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Current and Practical Information on the Management of Poisoning and Overdose Emergencies

THE TEN MOST LETHAL POISONS

The Specific Agents Responsible For Poisoning Fatalities

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INTRODUCTION

Nearly two million poisoning exposures are reported to poison information centers each year and there are an estimated two to three million additional unreported exposures.[1] Despite the voluminous number of poisoning exposures, the morbidity and mortality associated with these events is relatively low—only 0.04% of reported exposures are fatalities![1]

Approximately 60% of all reported poisoning exposures occur in children less than six years of age.[1] In contrast to the high pediatric mortality trends which existed prior to the advent of child-resistant closures, aggressive poison prevention intervention and treatment advances, approximately 87% of all fatalities now involve adults (Figure 1).[1] Putting this into perspective, the relative incidence of poisoning fatalities among adults increases to 0.13% (300% increase compared to the general population of poisoning cases!) due to the larger number of fatalities in a considerably smaller volume of reported cases.

There is tremendous disparity between children and adults as to the toxins which produce fatalities. For example, analgesics and antidepressants account for nearly 50% of all poisoning fatalities in adults,[1] but only 7% of pediatric poisoning fatalities.[1] In vast contrast, iron poisoning accounted for 25% of pediatric fatalities in 1991 but only 0.26% of adult fatalities involved the use of iron.[1] In addition to iron, children under six years of age were most commonly

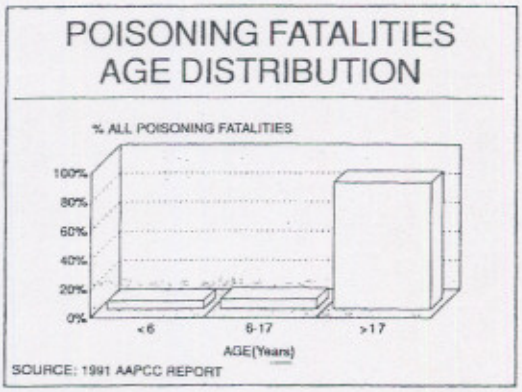

Figure 1

Only 0.04% of reported exposures are fatalities!

the victims of exposures to hydrocarbons (18%), fumes (16%), and household cleaning products (11%).[1] However, since the majority of poisoning fatalities occur in adults, the fatality data are significantly influenced by those agents which produce death in adults. This feature addresses the general categories of toxins and the specific agents which are responsible for the majority of poisoning fatalities (Figure 2) and introduces the concept of the fatality index—the percentage of exposures to a toxin or category of toxins that result in fatalities.

The most lethal category of prescription drugs is the antidepressants.

ANALGESICS

Analgesic overdosage only recently replaced antidepressant overdosage as the leading cause of death.[1] However, among the top ten lethal toxins, analgesics rank eighth in the percentage of all exposures that result in death and antidepressants produce fatalities at a frequency which is five times greater than analgesics!

Although acetaminophen, either alone or in combination, is responsible for the majority of the fatalities

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vs. acetaminophen 0.08%.[1] The gross metabolic imbalance which occurs following salicylate overdosage and the availability of an effective antidote, n-acetylcysteine, in acetaminophen poisoning may account for these marked differences.

Nonsteroidal anti-inflammatory agents have a very low fatality index compared to both acetaminophen and salicylates. Although reported poisoning exposures to nonsteroidal agents exceed salicylate exposures by nearly 100%, they result in 80% fewer fatalities.[1] Narcotic analgesic overdose fatalities accounted for only 21% of the analgesic-related deaths but have a 0.65% fatality index—significantly greater than that associated with salicylates and even cyclic antidepressants![1]

ANTIDEPRESSANTS

The most lethal category of prescription drugs is the antidepressants. Only street drugs and cardiovascular drugs approach this degree of lethality. Antidepressants have a very narrow therapeutic index—a therapeutic dose may be 150-300 mg whereas fatalities in adults may be the consequence of overdoses with only 750-1000 mg.

Within this category, cyclic antidepressants such as amitriptyline and imipramine account for 81% of the fatalities.[1] While there are numerous cyclic antidepressants represented in this category, there are insignificant toxicologic differences among the various agents and overdose treatment strategies do not differ among specific drugs.

Also included in this category are lithium overdoses which accounted for 6% of the antidepressant fatalities.[1] While lithium is effective in the treatment of bipolar disorders such as manic-depressive illness, it does not produce the classic antidepressant overdose toxidrome. Cardiovascular toxicity which is common to cyclic antidepressant overdosage is not as prominent with lithium poisoning where central nervous system toxicity dominates. It is extremely important to recognize the distinction between lithium and cyclic antidepressants since hemodialysis may be beneficial in the management of lithium overdosage, but it is ineffective in enhancing the elimination of other antidepressants.

SEDATIVE/HYPNOTICS/ ANTIPSYCHOTICS

Prior to the introduction of benzodiazepines, sedative/hypnotics like barbiturates, methaqualone (Quaalude®), glutethimide (Doriden®), ethchlorvynol (Placidyl®), chloral hydrate (Noctec®), and others were responsible for hundreds of fatalities each year. Benzodiazepines have an extraordinarily low fatality index and when taken as the sole ingestant they are regarded by many as having a safety margin which essentially prevents an individual from taking a fatal amount. While there are reports which cite benzodiazepine ingestion as the sole cause of death, this is not a common finding. Although benzodiazepine use has been identified in over 46% of the sedative/hypnotic-induced fatalities, it is almost always present in combination as a synergistic toxin with another agent such as ethanol or narcotics to produce the fatal outcome.[1] Aggressive supportive care is adequate therapy for the majority of benzodiazepine overdose patients. Additionally, the appropriate use of flumazenil (Mazicon®), the specific benzodiazepine antagonist, can reverse the central nervous system depression caused by benzodiazepines and may further reduce the mortality rate.

Barbiturates are rarely used as sedative/hypnotics but they still accounted for 13% of the fatalities in this category.[1] Aggressive supportive care is critical in the management of barbiturate overdoses. While there is no specific antidote, multiple dose activated charcoal administration has proven useful in the management of phenobarbital overdoses.

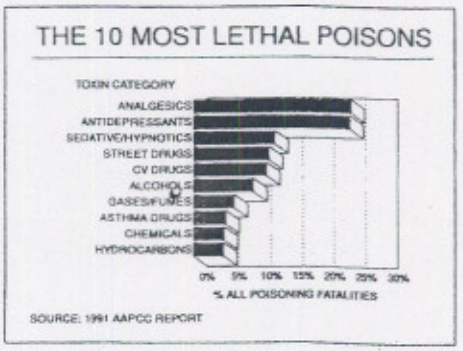

Figure 2

However inappropriate, phenothiazines are also included in this category. Nearly 22% of the fatalities involved exposure to phenothiazines.[1] Similarly to benzodiazepines, most fatalities involved a combination of agents—frequently other drugs used in psychiatric care such as antidepressants. Supportive care with special attention to maintaining hemodynamics is essential in the treatment of these cases.

STIMULANTS AND STREET DRUGS

A cursory review of the national data from poison information centers provides a false impression about the prevalence of drug abuse. For example, reported analgesic exposures outnumbered street drug and stimulant reports by over 160,000 cases![1] Drug abuse victims are not customary consumers of poison information and therefore, poison information center data inadequately represent the true incidence of street drug exposures and resultant fatalities. Unlike most overdose fatalities, the majority in this category are the consequence of abuse for psychoactive effects, not for the purpose of self-inflicted harm.

Not surprisingly, cocaine accounted for 67% of the reported street drug fatalities.[1] The mean age of those who died was only 32 years and is representative of the age group which is abusing cocaine. Fatalities even occur in "recreational" users and are not predictable, accounting for the young age of the victims. No specific antidotal therapy is available for the treatment of cocaine overdosage and therapy is directed at the treatment of problems such as hypertension, seizures, arrhythmias, hyperthermia, and rhabdomyolysis.

Heroin overdosage fatalities contributed to only 17% of the fatalities in this category which is a significant misrepresentation.[1] Heroin overdose victims die as a consequence of the rapid development of respiratory depression following intravenous drug injection and many die before treatment can be initiated in a health care facility. Therefore, the data reported by poison information centers is not representative of the large number of heroin fatalities.

CARDIOVASCULAR DRUGS

Cardiovascular agents rank second only to antidepressants as the most lethal category of prescription drugs. Within the cardiovascular drug category, calcium channel blockers are the most lethal, accounting for 36% of fatalities, followed by cardiac glycosides (24%), and beta blockers (20%).[1]

The calcium channel blockers are among the most commonly prescribed cardiovascular drugs and since 1989 they have been responsible for more fatalities than any other class of drugs within this category.[1,2,3] High mortality is associated with these overdoses because they effectively block calcium channel flux, even after the intravenous administration of large amounts of parenteral calcium. Aggressive supportive care is the cornerstone of patient management. Investigational research is being conducted to determine if 4-aminopyridine is an effective antagonist in calcium channel blocker overdoses.

Cardiac glycoside toxicity from digitalis derivatives has been recognized for centuries. While the fatality index is very high (0.9%),[1] the antidote, digoxin immune Fab, is a highly specific antagonist which can reduce the morbidity and mortality associated with digoxin toxicity. Beta blocker overdosage may respond to glucagon administration. Cardiovascular drug overdoses are often recalcitrant to intervention due to their polypharmacy nature—a patient may take an overdose of several cardiovascular medications which may include digoxin, calcium channel blockers, and beta blockers—a very complicated management dilemma.

ALCOHOLS

Methanol is perceived to be both the most toxic alcohol and associated with the largest number

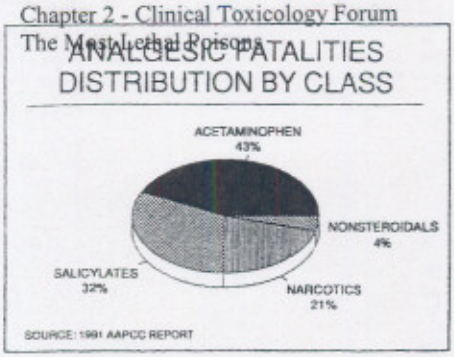

Figure 3

of fatalities. It is the most toxic of the common aliphatic alcohols—the fatality index exceeds 1%, making methanol exposure potentially even more lethal than narcotic, calcium channel blocker and cyclic antidepressant overdosage![1] However, ethanol, due to its ubiquitous nature, was responsible for 82% of the alcohol-related fatalities and the majority involved the ingestion of alcohol-containing beverages.[1]

Although isopropanol exposure is very common since it is the main component of most rubbing alcohols and known to be two times more inebriating than ethanol, it was incriminated in only 4% of the alcohol-induced fatalities.[1] Methanol exposure produced 14% of the alcohol-associated deaths and is associated with significantly greater morbidity than either ethanol or isopropanol, largely due to the toxic nature of its primary metabolites, formaldehyde and formic acid. Supportive care is critical to favorable patient outcomes. However, unlike most toxins, the aliphatic alcohols can be removed via hemodialysis. Furthermore, ethanol used in an antidotal agent can prevent the conversion of methanol to its toxic metabolites and prevent the severe toxicity associated with methanol poisoning.

GASES AND FUMES

Carbon monoxide accounts for 35% of the exposures and 76% of the fatalities in this category.[1] Despite the relatively low position of carbon monoxide in the fatality data derived from poison information centers, the National Center for Health Statistics actually ranks carbon monoxide as the leading cause of death due to poisoning with over 5,000 annual fatalities![4] This disparity is due to the nature of the calls to poison information centers, which are consultations on living patients.

Chlorine gas produced as a consequence of mixing an acidic agent, such as a drain cleaner, with a hypochlorite salt (bleach) resulted in 4% of the fatalities.[1] However, these victims had underlying pathology which was exacerbated by inhalation of chlorine fumes. Asphyxiants such as methane, natural gas, and propane were responsible for 8% of the fatalities.[1] These deaths are sometimes inappropriately attributed to carbon monoxide—a by-product of combustion, and not a component of these gases. The highly toxic gas hydrogen sulfide, which interferes with cellular respiration (like cyanide) was implicated in 10% of the fatalities in this category.[1]

ASTHMA THERAPIES

Theophylline toxicity produced 97% of the fatalities in this category.[1] The fatality index (0.56%) associated with theophylline rivals that of both calcium channel blockers and antidepressants: 50% of the patients who died of theophylline related toxicity did so after an intentional ingestion.[1] However, contrary to many poisoning fatalities (such as cyclic antidepressants), there were an alarming number of individuals who died as a consequence of accidental misuse of theophylline. Patient counseling and therapeutic monitoring of theophylline levels may reduce the number of accidental fatalities due to theophylline.

Beta agonists used to treat asthma, such as terbutaline and albuterol, accounted for 50% more poisoning cases than theophylline but had a fatality index of only 0.01%.[1]

CHEMICALS

All of the toxins which produce fatalities are chemicals. However, a limited number of chemicals which are not unique to a specific application class such as pharmaceuticals and household cleaning products, account for the fatalities within this category—cyanide (32%) and ethylene glycol (30%).[1] These agents have among the highest fatality indexes produc-

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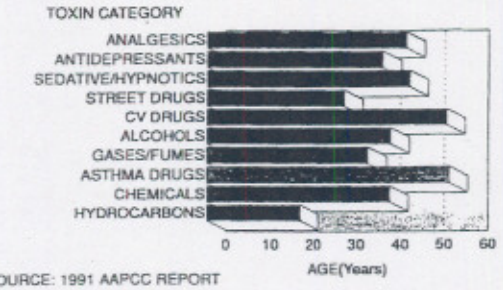
POISONINGS AT A GLANCE

THE 10 MOST LETHAL POISONS MEAN AGE AT DEATH



SOURCE: 1991 AAPCC REPORT

POISON INFORMATION CONSULTATIONS

"This is the poison information center, how may I help you?"

Q: A despondent 15 year old female consumed an unknown amount of ceramic glaze which was being used during occupational therapy on our mental health unit. Does that present any type of a toxic hazard to her?

A: Since many of the ceramic glazes contain high concentrations of lead, it is essential that the name of the product be ascertained to determine whether lead or any other toxic agents are present. If the product was produced in the United States since 1990, it must conform to the American Society for Testing and Materials (ASTM) standard for labeling conformance—ASTM D-4236. According to this standard, if the ceramic glaze contains lead, it must list lead as one of the hazardous components of the glaze. Furthermore, the label must include prominent cautionary signal words such as DANGER, WARNING, or CAUTION and recommend that the product be kept out of the reach of children or only used under adult supervision if lead is present. The products which are lead-free and free of other hazardous components would not include this precautionary labeling. Older ceramic glaze products which do not conform to ASTM D-4236 standards should be presumed to contain lead until proven otherwise, which may necessitate some therapy in a patient who ingests any appreciable amount of the glaze.

If the ceramic glaze contains lead and there is a short temporal separation between the time of the ingestion and the implementation of treatment, gastric evacuation with either syrup of ipecac or gastric lavage may be indicated. Since activated charcoal may not effectively adsorb lead, it should not be used as the sole means of gastric decontamination. Theoretically, the most effective way to evacuate the lead-containing ceramic glaze from the gastrointestinal tract is with whole bowel irrigation. Since the lead in the ceramic glaze is radiopaque, abdominal Xrays may be useful in both the confirmation of an ingestion and as an indicator of the effectiveness or of the gastric decontamination procedure. Emergent and serial blood lead levels are important to assess the extent of lead absorption, whether chelation therapy is necessary and the effectiveness of chelation.

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ing death in 2.5% and 1.8%, respectively, of all exposures. Despite the availability of antidotes to treat these chemically-induced maladies, the morbidity and mortality associated with exposure to cyanide and ethylene glycol remains high. The rapid progression of toxic effects leading to death from cyanide exposure often preclude antidote administration. Since most ethylene glycol ingestions are intentional, there is a significant delay from exposure to the antidotal administration of ethanol, allowing for the development of significant organ damage and systemic toxicity.

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HYDROCARBONS

Contrary to popular opinion, the ingestion and probable aspiration of hydrocarbons by children accounted for only 19% of the fatalities in the hydrocarbon category.[1] Intentional abuse of hydrocarbons such as butane, trichloroethane (commonly found in fabric protectors), and freon produced most of the fatalities. The abuse of these agents for their psychoactive effects is commonplace among teenagers. Not surprisingly, the average age of those dying from hydrocarbon abuse is 16 years.[1] Death produced by the inhalation of volatile hydrocarbons is commonly referred to as "sudden sniffers death syndrome" and is thought to be secondary to ventricular fibrillation induced by hypersensitization of the myocardium to endogenous catecholamines.

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CONTEMPORARY DRUG OF ABUSE SPOTLIGHT

MDMA

"Ecstasy and Toxicity"

According to data from the American Association of Poison Control Centers, amphetamines rank only third behind caffeine and cocaine as a leading cause of intentional street drug exposures.[1] Stimulants such as amphetamines account for nearly 84% of the street drug exposures which are reported to poison information centers. Extensive amphetamine abuse occurred in the 1960's and persisted until 1970 when amphetamines became controlled substances. Following the enactment of this restrictive control and the lack of easy access to amphetamines, amphetamine look-alikes which contained other sympathomimetic drugs such as phenylpropanolamine, ephedrine, and caffeine became very popular. The current scourge of cocaine abuse probably also evolved as a consequence of amphetamine control. Additionally, the synthesis and abuse of amphetamine congeners, also referred to as "designer drugs" also became popular.

Designer drugs were developed as a means of circumventing Drug Enforcement Agency (DEA) regulations. Newly synthesized amphetamine derivative designer drugs were not controlled substances, from a legal perspective, but maintained the psychoactive effects without the risk of incarceration secondary to their possession. However, DEA regulations soon encompassed all amphetamine-related designer drugs and the risk of legal penalties decreased their popularity.

The most common amphetamine-related designer drug is known as MDMA (methylenedioxymethamphetamine). Popular street names for MDMA include ecstasy, XTC, and ADAM. As a recreational street drug the psychoactive effects are a combination of amphetamine-induced stimulation and heightened awareness coupled with a psychedelic perspective that is common to mescaline. The customary adverse effects are secondary to excessive sympathetic discharge resulting in agitation, hypertension, and tachycardia. However, an array of alarming complications secondary to the abuse of MDMA have recently been reported in the United Kingdom.[2]

Severe complications have arisen after the recreational use of MDMA in a limited but growing number of patients. The toxidrome has included patients presenting with hyperthermia, seizure activity, disseminated intravascular coagulation, rhabdomyolysis, and even renal failure.[2] Fatalities have been reported as a consequence of these complications. Additionally, hepatotoxicity has been reported as an outcome of MDMA use. The etiology of the hepatotoxicity has not been elucidated, but it is conceivable that it may be due to a toxic by-product which is produced during its illicit synthesis.

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2. The Lancet. 1992;340:384-387

OVERDOSES IN CHILDREN

TOXINS/MEDICATIONS THAT COULD KILL A TODDLER OF 10-20 kg WITH ONE TABLET, TABLESPOON, OR SINGLE DOSAGE FORM

Tablets/Capsules
Amantadine
Amoxapine
Amphetamines
Beta-adrenergic blockers
Buspirone
Calcium channel blockers
Chlorpromazine
Chloroquine
Clonidine
Clozapine
Colchicine
Cyclobenzaprine
Diflunisal
Disopyramide
Fluoxetine
Haloperidol
Hydroxychloroquine
Hypoglycemic agents
Lithium
Lomotil®
Loxapine
LSD
Mefanamic acid
Meprobamate
Minoxidil
Molindone
Monoamine oxidase inhibitors
Nifedipine SR
Phenothiazine
Prazosin
Procainamide
Quinine/quinidine
Terazosin
Theophylline SR
Trazadone
Tricyclic antidepressants

Ointment/Cream
Camphor
Dibucaine (and other local anesthetics)
Doxepin
Lindane
Methylsalicylate
Theophylline

Patches
Clonidine
Fentanyl
Nicotine
Nitroglycerin

Ophthalmic
Atropine
Imidazoline

Nonmedicinal Solutions
Ammonia (>10%)
Diethylene glycol
Ethylene glycol
Formaldehyde
Hydrofluoric acid
Hydrogen peroxide (>10%)
Isopropyl alcohol
Methyl alcohol
Toluene

Other
Cigarettes (one entire cigarette or three smoked butts)
Boric acid
Bromates (2%)