EMERGENCY MANAGEMENT OF DRUG OVERDOSE

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MEDICAL GRAND ROUNDS

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INTRODUCTION

Drug overdose continues to be a major problem and challenge to those practicing internal medicine and emergency medicine. Over the past 10 to 15 years, new modalities of treating these patients have emerged, ranging from multidose charcoal and hemoperfusion to antibody fragments that complex drugs in the body. Even with these new techniques, however, considerable controversy still exists regarding the proper method of treating the simple as well as the complex overdose patient. Whenever possible, these controversies will be highlighted in this review. It would be impossible to review all aspects of poisoning in one hour so I have chosen to focus on the general treatment of overdose and poisoned patients without much emphasis on specific drugs except where they illustrate points and controversies.

SCOPE OF THE OVERDOSE AND DRUG ABUSE PROBLEM

In 1988, the American Association of Poison Control Centers (AAPCC) recorded 1,368,748 human poisonings reported by 64 poison centers in the United States[1]. Using the population served by these poison centers, it has been estimated that over 4 million poisonings occurred in the entire U.S. that year. While patients 13 years of age and older accounted for only 33% of poisonings, they accounted for 94% of the deaths reported by the AAPCC. Most of these deaths occurred in patients who took a drug overdose, and this group will be the focus of this discussion.

The drug abuse problems of patients using the Parkland Memorial Hospital emergency department consume a considerable amount of health care resources accounting for approximately 5% of visits to the medical part of the emergency department. From July through December, 1989, 757 patients were seen in the emergency department with problems directly related to drug abuse[2]. This number does not include children less than 14 except those involved in trauma episodes related to documented drug abuse. Of these patients, 372 (49%) were white and 301 (40%) were black. Males accounted for 54% of the visits, and 1377 drugs were mentioned in these visits. The top 10 drugs use by these patients are listed in Table 1. Alcohol is reported only when it is used in combination with other drugs.

TABLE 1

LEADING DRUGS OF ABUSE AT PMH

DRUG	% OF PATIENTS
1. Cocaine	46
2. Alcohol in combination	34
3. Marijuana	15
4. Heroin	9
5. Acetaminophen	5
6. Speed	5
7. Diazepam	4
8. Methamphetamine	3
9. Amphetamine	3
10. Ibuprofen	2

GENERAL APPROACH TO THE POISONED PATIENT

Poisoned patients present a complex clinical problem that can be properly treated only if a compulsive approach to the diagnosis and management is followed. A casual approach will frequently lead to misdiagnosis and consequently mismanagement. The general approach described below is designed for adolescent and adult patients who have been poisoned by mouth. When compared to children, this group tends to present later after exposure, have taken multiple substances, have more severe toxicity and tolerate treatment modalities better. I have not included the management of those patients with skin or ocular exposure but the same general principals apply.

STEP 1 STABILIZE THE PATIENT

This is obviously the most important step in the management of drug overdose patients. However, it is frequently overlooked in the initial few minutes of the care of the victim because of the health professional's desire to obtain an accurate history and search for an appropriate antidote. One must remember that over 90% of

overdose victims will survive with good supportive care alone without specific therapy.

Patients who present with unstable vital signs should be treated with accepted general therapy aimed at stabilization. Those with inadequate ventilation should have ventilatory support with endotracheal intubation if necessary. Hypotension should be treated with aggressive crystalloid infusion through a large bore intravenous catheter to maintain adequate right and left ventricular filling pressures. Sympathomimetic drugs should be avoided, if possible, because many drug overdoses such as cocaine have the possibility of sensitizing the myocardium to the arrhythmic effects of catecholamines. However, if blood pressure cannot be maintained with aggressive fluid management, vasopressors may be necessary. If pulmonary insufficiency or edema develop during treatment, measurements of pulmonary capillary wedge pressure should be made to distinguish between cardiogenic and noncardiogenic pulmonary edema, both of which can be caused by various drugs. Severe bradycardia and tachycardia should be treated if blood pressure cannot be maintained with crystalloid infusion and/or vasopressors.

Cardiopulmonary arrest when caused by a drug overdose should be treated by standard Advanced Cardiac Life Support (ACLS) protocols. Prominent exceptions to this rule are those patients who have taken a serious overdose of tricyclic antidepressants. If these patients have serious cardiac effects including cardiac arrest, sodium bicarbonate should be given to counteract the pH influenced toxicity of these drugs. In addition, phenytoin should be one of the drugs of choice in treating serious cardiac arrhythmias in these patients. Both of these recommendations are different than standard ACLS management of cardiac arrest.

The only other management one should attempt at this point is in the case of the comatose patient. These patients should have a quick estimation of blood glucose and intravenous glucose given if hypoglycemia is present. This is especially important if drug overdose is suspected because several drugs can present with hypoglycemia, e.g., propoxyphene. In addition naloxone should be given at a dose of 0.8-2.0 mg to reverse the potential effects of narcotics. Further information on naloxone infusion will be discussed under the section on antidotes. Thiamine also should be given parenterally if the patient is suspected of being an alcoholic.

STEP 2 OBTAIN A GOOD HISTORY, PHYSICAL EXAMINATION AND APPROPRIATE LABORATORY DATA

The history in patients who present with suspected poisoning or drug overdose is very important but frequently is inaccurate and difficult to obtain. Frequently, the patient is unable to give a history, or in the case of serious suicide attempts, the

history obtained may be intentionally inaccurate. One should always think of a drug overdose when presented with a patient with coma, an altered mental status, a known psychiatric history, trauma or a young patient with significant arrhythmias. It is obviously important to obtain all available information from friends, family, observers at the scene and paramedics regarding the situation of the suspected overdose, paraphernalia at the scene, previous drug history, medications taken, recent depression or personal trauma and the reason a drug overdose is suspected. One should always suspect that the information obtained regarding an overdose history is in error for several reasons such as guilt, fear of being found out, poor communication of drugs taken or the fact that many illicit drugs are very impure.

The physical exam of overdose patients should be thorough but directed to areas that may provide clues to the type of drug taken, complications of the overdose and areas that will be affected by treatment. Other than stabilizing vital signs and managing narcotic and hypoglycemic episodes described above, one should do this quick, directed exam before further therapy is undertaken. The examiner should remember that many medical and surgical conditions can mimic overdose and vice versa. The following is a summary of some of the information that can be obtained with respect to poisoning.

The vital signs should be carefully monitored throughout the management of the patient. Significant bradycardia should suggest an overdose of a beta-blocker; calcium channel blocker, especially verapamil; digoxin; hypoglycemic agent or cyanide. Tachycardia is a nonspecific finding and its presence gives little clue to the drug taken because of the vast number of drugs that cause it. Severe hypertension suggests the presence of a sympathomimetic drug such as cocaine, amphetamines and phencyclidine (PCP). Significant hyperthermia can be seen with anticholinergic drugs (tricyclic antidepressants and phenothiazines), amphetamines, cocaine, phencyclidine, salicylate and dinitrophenol.

The skin should be carefully examined looking for evidence of trauma and needle track marks signifying previous drug use. Cyanosis is an important finding suggesting the presence of significant hypoxia or methemoglobinemia. If methemoglobinemia is suspected, a drop of the patient's blood can be placed on a piece of white filter paper. A chocolate brown color suggests the presence of greater than 15 mg/dL of methemoglobin.

Focal cyanosis of an extremity may indicate regional ischemia and suggests accidental injection of a sympathomimetic drug into an artery. A similar appearance may be seen after arterial embolization of foreign material such as talc or cellulose during accidental arterial injection. Reddish coloration of the skin suggests poisoning with carbon monoxide or borates. Bullae, especially on pressure areas, can frequently be found with overdoses of barbiturates, glutethimide, ethchlorvynol and carbon monoxide.

The odor of the breath of the patient is generally more helpful in the evaluation of those who suffer from chemical poisoning than those with drug overdose except in those who take alcohol. A fruity smell suggests ketoacidosis. The smell of burnt almonds or that of silver cleaner is found with cyanide poisoning. Frequently, ingested hydrocarbons can be smelled on the breath.

Examination of the eyes can be very helpful. Pinpoint pupils, especially if associated with coma and respiratory depression, should suggest a narcotic overdose although this sign is not reliable since other conditions such as pontine hemorrhage can present with pinpoint pupils and narcotic overdoses can present with larger pupils, especially if the overdose is severe with respiratory depression and hypoxia. Dilated pupils can be found with many different drugs such as sedatives, alcohol, amphetamines, cocaine and anticholinergic drugs and consequently, should be considered a nonspecific finding. Examination of the ocular fundus may reveal hemorrhages from amphetamines, cocaine or phencyclidine. Poisoning with cyanide may cause the arteries and veins of the fundus to be the same bright red color.

The examination of the head and neck should include careful palpation and inspection for trauma. The frequent association of significant trauma and drug abuse or overdose is frequently forgotten in the rush to treat the drug overdose. Evidence of skull fractures should be carefully sought and any comatose overdose patient should be assumed to have a cervical spine injury until proven otherwise. Patients who snort cocaine or phencyclidine will occasionally have a perforated nasal septum. The neck should be examined for evidence of a "necklace sign" which suggests a narcotic overdose.

The lungs are frequently involved in drug overdoses. Aspiration can occur with almost any drug. Pulmonary edema is a frequent finding in patients with overdoses of intravenous narcotics and ethchlorvynol, methaqualone, tricyclic antidepressants and aspirin.

A careful heart exam should be undertaken looking primarily for evidence of cardiac failure suggesting a myocardial depressant such as a tricyclic antidepressant, valvular incompetence suggesting endocarditis and arrhythmias. Arrhythmias in a young healthy patient suggest the presence of a sympathomimetic drug (cocaine, amphetamines, phencyclidine, or an over the counter drug such as phenylpropanolamine), anticholinergic drug, hydrocarbon inhalation or ingestion, digoxin, quinidine or procainamide, tricyclic antidepressants, theophylline or chloral hydrate.

Examination of the gastrointestinal tract should include careful auscultation to detect mechanical obstruction ("body packer"), adynamic ileus or evidence of trauma.

Examination of the central nervous system is usually undertaken to rule out intracranial pathology because most drug overdoses that affect the nervous system cause a metabolic type of encephalopathy. Seizures can occur with many drugs but the most common ones are tricyclic antidepressants, cocaine, phencyclidine, propoxyphene, phenothiazines, lithium, isoniazid, amphetamines, pentazocine, hydrocarbons, cyanide and theophylline.

Baseline laboratory values should be obtained in moderate to severe overdoses or if a serum drug level makes a difference in treatment such as with acetaminophen. Usual labs obtained are a complete blood count, electrolytes, creatinine, BUN, glucose and urinalysis with serum osmolality, arterial blood gases, clotting studies and liver function tests drawn as indicated.

A general toxicology screen is not appropriate for most simple overdoses if serum levels of the drugs will not affect therapy, i.e., benzodiazepines. Such screens are appropriate in serious overdoses or comatose patients. If a specific drug is suspected, levels of that drug should be ordered instead of a general screen. Usually, one should ask specifically for alcohols, ethylene glycol, aspirin, acetaminophen, anticonvulsant drugs, cardiac drugs, carbon monoxide, lithium, and theophylline.

An electrocardiogram should be obtained on all patients with unstable vital signs, coma or an ingestion of a cardiotoxic drug.

STEP 3 REMOVE UNABSORBED DRUG

After initial evaluation, the clinician must next try to remove any unabsorbed drug from the patient. As will be discussed, this part of the treatment involves many controversies. The lack of good, definitive clinical trials to settle these controversies illustrates the difficulty in standardizing treatment for poisoned patients.

Patients may be exposed to toxic agents by ingestion, exposure to the skin or eyes, inhalation, envenomation or by injection into the vasculature or subcutaneous tissue. Agents that are injected intravenously or inhaled are already absorbed so recovery during this phase of treatment is not possible. In general, agents exposed to the eyes, especially acids and alkali, should be removed by irrigation with saline for at least 30 minutes. Patients who are exposed by skin contamination (most commonly pesticides, herbicides and hydrocarbons) should have these agents removed from the skin by washing extensively with soap and water to prevent further absorption and prevent exposure of the medical team to the poison.

The most common route of exposure to drugs and potentially toxic agents is by far through the gastrointestinal tract. Many methods of ridding the stomach and intestines of unabsorbed drug have been tried but the accepted methods used today can be found in Table 2.

TABLE 2

METHODS OF GASTROINTESTINAL DECONTAMINATION

Dilution
Gastric emptying
Activated charcoal
Cathartics
Neutralization

Dilution

Many poison centers recommend dilution of the toxic agent in the stomach with water or milk if immediate decontamination by other means cannot be accomplished. This procedure is probably acceptable in the home; but since it only dilutes the poison thereby slowing absorption somewhat, it is not recommended for most poisoned patients being treated in a health care facility where more definitive means of decontamination should be available. It is possible that the addition of large amounts of liquid volume increases gastric emptying and in some cases, may actually enhance absorption.

Gastric Emptying

Gastric emptying is usually accomplished either by making the patient vomit the unabsorbed material or by gastric lavage. Several methods of inducing vomiting have been used but most have been abandoned except the use of syrup of ipecac. Apomorphine can effectively induce vomiting in most patients, but it should not be used because it can cause central nervous system depression and it has a long half-life of several hours making prolonged vomiting and discomfort a problem. If one is faced with a patient who has been given apomorphine and has one of these complications, the effects of the drug can be reversed with naloxone. Mechanical methods for inducing vomiting, i.e., gagging, can be effective but should not be used unless other methods are not readily available.

Many patients present after a drug overdose with spontaneous vomiting, especially with drugs such as iron, salicylate, acetaminophen and theophylline. This vomiting has been found to be ineffective in removing adequate drug from the stomach, probably because of insufficient liquid volume of the vomitus.

Syrup of ipecac is a nonprescription drug that contains alkaloids from the dried roots of the Central and South American plants Cephaelis ipecacuanha or Cephaelis acuminata. Its active alkaloids are emetine and cephaeline. It has been used for many years as a method of inducing vomiting because it is effective in reducing absorption of many drugs by 28-50% [3]. It has been found with some drug ingestions to be as effective as activated charcoal as illustrated in figures 1 and 2 [4].

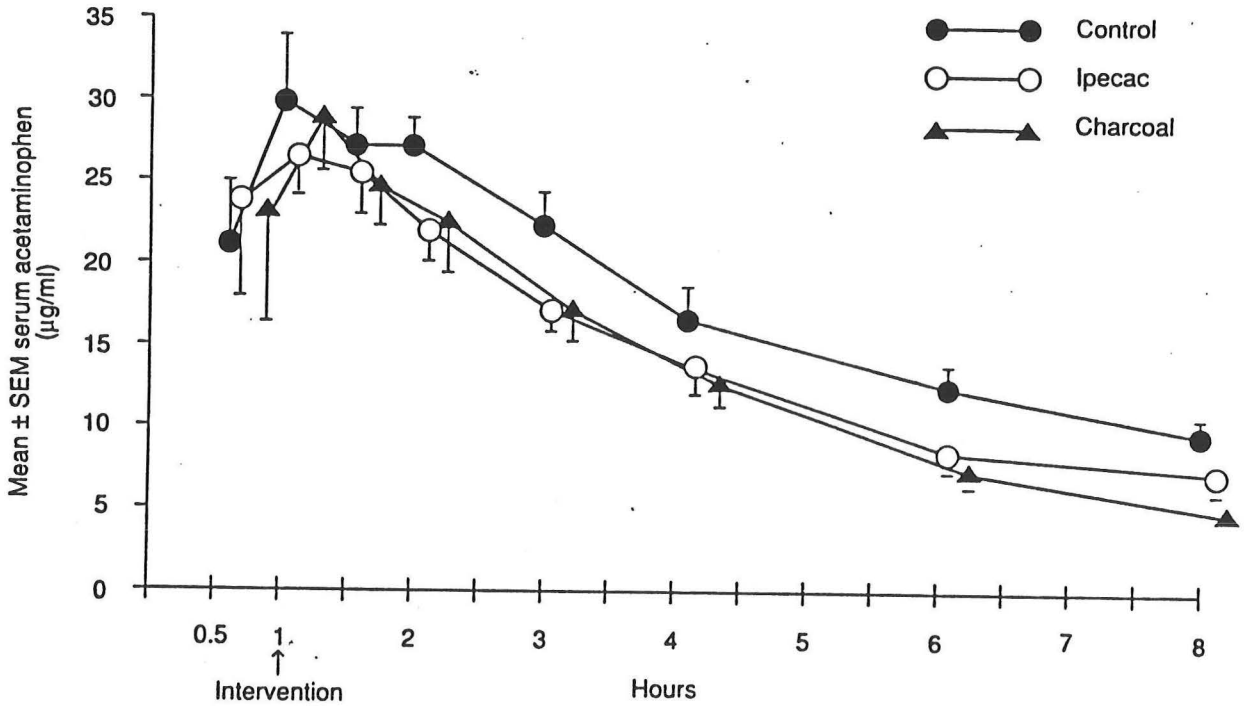

Figure 1. Graph of serum acetaminophen levels versus time after healthy subjects ingested 3 gm acetaminophen followed by no intervention, 30 mL syrup of ipecac, or 50 g activated charcoal-sorbitol at one hour [4].

	Corrected Mean Area Under the Curve
Control	119.41
Ipecac	94.32*
Activated charcoal—sorbitol	88.92*†

*Significantly different vs control ($P < .05$).
†No significant difference vs ipecac.

Figure 2. Corrected mean under the curve for data in figure 1.

Ipecac has little or no toxicity when used in adults at the recommended doses although toxicity has been reported in small children, primarily when large doses have been given intentionally [5,6]. Fluid extract of ipecac is a much more concentrated form of emetine and should not be used because proper dosing is very difficult and serious toxicity has resulted from its use.

Ipecac causes vomiting by stimulating the central nervous system chemoreceptor zone and a direct effect of emetine on the gastric mucosa. It is effective in producing vomiting in 85-90% of persons within 15 minutes of ingestion and its effects last 30-60 minutes.

Traditionally, ipecac has been thought to be more effective in removing stomach contents if given with one or two glasses of warm water. However, recent studies have indicated that fluid in the stomach may not increase the episodes of emesis[7,8,9] and may even increase the absorption of ingested material[10]. In children, at least, fluid volume does not seem to hasten the action of ipecac[11] as illustrated in Figure 3, with age being a more important factor with older children being more responsive than younger ones (Figure 4).

	Volume (oz)					
	0-2 (n = 27)	>2-4 (n = 33)	>4-6 (n = 26)	>6-8 (n = 21)	>8 (n = 17)	P*
Age (yr)	2.1 ± 0.1	2.2 ± 0.1	2.3 ± 0.2	2.6 ± 0.2	3.1 ± 0.2	≤0.05
Time to emesis (min)	15.5 ± 1.3	19.9 ± 1.7	18.7 ± 1.8	20.1 ± 1.9	19.2 ± 2.4	NS
Episodes of emesis	2.4 ± 0.2	2.8 ± 0.36	2.2 ± 0.2	2.3 ± 0.2	3.1 ± 0.4	NS

Values represent mean ± SEM.
*Significance (P ≤0.05) established using one-way analysis of variance; NS, not significant.

Figure 3. Effect of volume of fluid administered on ipecac-induced emesis[11].

	Age (yr)					
	0-1 (n = 7)	>1-2 (n = 61)	>2-3 (n = 36)	>3-4 (n = 17)	>4-5 (n = 3)	P*
Time to emesis (min)	19.4 ± 4.2	18.1 ± 2.2	19.1 ± 1.7	20.1 ± 2.7	13.3 ± 1.4	NS
Episodes of emesis	3.7 ± 0.8	2.5 ± 0.2	2.3 ± 0.2	2.9 ± 0.4	3.3 ± 1.1	≤0.05

Values represent mean ± SEM.
*Significance (P ≤0.05) established using one-way analysis of variance; NS, not significant.

Figure 4. Effect of age on ipecac induced emesis[11].

Although ipecac is relatively nontoxic, contraindications to the use of vomiting as a means of stomach decontamination do exist. These contraindications are summarized in Table 3.

TABLE 3

CONTRAINDICATIONS TO THE USE OF IPECAC

1. Coma or significantly altered mental status
2. No gag reflex
3. Seizures
4. Ingestion of sharp objects
5. Caustic ingestion (strong acids and alkali)
6. Petroleum distillate poisoning
7. Ingestion of rapidly absorbed, toxic drug

Obviously, patients with seriously altered mental status and/or poor gag reflex should not be made to vomit because of the risk of pulmonary aspiration. The same is true for patients who are seizing.

Patients who have ingested sharp objects should not vomit because the risk of retching with the object in the stomach can cause more serious injury. Fortunately, this is an unusual occurrence and most commonly occurs when someone bites off the end of a thermometer and swallows it.

Patients who have ingested caustic substances also should not be made to vomit. These are usually strongly alkaline substances that cause gastrointestinal burns and necrosis, especially in the esophagus and oropharynx. Repeated exposure of the esophagus to the substance during vomiting frequently causes worsening of the injury, which may lead to full thickness necrosis and rupture. If these patients do not have esophageal perforation at the time of presentation as determined by physical exam and x-ray, the caustic material should be diluted with water by mouth. Gastric lavage should not be attempted due to the risk of perforation during passage of the gastric tube. Careful upper endoscopy then should be performed to determine the extent and of necrosis and burn. Minor burns can be treated conservatively, but more serious injury frequently requires local mechanical and surgical measures to prevent esophageal stricture formation and perforation.

The management of petroleum distillate poisoning has been the subject of considerable controversy for many years. The controversy surrounds the advisability of gastric decontamination of these chemicals with low surface tension that are likely

to be aspirated. Aspiration of these substances frequently leads to a severe chemical pneumonitis with adult respiratory distress syndrome and respiratory failure. On the other hand, some hydrocarbons can be absorbed through the gastrointestinal tract and cause hepatic and cerebral injury if not removed. Consequently, authors have argued for decades if and how the hydrocarbon should be removed from the stomach. I think a reasonable compromise for the management of adult patients is as follows:

1) If the patient ingests less than 1 mL/kg of pure hydrocarbon, do not induce vomiting or undertake gastric lavage. The patient should be observed for several hours to monitor for spontaneous vomiting and aspiration. Most of these substances are good cathartics and will quickly pass through the gastrointestinal tract.

2) If the patient has ingested more than 1 mL/kg of the hydrocarbon, gastrointestinal decontamination should be considered[12,13] although controversy does exist[14,15]. If the patient is completely awake, this can be accomplished with ipecac since most feel that the risk of aspiration in an awake patient is less with the coordinated effort of vomiting than with unprotected gastric lavage. If the patient's mental status is depressed to any extent, endotracheal intubation should be accomplished by the most experienced person available and gastric lavage performed.

3) If the patient ingests any amount of hydrocarbon that contains other dangerous toxins such as organophosphates, the stomach should be cleaned using the guidelines outlined in number 2.

4) If the patient ingests a hydrocarbon with a very low surface tension, such as the mineral seal oil found in the red Old English furniture polish, gastrointestinal decontamination by vomiting or lavage should not be attempted no matter how much is ingested.

Patients who ingest hydrocarbons should be observed for several hours regardless of the type of treatment to monitor for the development of pulmonary complications. Any patient with coughing, dyspnea or abnormal pulmonary findings should be monitored by chest x-ray, arterial blood gases and serial pulmonary examinations.

Finally, ipecac should not be used if the patient has ingested a significant amount of a rapidly absorbed, toxic substance. The classic examples of this are cyanide and strychnine. However, more commonly one is presented with a patient who has taken a significant amount of isopropyl alcohol or a tricyclic antidepressant. These substances are rapidly absorbed and can cause an alert patient to become comatose in 10 or 15 minutes, before ipecac has a chance to work. This may result in a near comatose patient vomiting with subsequent aspiration. For these substances, gastric lavage should be used.

Relative contraindications to the use of ipecac can be found in table 4 (adapted from reference 16).

TABLE 4

RELATIVE CONTRAINDICATIONS TO THE USE OF IPECAC

1. Very young (less than 6 months of age)
2. Very old or debilitated
3. Late stages of pregnancy
4. Severe cardiac or pulmonary disease
5. Uncontrolled hypertension

The efficacy of ipecac compared to gastric lavage as the best method of gastric decontamination has been debated for years. The classic studies comparing the two showed vomiting to be superior[17,18,19]. However, many of these studies compared vomiting to nasogastric lavage using a relative small bore tube[20]. Today lavage is accomplished with large bore orogastric tubes[21] such as an Ewald and large volumes of lavage solution. Using these caliber lavage tubes, the two methods are probably similar in efficacy with lavage perhaps being superior if instituted very early[22] and emesis perhaps better if therapy is delayed for more than an hour after the ingestion[23]. A prospective, nonrandomized study comparing vomiting induced by ipecac and gastric lavage using a relatively large bore tube was published in 1986 from San Francisco General Hospital using thiamine introduced into the stomach as a marker[22]. Their published results can be found in figures 5 and 6.

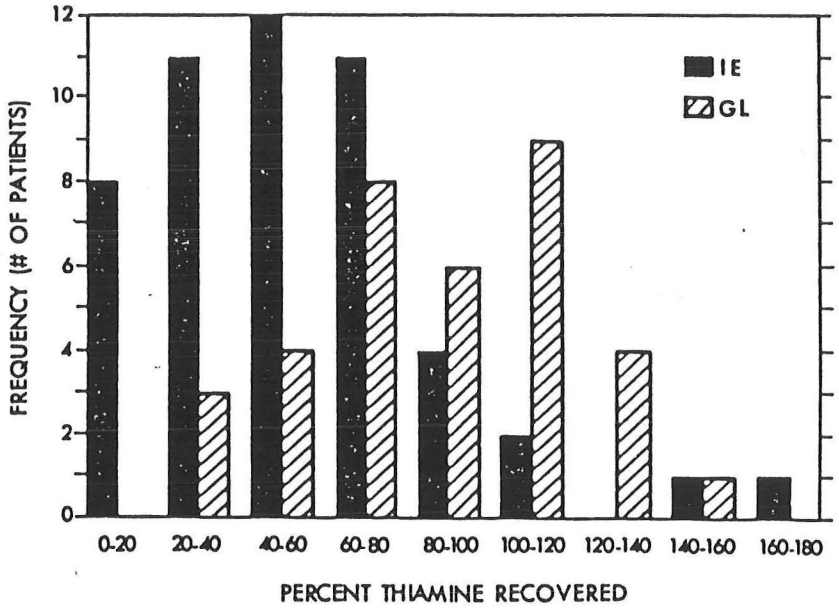

Figure 5. Recovery of thiamine following gastric lavage or ipecac-induced emesis.

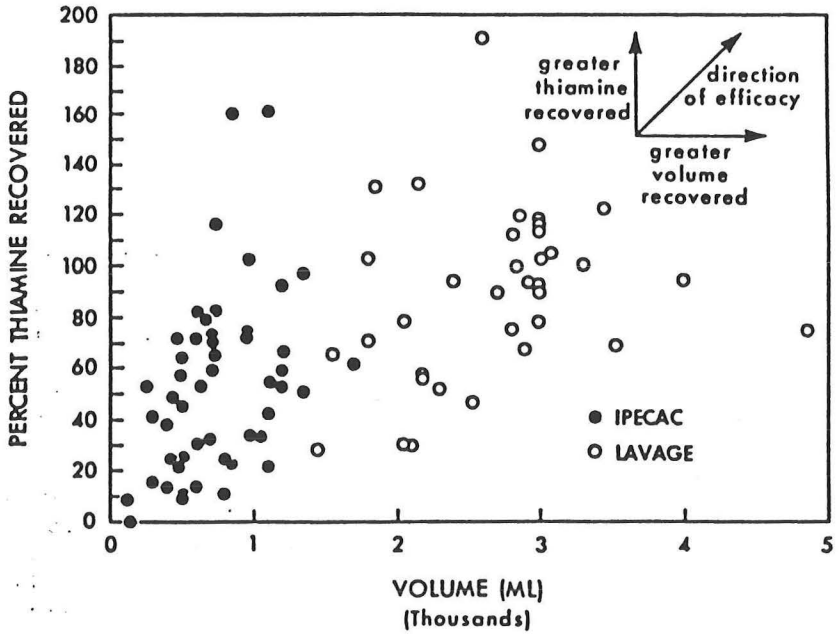

Figure 6. Recovery of thiamine as related to volume of recovery of gastric contents.

Gastric lavage seemed to be far superior to vomiting with both methods of analysis. However, too many patients fell outside an acceptable range of error to accept this study as definitive. Obviously a more carefully controlled, randomized study using similar patient groups needs to be done. In any event, it appears that gastric lavage and vomiting have at least similar efficacy with perhaps lavage having some advantage very early after ingestion[24]. The fact that many patients present to the emergency department an hour or more after ingestion[25] is an important consideration.

Fortunately, this controversy is rarely of clinical significance. Most patients are either wide awake and will refuse gastric lavage or have depressed mental status making ipecac a poor choice. Unfortunately, neither is very effective in removing more than 50% of drugs present in the stomach, except if performed within the first hour of ingestion.

The proper method of gastric lavage is to have the patient on the left side while the lavage tube is pushed into the stomach. The proper length of insertion should be measured to prevent kinking of the tube. 500 mL of lavage fluid should be poured into the tube via a funnel and immediately drained by gravity. One should never use a syringe to aspirate lavage fluid from the stomach because the tubes used do not have adequate ventilation capabilities.

The protection of the patient's airway during gastric lavage is at times difficult. In general, awake patients can tolerate gastric lavage with a large tube without tracheal intubation and have a low rate of aspiration. Comatose patients should have endotracheal intubation before lavage. Patients who are lethargic or stuporous present more of a challenge. Frequently they are too alert for endotracheal intubation without sedation. I personally prefer to have the airway protected in these patients and suggest nasotracheal intubation which usually can be accomplished easily in these patients without further sedation.

ACTIVATED CHARCOAL

Activated charcoal has become the primary means of treating most overdoses in many large emergency departments across the country. There is no question that it decreases the absorption of many drugs that bind to it and many authorities even question whether ipecac should be given before charcoal[26]. Albertson, et al.[27], studied the effect of activated charcoal alone compared with ipecac and activated charcoal on 200 adult patients treated in the emergency department at the University of California, Davis Medical Center. They found that patients treated with activated charcoal alone spent less time in the emergency department if discharged and had a lower treatment complication rate due to a decreased

incidence of pulmonary aspiration than the ipecac group. The clinical parameters studied can be found in figure 7. There was no significant difference in the number of patients requiring admission to the hospital or intensive care unit, or the time spent in each place.

Treatment	No.	Mean Time In ED (hr)	No. Hospitalized (%)	No. Days Hospitalized	No. Admitted to ICU (%)	No. ICU Days (Mean)	No. Complications
Ipecac and activated charcoal	93	6.8 ± 0.3*	13 (14.0)	2.4 ± 0.6	6 (6.5)	1.8 ± 0.4	5 (5.4)*
Activated charcoal only	107	6.0 ± 0.2	12 (11.2)	1.7 ± 0.5	5 (4.7)	1.0 ± 0.0	1 (0.9)

*$P \leq .05$ compared with activated charcoal only.

Mean ± SEM.

Figure 7. Effect of two decontamination procedures on acute toxic ingestions.

The efficacy of activated charcoal when compared to gastric lavage and ipecac has also been studied by Tenebein, et al., using normal subjects ingesting ampicillin as a marker[28]. Figure 8 reports their findings suggesting that activated charcoal alone is superior to gastric lavage in preventing the absorption of ampicillin. Note that the difference between charcoal and ipecac was not significant (figure 9).

Treatment Group	AUC (μg/hr/mL) Mean ± SE	% Not Absorbed
Control	50.2 ± 10.7	0
Gastric lavage	34.2 ± 4.3	32
Ipecac-induced emesis	30.9 ± 7.3	38
Charcoal/cathartic	21.8 ± 2.4	57

Figure 8. Efficacy of gastrointestinal decontamination procedures one hour after an oral dose of 5.0 gm ampicillin.

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Charcoal/cathartic	21.8 ± 2.4	57

Groups	*P*
Ipecac vs control	< .01
Charcoal vs control	< .01
Gastric lavage vs control	NS
Charcoal vs gastric lavage	< .05
Charcoal vs ipecac	NS
Gastric lavage vs ipecac	NS

Figure 9. Comparison between treatment groups.

Certainly the controversies of ipecac versus gastric lavage versus activated charcoal will continue. For now, the clinician should individualize treatment for each new situation.

Activated charcoal is given as a suspension either orally or via a gastric tube at a dose of 50-100 grams. It is not palatable but can be suspended in sorbitol or other liquids that make it acceptable.

Charcoal has few other side effects and these are related mostly to local gastrointestinal effects and accidental pulmonary aspiration. It has caused intestinal obstruction[29] primarily when given in multiple doses to patients who have taken drugs like tricyclic antidepressants and other anticholinergic drugs that decrease intestinal motility. Ray, et al.[30], have reported such a case in a 21 year old man who presented with a serious overdose of amitriptyline. His treatment included multiple doses of activated charcoal. He developed a small bowel obstruction on day 5 of his treatment which was confirmed by laparotomy to be a black bezoar due to inspissated charcoal. Although this is a rare complication of treatment, it does illustrate the need for careful serial physical examinations of the patient while treating overdose patients. Aspiration of charcoal has been noted to cause large and small airway obstruction, adult respiratory distress syndrome and hypoxia quickly after aspiration and bronchiolitis obliterans several days later[31,32]. Obviously the injury caused by the aspiration of gastric acid is a complicating factor.

Charcoal does absorb N-acetylcysteine that is used in the treatment of toxic acetaminophen ingestion. If it has been given to a patient who needs this drug,

adequate serum levels can be obtained if the dose is increased by about 40%[36]. The effect of charcoal on plasma levels of acetylcysteine can be seen in figure 10.

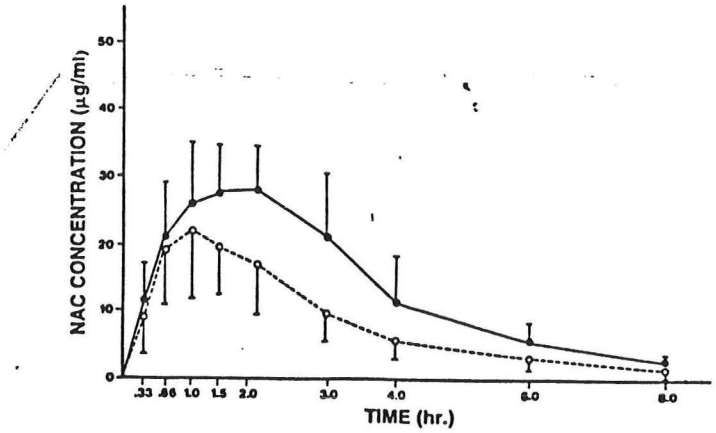

Figure 10. Plasma levels of N-acetylcysteine (NAC) following 140 mg/kg oral doses alone and after activated charcoal, plotted as a function of time. Solid circles indicate NAC treatment, and open circles, NAC plus charcoal.

A common problem is encountered when a drug that is absorbed by activated charcoal also causes vomiting such as theophylline. Protracted vomiting due to the drug's toxicity can significantly impair the clinician's ability to decrease theophylline levels with doses of charcoal, especially in the patients with very high serum levels that need it the most[33]. This has been nicely demonstrated by Amitai and Lovejoy[34] who found that patients with very high blood levels of theophylline vomited more and for a longer time than those with lower levels. Protracted vomiting in these patients sometimes responds to parenteral metoclopramide or continuous nasogastric infusion of activated charcoal. The latter was tried in two adolescents with serum theophylline levels of greater than 100 mg/L[35]. In these cases activated charcoal was diluted in normal saline and infused at a rate of 0.25-0.5 gm/kg/hr with a maximum of 50 gm/hr. Both patients had a good response with falling levels as illustrated in figure 11.

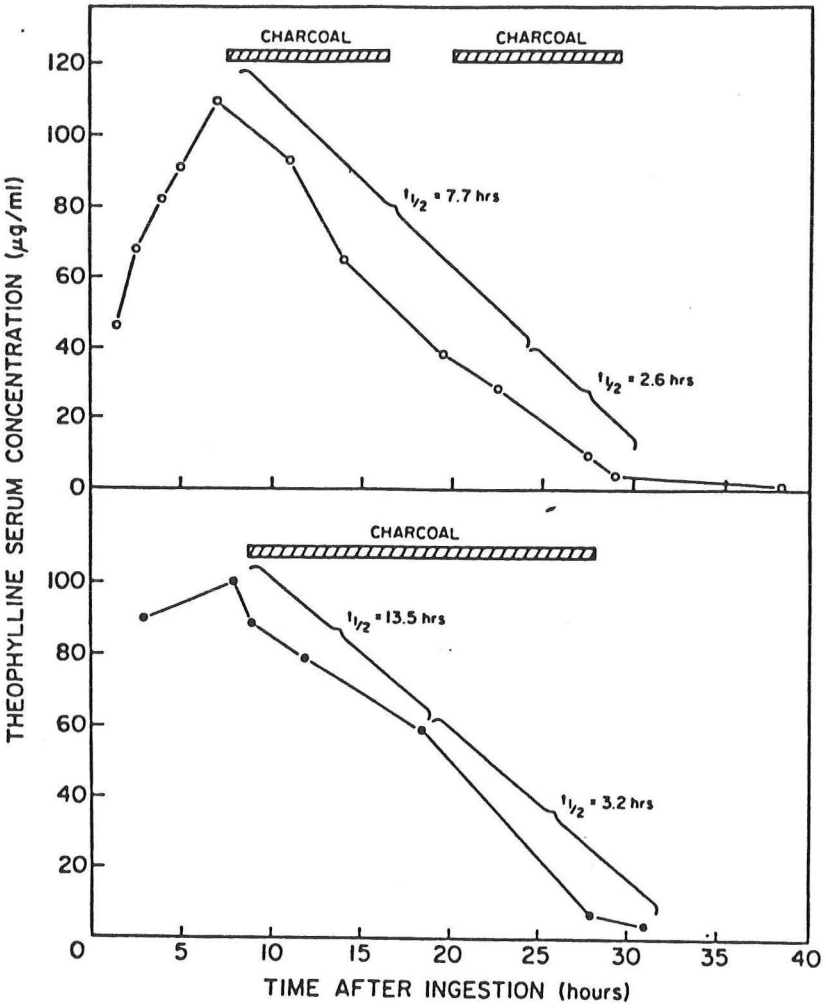

Figure 11. Numeric plot of serum theophylline concentrations versus time for case 1 (upper) and case 2 (lower) following ingestion. Dramatic changes in the apparent theophylline half-life are observed, which appear concentration dependent though overall theophylline elimination is augmented by charcoal administration[34].

A few drugs and chemicals are not absorbed by charcoal. A list of some of the more common of these can be found in Table 5.

TABLE 5

POISONS NOT ABSORBED WELL BY ACTIVATED CHARCOAL

Ethanol	Ethylene glycol
Methanol	Iodine
Iron	Lithium
Acids	Malathion
Heavy metals	Methylcarbamate
Alkali	Potassium
Bromide	Tobramycin
Cyanide	Tolbutamide
DDT	

CATHARTICS

Cathartics have been used in the treatment of drug overdoses and poisonings with the idea of decreasing the amount of time the toxic agent is exposed to the gastrointestinal tract and subsequently decreasing its absorption. Unfortunately, this method of treatment has never been confirmed by clinical studies. Cathartics do hasten the passage of charcoal through the system so they do have a place in the treatment of overdose patients. Sorbitol is probably the safest to use in adult patients and is probably the most commonly used. Castor oil is a reasonable alternative and is safe. Magnesium salts are good cathartics, but serious magnesium toxicity can occur, especially in patients with renal impairment[37,38]. Sodium sulfate has also been used but should be avoided in patients with congestive heart failure.

Cathartics must be used with caution. Repeated doses of cathartics in adult patients have been reported to cause serious hypernatremia within 24 hours such as that illustrated in figure 12[39,40].

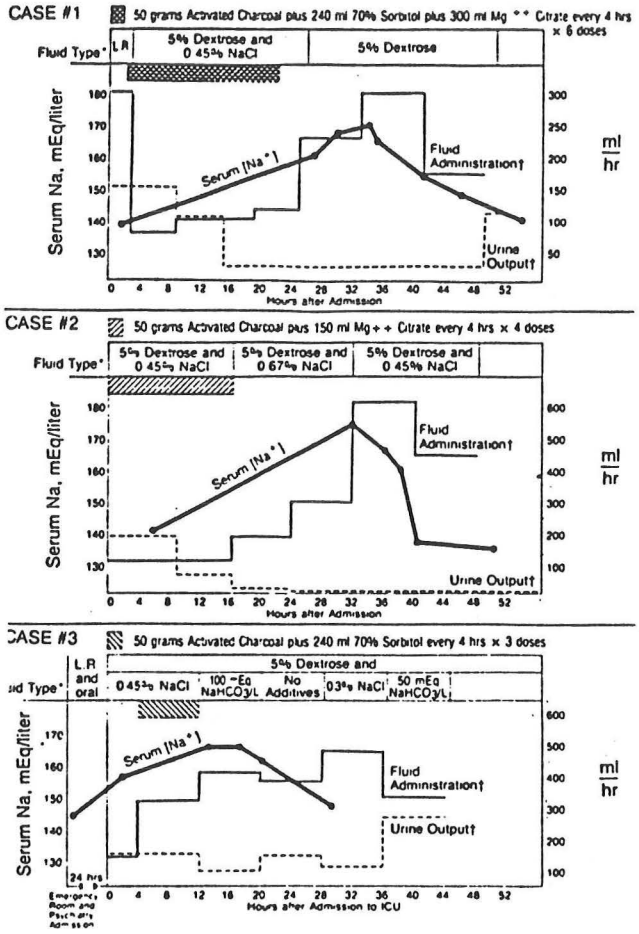

Figure 12[39]. The graph shows rising serum sodium concentrations accompanied by declining urine outputs despite the administration of fluids in excess of maintenance requirements in three patients who were administered multiple doses of cathartics and charcoal during overdose management.

A recent modification to gut decontamination has been to use whole bowel irrigation similar to that used for lower gastrointestinal endoscopy. Kirshenbaum, et al.[41], have reported the results of such a treatment compared to an activated charcoal-sorbitol mixture using enteric-coated acetylsalicylic acid as the ingested material. Whole bowel irrigation was accomplished using continuous nasogastric infusion of 1.5-2.0 L/hr. Treatment was stopped when the "rectal effluent was visibly similar to the infusate, with a minimum of 3 hours and a maximum of 5 hours of infusion". Whole bowel irrigation was superior to the activated charcoal-sorbitol

mixture when peak salicylate levels, time to zero salicylic acid concentrations and area under curve measurements were examined as illustrated in figures 13 and 14 below. No significant side effects were noted.

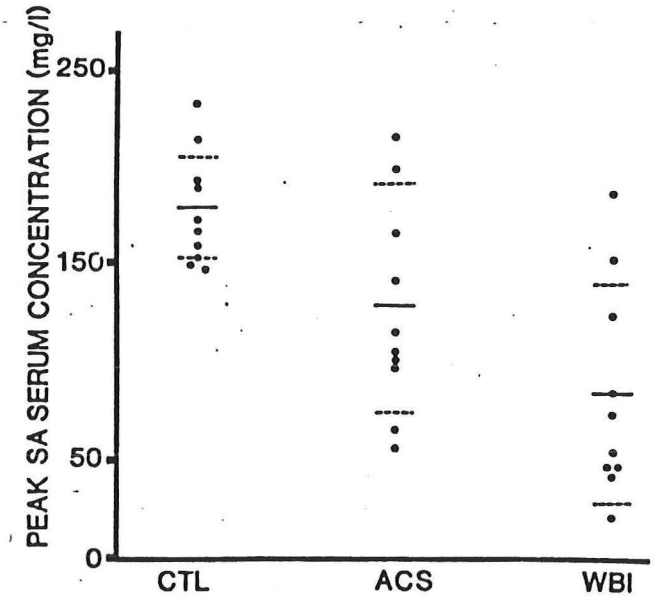

Figure 13. Peak serum salicylic acid (SA) concentrations for control (CTL), activated charcoal in sorbitol (ACS), and whole bowel irrigation (WBI) phases after ingestion of 2925 mg of enteric coated acetylsalicylic acid. A treatment effect was demonstrated ($p<0.01$), and treatments differed from each other ($p<0.05$).

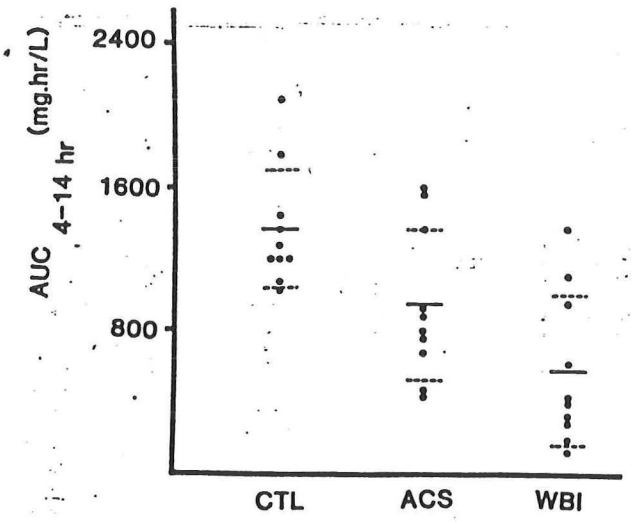

Figure 15.Area under the serum salicylic acid concentration versus time curves (AUC) between 4 and 14 hours for control (CTL), activated charcoal and sorbitol (ACS), and whole bowel irrigation (WBI) phases after ingestion of 2925 mg of enteric coated acetylsalicylic acid. Both treatments were different from the control ($p < 0.01$) and were different from each other ($p < 0.05$).

Whole bowel irrigation probably is effective for two reasons. First, its rapid transit through the gastrointestinal tract most likely washes unabsorbed drug through the gut as is presumed for any cathartic drug. Second, the rapid flow rates keep the concentration of the drug in the lumen of the gut very low, thereby creating ideal conditions for back diffusion of absorbed drug from the blood into the stool. This technique may have promise for certain overdose situations, but its obvious technical limitations will limit its use in busy emergency departments.

NEUTRALIZATION

Neutralization of a substance in the stomach is not appropriate in most poisonings but may be considered in the following situations:

1) Iron - Sodium bicarbonate
2) Mercury - Sodium formaldehyde sulfoxylate
3) Iodine - Starch in water
4) Strychnine, nicotine and quinine - potassium permangonate

STEP 4 CONSIDER GIVING ANTIDOTE IF APPROPRIATE

Antidotes are very helpful in the treatment of certain overdoses and poisonings, although no antidote is available for most drugs that patients take. The following drugs have antidotes that should be considered when severe poisoning or intoxication is present:

1) Acetaminophen - N-acetylcysteine is a effective antidote for acetaminophen poisoning. The initial dose is 140 mg/kg followed by 70 mg/kg every four hours for seventeen doses. It is most efficacious when given within ten to twelve hours of the ingestion, but may provide some benefit up to sixteen to twenty four hours.

2) Arsenic, gold, mercury - The most effective antidote for these heavy metals is BAL (British anti-lewisite). It is given as a dose of 5 mg/kg intramuscularly as soon as possible after the poisoning.

3) Carbon monoxide - Oxygen is the antidote for carbon monoxide poisoning. For severe cases, hyperbaric oxygen is indicated.

4) Cyanide - Amyl nitrite should be inhaled then sodium nitrite given intravenously. These should be followed by sodium thiosulfate which forms thiocyanate that is excreted by the kidney.

5) Ethylene glycol/methyl alcohol - Ethyl alcohol should be given to maintain a blood alcohol level of 100 mg/dL until dialysis can be arranged.

6) Iron - Desferoxamine should be given to chelate iron in overdose situations. It should be given if the total serum iron is greater than the total iron binding capacity of the blood, or if the total serum iron is greater than 350 mg%.

7) Lead - Calcium disodium versenate should be given to chelate this heavy metal.

8) Nitrites - Methylene blue will help if these drugs cause methemoglobinemia. The dose is 0.2 mL/kg of a 1% solution intravenously over 5 minutes.

9) Narcotics - Naloxone should be given at a dose of 0.2-2.0 mg. If a long acting narcotic such as propoxyphene or methadone has been taken, a continuous drip of naloxone can be given until the effects of the narcotic are gone.

10) Organophosphates - Atropine, 0.5-2.0 mg, should be given to control bronchial secretions and symptoms. Pralidoxime (2-PAM, Protopam), 1 gm, should then be given intravenously.

STEP 5 ENHANCE ELIMINATION OF ABSORBED DRUG

The final step in the general treatment of drug overdoses is to enhance the elimination of toxin that has been absorbed. In the past, this was done primarily through enhancing urinary excretion of certain drugs. Over the past few years, the development of hemodialysis and the technique of multidose charcoal has helped accomplish this task somewhat.

REPEATED DOSE CHARCOAL

Over the last few years, repeated dose activated charcoal has become a common method used to enhance drug elimination. It seems to work in reducing the serum half-life of some drugs by one of two methods. First, it binds drugs within the gastrointestinal tract that have a significant enterohepatic circulation thereby making the drug unavailable for reabsorption. Second, it keeps the functional concentration of the drug in the gastrointestinal tract at near zero, enhancing back diffusion across

the intestinal wall from the blood to the lumen. This is accomplished by giving 50 gm of activated charcoal every 2-4 hours with cathartics as needed.

Repeated doses of activated charcoal have been studied in the management of several drug intoxications. There is little doubt that this procedure is effective in dramatically enhancing the elimination of theophylline[42,43] and phenobarbital[44] from the body. It is probably effective in increasing the elimination of carbamazepine, nadalol, meprobamate[47], tricyclic antidepressants, propoxyphene, salicylate[45,46] and digoxin. Although data are conflicting, the technique is probably not effective in overdoses with phenytoin[48] or chlorpropamide.

Obviously, more studies are needed before multiple dose charcoal can be recommended for the general management of drug overdose patients. It does seem to be a safe and relatively inexpensive way to increase the elimination of some drugs.

DIALYSIS AND HEMOPERFUSION

With the advent of hemodialysis and later hemoperfusion columns, the question obviously arose as to whether these modalities could benefit severely poisoned patients. In order to be of benefit, it is generally accepted that the procedures must either improve morbidity and mortality, or at least remove a large portion of the toxic substance. For several reasons, these modalities have not proven effective in most intoxications. Drug overdoses that seem to benefit most involve substances that have a low volume of distribution and molecular weight and are poorly protein bound[49]. Very few drugs fit these characteristics, but a few have been found to be substantially removed by hemodialysis or hemoperfusion.

Isopropyl alcohol, in high doses, can result in serious toxicity. This alcohol is rapidly absorbed from the gastrointestinal tract. It is effectively removed by hemodialysis[50]. Indications for dialysis in isopropyl alcohol intoxication are coma, hypotension, cardiac toxicity and plasma levels greater than 400 mg/dL.

Hemodialysis is also indicated in significant methyl alcohol[51] and ethylene glycol[52] intoxication in conjunction with intravenous ethyl alcohol.

Both hemodialysis and hemoperfusion clear salicylate but the acid-base disturbances of this poisoning make hemodialysis the best method[49]. It should be considered in patients with high levels (>80 mcg/dL) with symptoms of serious intoxication or clinical deterioration.

Lithium is effectively removed by hemodialysis which should be employed in patients with significant symptoms of intoxication, a level greater than 2.5 mM, renal

insufficiency or other conditions that cause an increased sodium or lithium reabsorption.

Hemodialysis and hemoperfusion are effective in removing theophylline with hemoperfusion being the best. It should be performed on patients with levels greater than 80 mg/L and an acute intoxication or with patient whose levels are greater than 60 mg/L who are chronically intoxicated, greater than 60 years of age, or who have heart or liver disease. If hemoperfusion is not available, hemodialysis is an acceptable alternative.

Unfortunately, the rarity of other serious overdoses has made evaluation of hemodialysis and hemoperfusion difficult. It must be remembered, however, that most other intoxications will survive with good supportive care.

DIURESIS

In the past, fluid loading and forced diuresis were an accepted means of management of most overdoses. With better forms of therapy today, this modality should be reserved for specific indications. Drugs whose excretion can probably be enhanced by diuresis include phencyclidine, phenobarbital, salicylate, amphetamines, bromides and lithium. Alkalinization of the urine will ionize weak acids such as phenobarbital and salicylate thereby increasing their excretion. Acidification of the urine will increase the excretion of phencyclidine and amphetamine. This, however, can result in renal failure if significant rhabdomyolysis and myoglobinuria, which are common complications with these drugs, are present.

CONCLUSION

The treatment of drug intoxication has undergone many changes over the last few years. Unfortunately, many of the new treatment modalities have been inadequately tested in rigorous clinical trials. Fortunately, most patients do well with good supportive therapy and a common sense approach to management. Hopefully, the controversies regarding management of overdose patients discussed above will be resolved over the next few years.

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