be measured directly blood.

3.1 URINE

Xylene can be measured directly in the urine. Excretion of less than 2.1 grams in a 24 hour urine sample indicates exposure to less than 200 ppm.

IV. TREATMENT BY EXPOSURE ROUTE

4.0 INHALATION EXPOSURE

4.0.1 DECONTAMINATION

Move patient to fresh air. Monitor patient for respiratory distress. Emergency airway support and 100 percent humidified supplemental oxygen with assisted ventilation may be needed. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, pneumonitis.

4.0.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

4.1 DERMAL EXPOSURE

4.1.1 DECONTAMINATION

Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

4.1.2 TREATMENT

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

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4.2 EYE EXPOSURE

4.2.1 DECONTAMINATION

Exposed eyes should be irrigated with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

4.3 ORAL EXPOSURE

4.1.1 PREVENTION OF ABSORPTION

EMESIS: Probably not indicated following small amounts due to possibility of aspiration and the lack of substantial evidence of systemic toxicity from oral ingestion.

GASTRIC LAVAGE: Gastric lavage may be indicated when: the patient has ingested a large quantity of xylene (greater than 5 milliliters of pure substance), or there is a large amount of benzene contamination, and emesis is contraindicated (obtunded, comatose, convulsing). A cuffed endotracheal tube must be in place. The potential toxicity of the amount ingested must be weighed against the substantial risk of aspiration.

ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal as slurry. Charcoal slurry may be aqueous, or mixture of charcoal with saline cathartics or sorbitol.

4.1.2 TREATMENT

If the patient is already coughing upon arrival at the medical facility, aspiration has probably already occurred. Monitor arterial blood gases in cases of severe aspiration pneumonitis to assure adequate ventilation.

If aspiration is suspected (history of coughing/choking), obtain baseline chest x-ray and vital signs. Admit patient if symptomatic and/or chest roentgenogram is positive for signs of aspiration pneumonia.

If the baseline chest x-ray and vitals are normal, observe patient for 6 hours (obtaining hourly vital signs, when possible) and repeat the roentgenogram in 6 hours or sooner, if the patient becomes symptomatic.

If the serial vital signs indicate tachypnea, hyperpnea, fever or other signs/symptoms of aspiration pneumonia and/or the repeat chest x-ray is positive, admission should be considered. Asymptomatic patients with a negative repeat chest x-ray require no further observation.

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Chronic toxicity should include evaluation of the hepatic and renal status.

Hematologic evaluation is indicated if benzene contamination is suspected in cases of chronic inhalatiON.

Cardiac function should be monitored, and avoid epinephrine because of the possibility of myocardial sensitization.

V. OTHER INFORMATION

5.0 CASE REPORTS

No further information is available.

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