

Clinical Review

Activated Charcoal—Past, Present and Future

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Poisoned patients were first treated with charcoal more than 150 years ago. Despite its almost universal acceptance today, activated charcoal's role has been overshadowed by the emphasis on treating poisoned patients first with gastric emptying. We review the current use of activated charcoal and recent studies that suggest that activated charcoal may be the single most effective treatment in many types of poisoning. New explanations for the mechanisms of action include "back diffusion" and disruption of enterohepatic loops. Clinical data endorse a new and aggressive role for activated charcoal in the management of poisoned and overdosed patients.

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Activated charcoal is widely used in the treatment of overdoses and poisonings in conjunction with gastric emptying. The use of charcoal in the treatment of poisoned patients had gained universal acceptance only during the past 20 years.¹ Its current usefulness has been limited primarily to a one-time dose usually administered in an emergency department setting. Recent evidence suggests that frequent and repeated doses of charcoal may be important for the victim of a serious toxic ingestion. Furthermore, oral charcoal administration only without prior gastric emptying may have a role in the management of some poisoned patients.

History

The adsorbent properties of charcoal were described in the 1700s, and the first clinical applications occurred in the early 1800s. Early investigators such as Bertrand, Tovery, Hort and Garrod showed the effectiveness of charcoal in preventing clinical effects of poisoning in animals and humans.^{2,3} A classic and frequently cited early demonstration with charcoal was the ingestion of a lethal dose of strychnine mixed with charcoal by Tovery before the 1831 French Academy of Medicine. Tovery suffered no ill effects from the strychnine because of the simultaneous ingestion of charcoal.³ Similarly, the American physician Hort, by administering oral charcoal, reportedly saved the life of a patient in 1834 who ingested mercury bichloride.²

Over the next 150 years, charcoal was further refined, purified and activated to improve its adsorptive powers. Numerous studies were published describing the adsorbing characteristics and potential clinical benefits of charcoal.^{4,5} Despite this work, charcoal was not widely accepted as an

essential tool in the management of poisoned patients until the past 20 years. A review article published in the *Journal of Pediatrics* in 1963 has been credited with stimulating the more universal use of charcoal in poisoned patients.⁵ Despite the early recommendation that charcoal be given as a first-line antidote or mixed with lavage fluid, it is still frequently given only after gastric emptying has been completed by emesis or lavage.

Activated Charcoal

Activated charcoal can be prepared from one of a variety of carbon-containing materials.⁶ Wood pulp with a low ash content, coal, lignite and rye starch are some examples of sources. Once the charcoal (nearly pure carbon) is obtained through chemical means, it is broken down into a fine granular form. To activate it, a further process of treating it with steam, oxygen, carbon dioxide, certain acids and other chemicals is undertaken. This activating process removes impurities and creates fine, small granules. As a result, currently used activated charcoal has a surface area of about 1,000 m² per gram, while experimental activated charcoal with surface areas of up to 3,500 m² per gram has been manufactured.⁷ Activated charcoal will adsorb most drugs and toxins,^{8,9} but not all compounds are well adsorbed (Table 1).¹⁰

Present Use

Activated charcoal is now widely used in the treatment of poisoning and overdoses but in conjunction with gastric emptying.¹² Gastric emptying is usually carried out by one of two means. In an alert and awake adult patient, syrup of ipecac is usually administered orally in a dose of 30 ml (smaller doses

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TABLE 1.—Compounds Poorly Adsorbed or Not Adsorbed by Charcoal

Alkali*	<i>N</i> -Methyl carbamate*
Boric acid*	Malathion*
Cyanide†	Electrolytes*
Dichlorodiphenyltrichloroethane (DDT)*	Water-insoluble compounds such as methanol‡
Ferrous sulfate*	Tolbutamide*
Mineral acids*	

*From Decker et al.¹⁰
†From Andersen.²
‡From Berlinger et al.¹¹

in pediatric patients). This generally will induce emesis, but if it fails, the dose of ipecac may be repeated about 15 to 30 minutes after the initial dose. After the patient has finished vomiting, activated charcoal in a dose of about 1 gram per kg of body weight is administered orally to the patient.

Gastric lavage is carried out on patients who are not alert or who have a diminished gag reflex. Before the gastric tube is passed, the patient's airway must be protected, which requires positioning in the left lateral decubitus position and often requires endotracheal intubation. A total of 3 liters or more of fluid in small 200- to 300-ml aliquots is used until the return is clear (smaller amounts of normal saline solution can be used in pediatric patients to prevent hyponatremia).¹³ Repeated lavage with warmed saline has recently been advocated.¹³ After gastric lavage, activated charcoal can be placed directly through the lavage tube into the stomach. One should preferably attempt to achieve an activated charcoal-to-toxin or drug ratio of about 10:1.¹⁴

Following the administration of activated charcoal, cathartics are indicated to evacuate the charcoal-poison bonded complex from the gastrointestinal tract. The relative risks and benefits of cathartics have recently been reviewed.¹⁵ Although the efficacy of cathartics in the treatment of poisoned patients has never been documented, they were recommended by most (20 out of 27) medical toxicologists surveyed.¹⁵ With the use of repeated doses of activated charcoal in the treatment of a poisoned patient, cathartics have been used to reduce the charcoal-induced constipation that occurs in some patients.¹⁶ The use of oil cathartics should be avoided.¹⁵ Relative contraindications for saline cathartics (sodium, phosphate and magnesium salts) include renal disease, profound electrolyte imbalance, hypertension, bowel obstruction and congestive heart failure. Profound electrolyte and free water loss can occur with repeated or large doses of either saline or osmotic (sorbitol or lactulose) cathartics. Activated charcoal can now be purchased premixed in a sorbitol solution. This solution is particularly useful when a lavage tube is in place, saving mixing time and the potential mess of mixing.

Because activated charcoal administration follows gastric emptying, many people consider charcoal only a second-line agent in the treatment of overdoses and poisonings. This backseat role may be unjustified. First of all, ipecac-induced emesis results in a variable return of ingested poisons. One study found that less than 30% of the ingested substance was vomited even when ipecac was given immediately post-ingestion.¹⁷ It has been shown that when delayed 30 minutes post-ingestion, ipecac-induced vomiting alone has only a limited effect on reducing the total absorption and peak concentra-

tions of acetaminophen, aminophylline and tetracycline and is significantly less effective in reducing absorption compared with activated charcoal given alone at the same post-ingestion time.¹⁸

Additionally, giving ipecac may waste valuable time. It has been well established that activated charcoal is more effective the earlier it is administered to a poisoned patient.^{1,18} The current emphasis on ipecac-induced vomiting may undermine this effectiveness. A delay of one to six hours¹⁹ may ensue before charcoal can be administered because of the time required for ipecac to induce vomiting and the time of continued vomiting. Furthermore, if repeated doses of ipecac are necessary to induce vomiting, the administration of charcoal will be delayed further. Finally, it is not unusual for a patient to vomit the activated charcoal when given immediately after the cessation of ipecac-induced emesis. In a patient given gastric lavage, delays in administering activated charcoal are usually less and are more directly related to the actual time it takes to lavage the stomach and secure an airway.

New and Future Uses

Emesis and Charcoal

Recent studies have challenged the traditional approaches to a poisoned patient.¹⁹⁻²¹ The use of only activated charcoal without prior emesis may be the most effective treatment modality for some types of poisonings. Activated charcoal has been shown to bind and prevent the absorption from the gastrointestinal tract of many ingested drugs and chemicals.

A recent study addresses the clinical usefulness of emesis in preventing aspirin absorption in adult volunteers. When ipecac was given alone and resulted in emesis, an approximate 30% reduction in salicylate absorption from control values was found compared with nearly a 50% reduction in absorption when activated charcoal alone was given. Subjects first given ipecac, then followed after cessation of emesis by activated charcoal also had only about a 30% reduction from control salicylate absorption. This was explained in part by the fact that eight of the ten subjects in this group immediately vomited the activated charcoal.²⁰ This experimental finding is consistent with clinical experience with combined emetic and activated charcoal therapy in overdosed patients.

In a recent study, more than 592 patients were randomly treated with either gastric emptying (emesis or gastric lavage, depending on clinical status) in conjunction with charcoal and cathartic, or with activated charcoal and cathartic alone.¹⁹ No difference in mortality, morbidity or clinical outcome was found between the emesis and charcoal versus the charcoal-alone group. In obtunded patients, however, who presented within an hour after ingestion, those receiving lavage before charcoal had a better clinical course.¹⁹ This must still be considered a preliminary study awaiting duplication in other centers with additional patients so that an analysis and comparison of the outcome of the two approaches with various toxic substances and categories of related drugs can be made.

In another study, dogs were used to further examine the relationship between gastric lavage and activated charcoal in the treatment of overdoses.²¹ When dogs were administered 500 mg per kg of aspirin, followed 30 minutes later by activated charcoal, a significant reduction (17%) in peak salicylate levels compared with controls occurred.²¹ Larger reductions (37%) occurred when gastric lavage preceded the

instillation of activated charcoal or when gastric lavage preceded and followed activated charcoal administration (48% reduction).²¹

Although the above studies tend to support the traditional concept of lavage before instillation of activated charcoal in obtunded patients, they suggest forgoing gastric emptying in an alert patient. Further studies in animal models with other compounds and further clinical trials with poisoned patients are needed to determine objectively whether gastric emptying followed by activated charcoal or activated charcoal alone is the best approach for various poisonings.

Effects of Gastrointestinal Charcoal on Systemic Drug Levels

A new and exciting role for the use of charcoal in poisoning has emerged. This is the concept of lowering serum concentrations of already systemically absorbed drugs or poisons. Two recent studies have shown the potential importance of activated charcoal in the gastrointestinal tract in reducing the serum half-life ($T_{1/2}$) of intravenously administered substances such as phenobarbital,²² theophylline¹¹ and digoxin.²³ Although the exact mechanism of $T_{1/2}$ reduction is not known, nonrenal elimination was enhanced when activated charcoal was given orally after intravenous administration of either phenobarbital or theophylline to normal volunteers. The reduction in $T_{1/2}$ when activated charcoal was given orally approached 50% for both drugs compared with control values.

There are at least two possible explanations for this finding. Many drugs and toxins that undergo significant hepatic metabolism are conjugated with glucuronides or other substances—for instance, bilirubin, morphine, glutethimide and chloramphenicol—and then eliminated via the bile into the small intestines.²⁴ When these conjugates reach the gut, they can undergo hydrolysis by enzymes such as β -glucuronidase followed by reabsorption into the portal venous system (enterohepatic circulation) (Figure 1).²⁴ One explanation for the effects of charcoal would include the ability of activated charcoal to bind the conjugated drug before hydrolysis or the free deconjugated drug before reabsorption (Figure 2). Another explanation uses the concept of “back diffusion” of free drug from the systemic circulation across the gastrointestinal tract into the intestinal fluids and, finally, binding to the activated charcoal in the gut (Figures 2 and 3).²⁵ The equilibrium for “back diffusion” is strengthened by the characteristic of an “infinite sink” in the intestinal tract brought on by the large binding capacity of charcoal and by the use of repeated doses of charcoal, which replaces charcoal that has moved out of the gastrointestinal tract by intestinal motility (Figure 3).²⁵ Collectively, the use of repeated doses of activated charcoal to disrupt enterohepatic loops, strengthen back-diffusion of drugs into the gastrointestinal tract and hasten elimination has been termed “gastrointestinal dialysis” by some.²⁵ The use of this treatment for severe overdoses, including intravenously introduced drugs, is a major advancement in clinical toxicology.

Earlier data have shown that a single dose of activated charcoal given 30 minutes after an oral dose of the tricyclic antidepressant nortriptyline hydrochloride reduces blood concentrations.^{26,27} Further reductions in peak concentrations and the amount of total drug absorbed (measured from calculations of the area under the time versus drug concentration

curve) were noted when four repeated doses of activated charcoal were given 30 to 360 minutes after a single dose of nortriptyline in human subjects.²⁷ These limited data are the only experimental evidence regarding the potential efficacy of

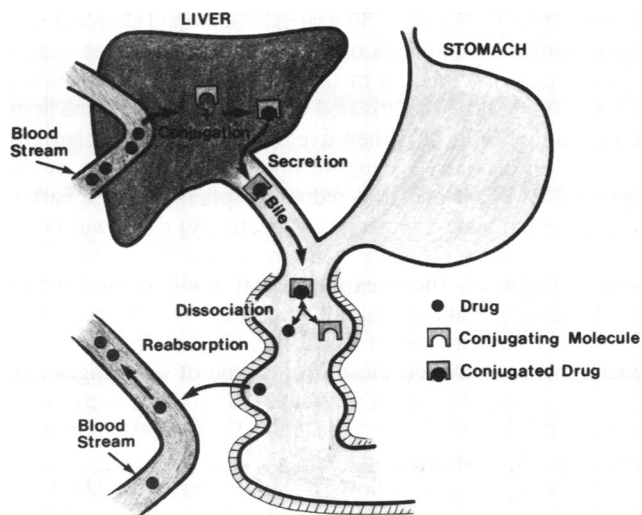


Figure 1.—Normal enterohepatic recirculation of drugs.

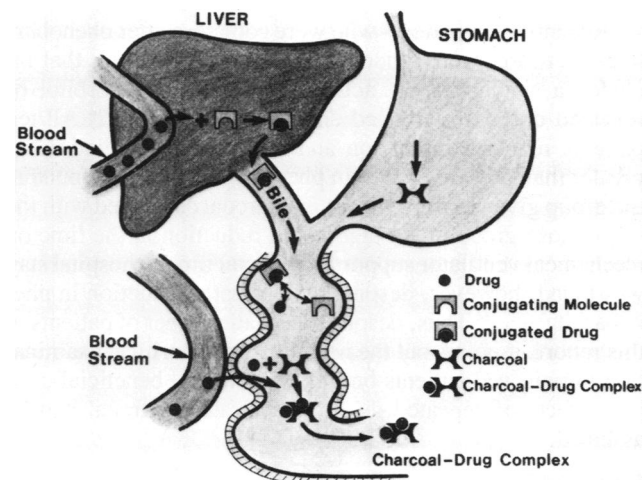


Figure 2.—Effect of charcoal on enterohepatic recirculation of drugs.

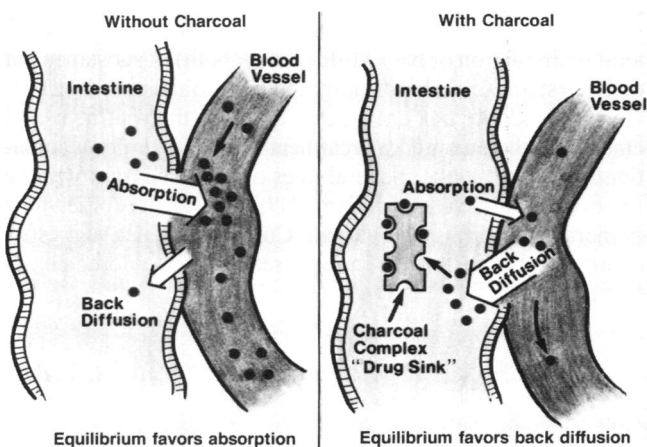


Figure 3.—Diffusion of drug with and without the use of charcoal.

repeated doses of activated charcoal in reducing the toxicity of troublesome overdoses of the tricyclic antidepressant.

A similar study has shown that the absorption of ingested carbamazepine (an anticonvulsant with a tricyclic structure), phenobarbital and phenylbutazone was almost completely prevented (>95%) when 50 grams of activated charcoal was taken within five minutes of the drugs.¹⁵ Significant reductions in the total amount of drug absorbed were also noted when a single dose of activated charcoal was given one hour after drug ingestion.¹⁵ When five doses of activated charcoal were given between 10 and 48 hours after ingestion of the drug, a 72%, 45% and 30% reduction (phenobarbital, carbamazepine and phenylbutazone, respectively) in $T_{1/2}$ was noted for the three drugs compared with the case with control ingestion.¹⁵ Together, these experimental findings in humans would suggest that the oral administration of activated charcoal can reduce or prevent absorption of many ingested compounds when provided close to the time of drug ingestion. Further, repeated doses of activated charcoal can even, when started after several hours, reduce the $T_{1/2}$ of ingested or intravenously administered compounds.

A number of case reports have attested to the ability of repeated doses of activated charcoal to reduce the $T_{1/2}$ of digoxin,²⁸ phenobarbital,²⁹ phenytoin,³⁰ dapsone³¹ and theophylline.^{32,33}

Recently, ten patients who were comatose after phenobarbital overdoses were randomly assigned to protocols that included a single dose of activated charcoal and sorbitol or repeated doses of activated charcoal and sorbitol.³⁴ All ten patients required intubation and mechanical ventilation. A greater than 50% reduction in phenobarbital $T_{1/2}$ was found in the group given multiple doses of charcoal compared with the single-dose group.³⁴ No significant reduction in the time on mechanical ventilator support or the total time of hospital stay was found, however, despite this dramatic reduction in phenobarbital $T_{1/2}$.³⁴ Thus, despite the small number of patients in this report, it points out the need for further critical examination in poisoned patients before the potential beneficial clinical effects of repeated doses of activated charcoal can be assumed.

Conclusion

Charcoal's effectiveness in treating poisoning occurs through its direct adsorption of the toxic substance in the gastrointestinal tract. In some instances, further benefit is gained through interference with enterohepatic or gastrointestinal recirculation or back-diffusion (or both) of substance out of the systemic circulation across the gastrointestinal mucosa. Current evidence has drawn into question the routine use of emetics in the emergency treatment of mild overdoses in patients who are awake. Several lines of evidence reinforce the importance of the use of activated charcoal as the cornerstone of therapy for a poisoned patient. Current evidence suggests a continued role for lavage in more seriously overdosed comatose patients.

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