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**USE OF ACTIVATED CHARCOAL IN PEDIATRIC POPULATIONS**

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## **Literature review**

The studies for this review were identified by performing a search of the PubMed and Medline databases using the search terms: “activated charcoal” and “poisoning”, “activated charcoal” and “toxicity”, “activated charcoal” and “decontamination”, “multiple dose activated charcoal” and “poisoning”, “multiple dose activated charcoal” and “toxicity”, and “multiple dose activated charcoal” and “decontamination”. The dates included 1970-2007. The Cochrane Database for Systematic Reviews was also searched; however, no pertinent reviews were found. The bibliographies of selected articles were also reviewed to identify any studies not found by the original literature search. Inclusion of articles was dependent on the age of the subjects or patients included in the literature, with primary focus on children under the age of 21 years.

## **Background**

In 2006, childhood poisonings accounted for 64% of the 2.4 million human toxic exposures reported to the American Association of Poison Control Centers.<sup>1</sup> Of the 1,229 fatalities, 8% were in children under the age of 19 years. Of the total human exposures, 62.5 % of these patients received decontamination. While 42% of patients received decontamination by way of dilution and irrigation, far fewer received gastrointestinal decontamination. The modalities included single-dose activated charcoal (4.6%), cathartics (1.4%), gastric lavage (0.4%), emetics (0.1%) and whole bowel irrigation (0.1%). In addition, multiple-dose activated charcoal was used to enhance elimination in 0.1% of human exposure patients. As children are more likely to be managed at home and not require decontamination, activated charcoal was used in only 1% of children exposed. Likewise, other gastrointestinal decontamination modalities were used less in children. While the use of other forms of decontamination has decreased significantly over the last 20 years, the use of activated charcoal has declined at a slower rate over this period of time (1.7% in 1985 versus 1.0% in 2006 for all children’s exposures).

The American Academy of Clinical Toxicology and the European Association of Poison Centres and Clinical Toxicologists released a position statement in 1997 (updated in 2005) on the use of single-dose activated charcoal.<sup>2,3</sup> In preparing the position statement, relevant scientific literature was identified and reviewed. The recommendations from this literature review can be found in Table 1. The Position Statement can be found in Appendix 1.

Of particular note, however, is that many of the studies available were performed in adult volunteers or adult overdose patients. While the position statement offers sound advice on the administration of activated charcoal to the poisoned patient, little available literature provides a review of use of activated charcoal specific to the poisoned child.

**TABLE 1: Summary of Single-Dose Activated Charcoal Position Statement**

- There are no appropriately designed clinical studies assessing the benefit from single-dose activated charcoal.
- Benefit from activated charcoal is more likely to occur if administered within one hour of the ingestion of a potentially toxic amount of a poison.
- There is the potential for some benefit of activated charcoal if administered after one hour of ingestion.
- The optimal dose is unknown but recommended as:
  - Children up to one year of age: 10-25 gram or 0.5-1.0 gram/kilogram
  - Children 1 to 12 years of age: 25-50 grams or 0.5-1.0 gram/kilogram
  - Adolescents and adults: 25-100 grams
- Activated charcoal is contraindicated if the patient has an unprotected airway, if its use increases the risk of aspiration (e.g. hydrocarbons), or if any anatomical or medical conditions exist that may be compromised by its use.
- The most common complication of activated charcoal is aspiration or direct instillation of activated charcoal into the lungs.
- Activated charcoal may not be effective for some ingestants, including heavy metals, metal salts (lithium and iron), alcohols, cyanide and other rapid-acting medications.

The use of activated charcoal was first described in 1791 by Lowitz, but used only occasionally until the merits of its use were described in the literature in 1963.<sup>4,5</sup> Since that time, it has been more frequently used in the United States and elsewhere for the treatment of poisoned patients, especially in children. Activated charcoal is an inert, nontoxic adsorbent with a surface area up to 2000 m<sup>2</sup>/gram.<sup>3,4</sup> It is made from a controlled pyrolysis of coconut shells, bone, sucrose, peat, lignite (coal), wood or petroleum that ultimately, produces charcoal. It is activated by heating it in steam, air or carbon dioxide at high temperatures (600-900° C). It is washed with organic acids and dried. This “activation” creates the highly developed internal pore structure and small particle size needed for effective gastrointestinal decontamination. This “activation” also removes substances previously adsorbed by the charcoal. For optimal adsorption, charcoal should have small particle size, a large total surface area, and a low mineral content. Optimal activated charcoal should have a surface area of up to 1,000 m<sup>2</sup>/gram.<sup>6</sup>

The amount of drug that adsorbs to the activated charcoal is dependent on the charcoal-to-drug ratio, with the optimal ratio proposed to be 10:1.<sup>7</sup> As the dose of drug is rarely known, a standard dose of charcoal is normally given. Toxin adsorption may be pH dependent, as these substances are more likely to bind to activated charcoal in the unionized state. Higher doses may be needed in the presence of food. Activated charcoal has been shown to be variable in its ability for drug adsorption, but the list of drugs known for its effectiveness is exhaustive<sup>3,8</sup>. Drugs and chemicals known to have little effect from the administration of activated charcoal include common electrolytes, iron, mineral acids or bases, alcohols, cyanide, most solvents, water insoluble compounds such as hydrocarbons, lithium and other heavy metals.<sup>3,9</sup>

The position statement for a single dose of activated charcoal suggests a dose of 1 gram per kilogram of body weight in a child up to 1 year of age, 25 to 50 grams in

children 1 to 12 years of age, and 25 to 100 grams in adolescents and adults. However, most children up to 12 years of age receive a dose of 1 gram per kilogram of body weight.<sup>3</sup>

### **Efficacy of Single-Dose Activated Charcoal in Children**

In November 2003, the American Academy of Pediatrics released its policy statement for treatment of poisoning in the home.<sup>10</sup> After reviewing much of the literature, the AAP recommended that ipecac no longer be used routinely as a strategy for managing poisoning. As a result, more children who ingest a potentially toxic amount of a drug are referred to the Emergency Department for activated charcoal. While efficacy studies of the use of activated charcoal have been documented in adults and summarized in the AACT/EAPCCT Position Statement, few pediatric studies have been performed. The majority of what is known about the efficacy of activated charcoal in children is found in case reports scattered throughout the literature. However, there are a few studies worth mentioning.

Theophylline was a drug commonly used in the United States for the treatment of asthma. Due to its narrow therapeutic index, many patients experienced overdoses while on chronic therapy. After a group of study patients (ages 8 to 18 years) took a therapeutic dose of sustained-release theophylline, blood for theophylline serum concentrations was obtained for pharmacokinetic evaluation. After a 72-hour washout period, subjects were randomly assigned to one of four study groups and given the same dose as used for the pharmacokinetic evaluation. One group received oral activated charcoal one hour after the dose of theophylline. The second group took four doses of oral activated charcoal at three-hour intervals beginning at one hour after dosing. The third group also received four doses of oral activated charcoal at three-hour intervals but did not start until three hours after the theophylline dose. The fourth group received three doses of oral activated charcoal at three-hour intervals but did not start until six hours after the theophylline dose. Oral activated charcoal reduced the 12-hour area under the concentration time curve (AUC) by 61% in group 1, 68% in group 2, 37% in group 3 and 18% in group 4. All differences in the area-under-the-curve between treated and untreated times were significant except for Group 4.<sup>11</sup> These results validate the need for early decontamination in the child and the possible role for multiple doses of activated charcoal in theophylline poisoning. However, because it was a volunteer study, suprathreshold doses of theophylline were not given, and the role of activated charcoal in an overdose was not assessed.

Likewise, a volunteer study on therapeutic doses of isoniazid was performed after two adolescent cases of overdose were reported.<sup>12</sup> While the patients in the case reports did not receive activated charcoal, pharmacokinetic analysis was performed after the overdose. In addition, one patient received hemodialysis. These pharmacokinetic parameters were compared to those determined from patients who ingested therapeutic doses of isoniazid. The study patients were given a dose of isoniazid at two different times one week apart. During the second phase, activated charcoal was given immediately after the dose of drug. Blood sampling was again obtained for pharmacokinetic analysis. After activated charcoal was given, no isoniazid was measured in plasma in any of the subjects over the same time period. While this study reveals the efficacy of activated charcoal for isoniazid ingestions, the analysis was performed on study subjects that received therapeutic doses and received the activated

charcoal immediately after the drug dosing. As patients with overdose do not receive activated charcoal within minutes after their ingestion, this study cannot be generalized to overdoses in the clinical setting.

Acetaminophen (paracetamol) is a common ingestant in adults and children. The efficacy of activated charcoal in addition to N-acetylcysteine has been studied. Many of these studies have included children in their analysis. One study evaluated gastrointestinal decontamination using gastric lavage and/or activated charcoal in acetaminophen poisoning.<sup>13</sup> Of the 981 patients (ages 13 to 89) admitted over the 10-year period, 10% had serum concentrations that indicated probable or high risk of hepatotoxicity. Patients who received activated charcoal (with or without gastric lavage) were less likely to have plasma concentrations predicted (using the Rumack-Matthews nomogram) to be associated with significant hepatocellular injury, thereby, minimizing the need for hospitalization and treatment with N-acetylcysteine. Gastric lavage did not offer any additional benefit to activated charcoal in this study.

After the AACT/EAPCCT Position Statement was released in 1997, many Emergency Departments curbed their use of activated charcoal. One study assessed the outcomes of patients after deliberate self-poisoning to determine if worsening occurred over time.<sup>14</sup> A retrospective chart review was performed on patients discharged from an Emergency Department after a suicide gesture from three-year time points. There were 561 presentations during those three years. The average age was 31.8 years (ages 14 to 82). The most popular drugs ingested were antidepressants, paracetamol (acetaminophen), benzodiazepines, and antipsychotics. In the first year evaluated, gastrointestinal decontamination was performed in 72% of patients presenting with deliberate self-poisoning. In contrast, gastrointestinal decontamination was performed in only 81 patients seven years later. Specifically, 13.2% of all patients received activated charcoal alone and 85.6% received no gastrointestinal decontamination. There was no significant difference between the two groups in regard to the number of patients who were admitted for hospitalization or died. However, there was a significant difference in that the number of patients admitted to the intensive care unit compared to a general medical bed decreased over the time period. Thus, this would suggest that activated charcoal does not change the clinical outcome of patients. While the study results included all ages of patients who were admitted, the two deaths in the final year studied occurred in men in their 30s.

These studies suggest that while activated charcoal may be efficacious in the treatment of the poisoned patient, much of the efficacy decreases over time; an anticipated conclusion given that the efficacy of a single dose of activated charcoal is dependent upon contact between this non-selective organic adsorbant and un-absorbed drug/toxicant in the lumen of the gastrointestinal tract. The AACT/EAPCCT Position Statement indicates that it is more likely to produce benefit if given within one hour. However, few children receive activated charcoal in that time frame. In one study, 55% of children were administered activated charcoal within one hour of presenting to the Emergency Department, but only 7.8% received charcoal within one hour of the ingestion.<sup>15</sup> In addition, the median time it took to completely ingest the activated charcoal was 15 minutes in children less than 6 years of age.

In a review of the literature cited in the AACT/EAPCCT Position Statement on single dose activated charcoal, none of the articles specifically mention the efficacy in

children. Given that children are more likely to ingest smaller doses of a poison and the adsorptive capacity of the charcoal dose relative to the amount of toxicant present, one can assume that efficacy between children and adults would be comparable. Given the paucity of evidence, no change in the position statement's current recommendations regarding the use of activated charcoal appear warranted. Thus, the administration of activated charcoal may have benefit in a child if it occurs within one hour of the ingestion, but this is difficult to accomplish given the time of presentation of most patients.

## **Palatability**

While the efficacy studies suggest that the dose of activated charcoal should be given within one hour of ingestion, many children may choose not to ingest it during that time frame. As activated charcoal is commonly administered as a slurry consisting of activated charcoal in water, its gritty nature and black color often adversely affect the child's willingness to drink it. In that regard, studies have been performed to assess the optimal way for charcoal administration to ensure that the treatment is given in a timely fashion.

One study compared flavoring agents added to activated charcoal by performing a prospective masked trial on 54 healthy volunteers between the ages of 3 and 17 years.<sup>16</sup> Five identical pitchers were prepared containing activated charcoal alone and others with activated charcoal mixed with flavoring: chocolate milk, Coca-cola®, cherry-flavored syrup and sorbitol. All children were asked which mixture was best. Taste scores for chocolate milk, Coca-cola®, and cherry-flavored syrup were significantly better than those with no flavoring or sorbitol. Chocolate milk received the highest score, with 39% choosing it over the other flavors.

In a similar study<sup>17</sup>, four flavorings (chocolate milk, orange juice, cola, and water) were added to activated charcoal. Thirty volunteers aged 5 to 9 years were blinded to a taste test and rated the taste using a visual analog scale. There was a significant difference in the taste scores between the cola drink and the other flavors ( $p = 0.01$ ). The cola drink was the most preferred flavor with 50% choosing it over the other flavors. Water was the least preferred flavor. There was no demonstrable preference of chocolate milk or orange juice over water.

In contrast, an earlier study assessed the validity of the assumption that activated charcoal is difficult to administer to children.<sup>18</sup> Fifty young children who presented to an Emergency Department after an accidental ingestion were given 10 grams of activated charcoal in water after other emergency treatment had been administered. If ipecac had been given, the activated charcoal was given only after emesis had stopped. The activated charcoal was given to the child by the nurse or parent. The child was "told in a firm but kindly manner to drink the contents of the cup, that the substance did not taste bad, that it would not make him sick, that it would make him feel better". Even after vomiting, 86% of the children drank the slurry of activated charcoal and water. Seventy-six percent of these children drank the complete dose. This implies that the perception that children will not take the activated charcoal may be erroneous and that discomfort may be mainly felt by the emergency personnel administering it.

## **Complications**

It must be noted that there are children who (1) will not ingest the activated charcoal willingly or (2) are not capable of ingesting the charcoal on their own. Activated charcoal is contraindicated in patients that do not have a protected airway, such as in the patient who has central nervous system or respiratory depression without endotracheal intubation.<sup>2</sup> Additionally, its administration is contraindicated if its use increases the likelihood of aspiration or there is any pathology that can be further complicated by its use. Notably, the single most serious adverse event that occurs with its administration is aspiration into the respiratory system. This can occur consequent to emesis following charcoal administration or by direct instillation into the lung. The incidence of emesis has been shown to be greater if activated charcoal is administered with sorbitol.<sup>2</sup> In addition, certain ingestants such as hydrocarbons can increase the incidence of emesis resulting in the potential for aspiration of the charcoal and hydrocarbon.

With the difficulty that health care professionals face when administering activated charcoal in small children, it is not uncommon to recommend administration via a nasogastric tube to optimize the timing. However, available data suggest that nasogastric administration may increase the incidence of vomiting.<sup>19</sup> A prospective study cohort of children who received activated charcoal was performed to assess the risk factors for emesis. Fifty-six of the 275 patients vomited. The median time to vomiting was 10 minutes after administration. Previous vomiting and instillation by nasogastric tube were the most significant independent risk factors for vomiting after activated charcoal. Combining activated charcoal with sorbitol, increased volumes or administration rate did not increase the risk of vomiting.

Case reports that document aspiration of activated charcoal in children commonly refer to the use of a nasogastric tube.<sup>20-22</sup> While ipecac and gastric lavage were performed in two of these children<sup>20,21</sup> and may account for the emesis, the risk of aspiration cannot be discounted. Complications such as bronchospasm, obstructive laryngitis and bronchiolitis obliterans have developed as a result of activated charcoal inadvertently entering the lungs. Additionally, direct instillation of activated charcoal directly into the lung using a nasogastric tube can occur despite the belief that adequate placement of the tube has occurred.<sup>23-26</sup> Finally, corneal abrasions may result from activated charcoal directly entering the eye during emesis or other contact.

## **Alternatives to Activated Charcoal in the Emergency Department**

### **Syrup of ipecac**

Ipecac syrup is an emetic agent that is derived from two plants found in South America in the family Rubiaceae, *Cephaelis acuminata* and *Cephaelis ipecacuanha*.<sup>27</sup> Cephaline and emetine are the two components of these plants thought to contribute to its emetic effect. Other alkaloids are also present in lesser concentrations. They induce emesis by a local irritation of the gastric mucosa and a central stimulation of chemoreceptors in the medulla. Syrup of ipecac has been used clinically as an emetic for centuries but became more widely used in the 1900s as other emetics went out of favor.

The efficacy and usefulness of ipecac syrup has long been debated. Many adult studies have assessed its efficacy after therapeutic doses to determine if serum concentrations of a poison differ over time after treating with ipecac syrup. Many have found that it is more efficacious the sooner it is given after the ingestion. In a pediatric chart review, the effect of ipecac syrup after an acetaminophen ingestion and induced vomiting was assessed by observing the four-hour acetaminophen serum concentration.<sup>28</sup> Emesis within 60 minutes lowered the mean serum level by 50% (16 mg/dl versus 33.1 mg/dl). After 90 minutes, no differences between groups could be found. Overall, many of the studies imply that the efficacy of ipecac decreases over time and that it should be used within 30 – 60 minutes of an ingestion in order to minimize risk and maximize benefit. However, none of the studies could demonstrate that ipecac syrup at any time (at home or in a health care facility) improved the patient's clinical outcome.

At the same time, studies comparing the efficacy of syrup of ipecac and activated charcoal were also performed. In a pediatric, prospective trial, children under the age of 6 years who presented with mild-to-moderate acute ingestions were randomized into two groups (syrup of ipecac prior to activated charcoal versus activated charcoal alone).<sup>29</sup> Those that received syrup of ipecac took significantly more time to receive the activated charcoal after presentation to the Emergency Department (2.6 versus 0.9 hours) and spent more time in the ED. In addition, as one would expect, they were more likely to vomit the activated charcoal. There were no differences between the groups in regard to clinical outcome. The authors conclude that activated charcoal should be the sole mode of decontamination in children due to the delay in administration and prolonged emergency room visit if ipecac is used first.

A representative panel from the AACT and EAPCCT provided a position statement on the use of ipecac syrup in addition to their statement on activated charcoal.<sup>30</sup> Given the literature, such as stated above, they concluded that syrup of ipecac should not be routinely administered in the management of poisoned patients. This is largely due to the lack of efficacy studies and to the fact that its use delays the administration or reduces the effectiveness of activated charcoal and oral antidotes. They suggest that it be administered within 60 minutes but acknowledge that its clinical efficacy at that time is in doubt.

The American Academy of Pediatrics had long advised parents to keep a 30-milliliter bottle of syrup of ipecac in their home to be used under the advice of a physician or poison control center. However, in 2003, after reviewing all of the available literature, they released a policy statement advising that syrup of ipecac should no longer be used in the home as a poison treatment and that the bottles should be discarded.<sup>31</sup> Alternatively, caregivers should post the number to the local poison control center to be advised on whether treatment of an ingestion is necessary and what the next steps should be.

### **Gastric lavage**

The use of gastric lavage in children is also controversial. Gastric lavage involves placement of a large bore tube through the oral cavity into the stomach for removal of a drug or chemical from the stomach. The largest possible tube should be used as the

purpose is to remove un-dissolved toxicant from the stomach. The utility of a standard nasogastric tube is limited due to the likelihood that fragments of solid oral drug dosage forms or other solid toxicants will be too large to pass through the small openings. Although children may benefit from the procedure, the risk from placement of such a large tube precludes its use due to the size of the child's esophagus.<sup>32</sup>

In addition, adult studies have compared the efficacy of gastric lavage to activated charcoal and found gastric lavage to be lacking with the amount of drug removed being variable and as expected, diminished with increasing time after ingestion. Many conclude that, like ipecac, gastric lavage delays the use of activated charcoal.<sup>33</sup> In addition, the use of gastric lavage in addition to charcoal is only as efficacious as activated charcoal alone.<sup>34</sup> The AACT and EAPCCT evaluated the literature and suggest that gastric lavage not be used routinely in the poisoned patient. Like syrup of ipecac, they suggest that it be administered within 60 minutes but acknowledge that its clinical efficacy at that time is in doubt.<sup>35</sup>

### **Cathartics**

As with the other gastrointestinal decontamination modalities, the use of cathartics has also been evaluated in the poisoned patient.<sup>36</sup> Cathartics are used to decrease the absorption of the substance by altering gastrointestinal motility and thereby, decreasing the transit time of the drug in the gastrointestinal tract. Sorbitol is more commonly used as it improves the palatability of the activated charcoal by providing a sweet flavoring. Other cathartics (magnesium citrate, magnesium sulfate, and sodium sulfate) have been used with activated charcoal but generally, are far less palatable than sorbitol. The use of cathartics has been associated with electrolyte abnormalities and volume depletion due to the osmotic nature of the cathartics. Single-dose use of cathartics with activated charcoal has been associated with nausea, vomiting and abdominal cramps. In addition, with multiple or excessive doses, dehydration, hypernatremia in patients receiving sodium-containing cathartics and hypermagnesemia in patients receiving magnesium-containing cathartics have been noted.<sup>36-38</sup>

While efficacy studies have been performed in adult volunteers, no clinical trials assessing the effectiveness of cathartics in children have been done. The literature does provide a few case studies in which cathartics have been used in children receiving multiple doses of activated charcoal. In one case series, 5 adolescents received multiple doses of activated charcoal followed by regularly scheduled doses of magnesium sulfate.<sup>39</sup> The authors concluded that the patients had a rapid clinical improvement without complications. However, no magnesium serum concentrations were obtained to assess the toxicity associated with the cathartic. In one adult study, the addition of sorbitol to activated charcoal did not increase the efficacy of the decontamination, but did increase the side effects.<sup>40</sup> Based on the assessment of the risk-benefit ratio, cathartics are not recommended for use in the poisoned child.

### **Pre-hospital activated charcoal**

The debate over decontamination of the poisoned patient largely lies in assessing the risk:benefit ratio. The AACT and EAPCCT statement and available literature support diminished efficacy of activated charcoal as the time from ingestion increases. Not

surprisingly, the use of pre-hospital activated charcoal has been discussed to optimize the time to decontamination.

In the 1990s, Poison Information Centres in Finland recommended that families with children have activated charcoal in the home to decrease the delay in administration if a child should have a poisoning. Data from calls received at the Centre were assessed to determine the availability of activated charcoal in the home and the ability to safely administer the charcoal in the home.<sup>41</sup> Data from 174 children (mean age: 1.6 years) who had mild ingestions were included. Activated charcoal was not available in more than half of the homes. Charcoal was more often in tablet form rather than the recommended powder form. Those who did not have it at home (103 families) always found it at the local pharmacy. Most children who received the charcoal had no problems with its administration. While vomiting was reported in 5 children, it was difficult to discern whether it resulted from activated charcoal and/or the ingestant. It is also important to note that 7 patients in this reported series had continued development of symptoms from their ingestion despite the early charcoal administration. No children had severe complications from the activated charcoal. The charcoal was administered significantly faster when it was available in the home as compared to a hospital (38 versus 56 minutes). The authors concluded that home charcoal administration could be a safe first-aid therapy to prevent transport to a health care facility.

The above study was validated in the United States when researchers sought to evaluate home use of activated charcoal.<sup>42</sup> In 1996, the Kentucky Regional Poison Center advised parents to stock activated charcoal in the home and pharmacies to stock it on their shelves. Data were collected over 18 months in patients for which activated charcoal was recommended in the home. The data included the availability in the home and/or local pharmacy, time after ingestion for activated charcoal administration, complications or difficulties with administration of activated charcoal, age and gender of the patient and the medical outcome. Out of the 138 cases in which charcoal was recommended, 115 (mean age of patient: 3 years) received it in the home with no apparent problems reported in association with its administration. The time to administration of activated charcoal from the time of ingestion averaged 38 minutes for home treatment and 73 minutes for treatment in the Emergency Department. Eight of the 116 patients treated in the home vomited after administration of charcoal, compared to 3 of the 23 who were treated in the emergency department. No complications, such as aspiration, were noted in the children treated at home. The taste of the activated charcoal was the most common problem in the administration to the children. However, this was alleviated by alternating the activated charcoal with sips of juice or mixing it with juice or carbonated beverages prior to administration. The majority of patients treated at home were children with mushroom ingestions. No mention is made of whether any children became symptomatic from their ingestions or if they were referred to the Emergency Department after home administration of activated charcoal. In addition, it should be noted that the actual dose given was based on the parent's estimation and, more likely, a subtherapeutic dose (less than 1 gram per kilogram) was given.

Another group of investigators in Finland sought to assess the feasibility of administering activated charcoal by emergency medical services (EMS) to patients with suspected acute overdose and fulfillment of criteria for activated charcoal.<sup>43</sup> A

prospective follow-up study was performed on 2047 (age 10 months to 98 years) patients over a 12-month period of time. Based on a medical assessment, activated charcoal was indicated in 722 patients based on presentation within 120 minutes of the ingestion. Of these, charcoal was administered to 405 patients. In addition, 149 patients received charcoal when it was not indicated. Administration of charcoal was unsuccessful in 101 patients because of patient refusal, inability to ingest the charcoal, difficulty in administration due to technical problems, or hospital personnel recommendations against the administration of charcoal to the patient. The average time from the arrival of EMS personnel to charcoal administration was 13 minutes if the person drank it and 38 minutes if given by nasogastric tube. The median time from ingestion to administration of activated charcoal was 60 minutes. Vomiting was the most common adverse event, but it was more likely to occur before administration of activated charcoal. Two patients had cardiopulmonary arrests with one death. However, these incidences were believed to be due to the ingestion rather than the activated charcoal. One patient received activated charcoal after the cardiopulmonary arrest. The authors conclude that activated charcoal administration by EMS providers is feasible even in severe poisonings. While the adverse events were rare, it should be noted that activated charcoal should be given only in those situations when it is indicated and previous guidelines on time to administration are followed.

Despite this evidence, the routine use of pre-hospital activated charcoal has not been advocated in the United States and elsewhere. In an editorial linked to the study by Spillers and Rodgers<sup>42</sup>, Bond points out that poison control centers have become more judicious in their recommendations of activated charcoal in the Emergency Department.<sup>44</sup> This is validated by the decline in the use of activated charcoal in the emergency rooms.<sup>1</sup> Furthermore, in the policy statement of poison treatment in the home, the American Academy of Pediatrics does not support the recommendations of home use of activated charcoal and states that parents should consult with their regional poison control center for recommendations for referral to the Emergency Department.<sup>31</sup>

## **Multiple-Dose Activated Charcoal**

### **Efficacy**

Multiple-dose activated charcoal (MDAC) is defined as the administration of more than 2 doses of activated charcoal in the treatment of a given poisoning. It is believed that drugs with a prolonged elimination half-life, low plasma protein binding and a small apparent volume of distribution (eg.,  $\leq 0.6$  L/kg) may be more quickly eliminated by use of multiple doses of activated charcoal and as a result, the clinical course of the patient improved. In addition, some drugs undergo enterohepatic or enteroenteric recirculation which, in the case of an overdose, may be enhanced by MDAC. As with single-dose activated charcoal, the AACT and EAPCCT drafted a position statement and practice guideline on the use of multiple-dose activated charcoal in the treatment of the poisoned patient. The recommendations are based on adult volunteer studies and case series/reports.<sup>45</sup> Recommendations from this literature review can be found in Table 2. The Position Statement can be found in Appendix 2.

**TABLE 2: Summary of Multiple-Dose Activated Charcoal Position Statement**

- There are no published reports demonstrating that multiple-dose activated charcoal reduces morbidity and mortality in the poisoned patient
- Volunteer studies have documented that drug elimination is enhanced by multiple-dose activated charcoal for the ingestion of carbamazepine, dapsone, phenobarbital, quinine and theophylline.
- Multiple-dose activated charcoal should be considered for life-threatening ingestions of carbamazepine, dapsone, phenobarbital, quinine and theophylline.
- The decision to use multiple-dose activated charcoal should be based on the physician's clinical judgment, lack of contraindications to its use, and the effectiveness of alternative therapies.
- The addition of a cathartic is not recommended.
- Multiple-dose activated charcoal is contraindicated if the patient has an unprotected airway, if its use increases the risk of aspiration (e.g. hydrocarbons), or if any anatomical or medical conditions exist that may be compromised by its use.
- Rarely, constipation and bowel obstruction have occurred with the use of multiple-dose activated charcoal. Aspiration has occurred, but more commonly with concomitant use of sorbitol.

The recommended indications for the use MDAC are if: (1) the patient has ingested a potentially life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine, or theophylline and other invasive extracorporeal measures are being considered, (2) in the clinical judgment of the clinician the benefits outweigh the risks, and (3) alternative methods of treatment are not effective. MDAC should be given by nasogastric tube if the patient is unconscious, nauseated or vomiting. An antiemetic may be needed if the latter occurs. The dose of the charcoal is more important to its efficacy than the surface area, implying that smaller doses more often may prevent vomiting and have led to greater decreases in half-life of the ingested poison. The recommended dose is the initial charcoal dose of 50-100 grams in an adult (or recommended single dose of activated charcoal) followed by hourly, every 2 hours or every 4 hours doses equal to 12.5 grams per hour (in an adult). In children, smaller doses are recommended due to the volume capacity of the intestinal lumen and the likelihood that smaller doses of the poison have been ingested.

As mentioned above, the clinical experience of MDAC is only documented in case reports and case series. While the majority of these are in adults, there are scattered reports of its efficacy in children. Theophylline is a drug that, while commonly used in the past in the United States, may continue to be used elsewhere for the treatment of asthma and apnea of prematurity. It is not uncommon for dosing errors to occur resulting in toxicity to the young child or infant. Several cases have documented the apparently successful use of MDAC in the treatment of theophylline overdoses in infants as young as 2 weeks of age without complications.<sup>46-48</sup> In these cases, charcoal was administered at different doses ranging from continuous infusions (0.25 to 0.5 gram/kilogram/hour) to 1 gram per kilogram every two to four hours. MDAC was able to decrease the anticipated half-life of theophylline from 14-30 hours to 2.5-12.5 hours in these young children.

Phenobarbital is a drug that, while not commonly used in adults to treat seizures, is used in children frequently due to its known pharmacokinetic properties compared to other newer antiepileptics. However, like theophylline, dosing errors occur that can result in toxicity and extreme sedation in the small child. Given that this drug has a prolonged half-life in children, its adverse effects in overdose can persist for days, thereby complicating and prolonging medical care. MDAC has been used in children when these events have occurred, resulting in increased phenobarbital clearance and faster than expected clinical improvement.<sup>49</sup> In a unique case,<sup>50</sup> a neonate was given MDAC due to the need to diagnose brain death by electroencephalogram. The child had asphyxia at birth resulting in seizures requiring phenobarbital at concentrations above 80 micrograms per milliliter for control. However, to establish brain death the serum concentration needed to be less than 30 mcg/ml. Phenobarbital serum concentrations were 89.4 mcg/ml 9 hours after admission and had only decreased to 79.0 mcg/ml at 54 hours. Due to the urgency for this diagnosis to be made, MDAC was instituted at 2 grams every six hours. The serum concentration dropped to 52.8 mcg/ml after two doses and to 22.0 mcg/ml after six doses.

Dapsone is a medication that when ingested, especially in overdoses, can result in methemoglobinemia. MDAC was instituted in an 18-month-old child after an overdose of dapsone.<sup>51</sup> After ingestion, the patient developed a methemoglobin level of 27% and continued to have cyanosis after methylene blue was administered. MDAC was given at 10 grams every 6 hours until the methemoglobin level was 2.3% 64 hours after ingestion. The average half-life of dapsone in therapeutic doses is 30 hours. Although the authors were not able to obtain dapsone levels, the patient could be discharged four days after ingestion where other patients have been documented to be symptomatic for up to 8 days.

While carbamazepine has been recommended by the AACT and EAPCCT to have benefit from MDAC, one study in children did not find that its use resulted in clinically significant improvement.<sup>52</sup> Four children received MDAC after an overdose of carbamazepine with resulting significant decrease in the half-lives. However, the children were not discharged from the hospital earlier compared to those that did not receive MDAC. The authors conclude that while MDAC may decrease the half-lives and the serum concentrations, it did not decrease the time to resolution of symptoms.

While the AACT and EAPCCT Position Statement make recommendations for the drugs whose effects can be decreased or counteracted by MDAC, there may be other drugs that have decreases in serum concentrations and clinical improvement with its use. Children who have ingested drugs such as phenytoin and aspirin have benefited from MDAC.<sup>39, 53-54</sup> In each of the documented cases, the half-lives were decreased with MDAC use, resulting in decreased hospital stays. In addition, MDAC has been used successfully in the treatment of children used as body packers to transport drugs of abuse.<sup>52</sup> While single-dose activated charcoal may be of benefit for most drugs, it is especially useful for those drugs that do not have an antidote, such as cocaine. Use of MDAC may increase the amount of charcoal surrounding the packets of drug should they burst and a bolus of free drug ensue. It is suggested that 1 gram per kilogram (maximum of 50 grams) be administered every 4-6 hours for 4 doses to aid in the treatment and prevention of symptoms.

## **Complications**

Like single-dose activated charcoal, MDAC may have adverse effects that precludes its routine use in overdoses.<sup>45</sup> MDAC is more likely to cause small bowel obstruction and intestinal perforation requiring surgery in the poisoned patient. In addition, respiratory complications have occurred and are more likely as a consequence of aspiration. Some of these cases have resulted in fatalities. However, the only pediatric literature to document complications of MDAC occurred with concomitant use of a cathartic, namely sorbitol, in the charcoal resulting in electrolyte abnormalities.<sup>37-38, 57</sup>

## **Summary**

Activated charcoal is now considered the decontamination treatment of choice for most poisonings in adults and children. However, much of the literature reviews to date have focused on its use in adults. Children are different from adults in that they continue to develop not only physically in regard to maturation of organs and growth but also in regard to their disposition of drugs and chemical within the body.<sup>58</sup> While much of the literature does support the use of activated charcoal in children, the majority of information is based on case reports and case series. The recommendations made by the AACT and EAPCCT remain sound in regard to adults. And, while the evidence is lacking in children, these recommendations should be followed, cautiously, if activated charcoal is to be used in children. One must remember, however, that the use of activated charcoal should not be used as a treatment in the symptomatic child but rather, as a highly effective adjunctive agent for gastrointestinal decontamination. When activated charcoal is given as a single dose within 1 hour after ingestion of a solid toxicant, it can significantly reduce the extent of absorption and as a consequence, reduce and/or ameliorate symptoms associated with poisoning. Its risk:benefit profile changes in relation to the time of administration and its efficacy is limited for ingestion of liquid toxicants (due to more rapid rate of absorption) and inorganic substances (eg., metals). In the absence of an antidote, symptomatic and supportive care should be the mainstay of treatment.

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## **Draft Formulary for Activated Charcoal in the Pediatric Patient**

**Uses:** Decontamination (reduction of absorption) of the poisoned patient who has had a potentially life threatening poison.

Given by mouth **activated charcoal** can bind many poisons in the gastrointestinal system, thereby reducing their absorption. The sooner it is given, the more effective it is, but it may be effective for up to 1 hour after ingestion of the poison. It may be effective several hours after poisoning with modified-release preparations or drugs with anticholinergic (antimuscarinic) properties. It is relatively safe and particularly useful for prevention of absorption of poisons which are toxic in small amounts, for example, antidepressants. Furthermore, repeated doses of activated charcoal enhance the fecal elimination of some drugs (that undergo enterohepatic or enteroenteric recycling) several hours after ingestion and after they have been absorbed, for example phenobarbital, theophylline.

**Contraindications:** Use in a child with an unprotected airway or absent gag reflex.; poisoning by hydrocarbons with high potential for harm if aspirated; poisoning by corrosive substances as AC may prevent visualization of lesions caused by poison and cause more complications with perforation.

**Precautions:** Sedated or unconscious patients as there is an increased risk of aspiration. Intubation or administration via a nasogastric tube may be necessary if the ingestion has occurred within 1 hour of the ingestion. AC is not effective for poisoning including heavy metals, metal salts (lithium and iron), alcohols, cyanide and other rapid-acting medications.

### **Dose:**

Poisoning (reduction of absorption), *by mouth*,

Children up to one year of age: 10-25 gram or 0.5-1.0 g/kg, as a single dose

Children 1 to 12 years of age: 25-50 grams or 0.5-1.0 g/kg, as a single dose

Adolescents and adults: 25-100 grams, as a single dose

Poisoning (active elimination), *by mouth*,

Children up to one year of age: 10-25 gram or 0.5-1.0 g/kg every 4-6 hours

Children 1 to 12 years of age: 25-50 grams or 0.5-1.0 g/kg every 4-6 hours

Adolescents and adults: 50 g every 4 hours (in case of intolerance 25 g every 2 hours).

**Adverse-effects:** black stools; vomiting, constipation or diarrhoea; pneumonitis secondary to aspiration