CASE REPORT

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Suicide by Ingestion of Methyl Ethyl Ketone Peroxide

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ABSTRACT: Methyl ethyl ketone peroxide (MEKP) is a free radical-generating compound used as a fiberglass resin hardener. A 41-year-old Haitian man developed severe metabolic acidosis, hemolysis, esophageal and gastric necrosis, and perforation of the stomach after drinking an undetermined amount of MEKP in a successful suicide attempt. The biochemical effects of free radicals explain the necrosis and hemolysis observed.

KEYWORDS: toxicology, suicide, methyl ethyl ketone peroxide

Because of their poisonous and often corrosive nature, industrial chemicals and solvents may be the agents chosen in suicide by ingestion. Easy availability to factory workers of certain chemicals may be a deciding factor. Methyl ethyl ketone peroxide (MEKP) has been used for a few decades in the fiberglass industry. After early experimental work in Germany in the late 1900s, MEKP was patented in the mid-1930s and was introduced to the American public in 1949 [*1*]. This chemical belongs to the organic peroxides which have received usage in the production of rubber, optical and dental castings, and even the bleaching of flour. In addition, these organic peroxides, particularly MEKP, are used for their production of free radicals providing catalyzation for the polymerization process which hardens fiberglass resin [*2,3*]. MEKP may be found in various commercial preparations (for example, Cadox® M-50, Lupersol®, and Norox®), and is dangerous to handle as the result of explosion and fire hazards. Adequate safety standards and procedures for storage, handling, supervision and maintenance, and fire protection are desirable [*4*]. The threshold limit value in workroom air is 0.2 ppm (8-h day—40-h week) [*5*].

In 1980, the Dade County Medical Examiner Department investigated a case of suicide by ingestion of MEKP. A few reports [*6-8*] of both accidental and suicidal ingestions have been published in the medical literature. In addition, the National Injury Information Clearing-

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house of the U.S. Consumer Product Safety Commission lists four incidents related to MEKP from 1974 to the present (Table 1). Inquiries of the Environmental Protection Agency (EPA) and the National Institute for Occupational Safety and Health (NIOSH) as well as other state and local authorities did not result in data regarding the national or local annual incidents of toxicities or fatalities. In addition, the 1983 annual report [9] of the American Association of Poison Control Centers did not directly mention MEKP in their list of "fatal exposures."

Case Report

A 41-year-old Haitian male was taken by Fire Rescue to a Miami hospital after ingesting an undetermined amount of an unidentified chemical at home. Hours before, he had an argument with his wife. Upon arrival, he was alert, active, very belligerent, and in mild to moderate respiratory distress. He required intubation because of copious, brown, foamy secretions and deteriorating blood gases. The patient extubated himself four times, repeatedly stating that he wanted to either return to Haiti or die. He was admitted to the medical intensive care unit where he was reintubated and sedated. Physical examination revealed a foul breath odor, white areas on the oral mucosa consistent with chemical burns, bilateral rales and rhonchi with large amounts of brown secretions, greatly decreased bowel sounds, an initially nontender abdomen, and heme negative stools. An abdominal film was normal, as was the chest X-ray. Over the next several hours the patient developed left upper quadrant and epigastric tenderness, heme positive stools, and hypotension.

Laboratory examination showed a severe metabolic acidosis. Blood pH was as low as 6.70 and remained less than 7.0 even with appropriate ventilation and repeated sodium bicarbonate administration. Serum bicarbonate was recorded as low as 10.0 meq/L and base deficit as high as 30. Serum lactic acid was elevated at 2.5 mg/dL (normal range 0.5 to 2.2 mg/dL). Serum creatinine was slightly elevated and alkaline phosphatase was normal. Hemoglobin and hematocrit were initially normal, but hematocrit later dropped to 24% and the serum became 3+ icteric. Prothrombin time (PT) and partial thromboplastin time (PTT) were also normal on admission, but increased to 20.8 s (control 11.3 s) and 68 s (no control), respectively. Urine was heme positive with clumps of red blood cells (RBCs), no myoglobin was present.

The patient was treated supportively with ventilation, pancuronium bromide (Pavulon®) for paralysis, sodium bicarbonate, methyl prednisone sodium succinate (Solu-Medrol®), mannitol, and cemetidine. He was also given penicillin G. Dopamine was added when hypotension ensued. Endoscopy was attempted, showing oral mucosal burns and an edematous pharynx, but the instrument could not be passed beyond this point. A peritoneal lavage was performed with return of necrotic coffee ground-like material. The pH of the gastric contents was 5.0. The patient was taken to surgery approximately 12 h after the ingestion. At the time of laparotomy, a necrotic, perforated stomach was found with diffuse necrotic areas on the external surfaces of the small intestine, colon, and liver. There was a large amount of black, watery fluid in the abdominal cavity. The injuries were considered to be incompatible with life, and the patient died shortly thereafter. The body was transported to the Dade County Medical Examiner Department and then placed in the morgue refrigerator (4°C). A postmortem examination was performed 20 1/2 h after death.

At autopsy, the mucosa of the lips was white with superficial denudation. The esophageal wall was edematous with dusky gray, eroded mucosa (Fig. 1). The edematous stomach was black with a prominent fundic perforation (Figs. 2 and 3). The intestines were intact but had a gray-black appearance. The liver, spleen, and kidneys were unremarkable except for a grayish discoloration of the superficial portion of their external surfaces. The abdominal cavity contained a large amount of black watery fluid. There was patchy blood extravasation about the base of the brain extending to the superolateral aspects of the temporal and parietal lobes and prominent subdural blood at the base of the posterior fossa. The brain was of the usual size and shape except for small focal disruption of the lateral aspect of the right cerebellar hemisphere.

FIG. 1—*Necrotic esophageal mucosa.*

In addition, there were small foci of blood extravasation within the tissue immediately adjoining the fourth ventricle. The brain was otherwise unremarkable. Careful examination of the cerebral vasculature failed to reveal aneurysm, vascular anomaly, or arteriosclerosis. The scalp, skull, and neck were free of trauma.

Microscopic examination of the esophagus and stomach revealed extensive necrosis. The mucosa was almost completely absent. The submucoa contained mostly remnants of severely congested capillaries surrounded by necrotic tissue consisting predominantly of red blood cell fragments. The muscular layer showed various stages of necrosis (Fig. 4). There was superficial necrosis of the small intestinal serosa and musculature in a few random samples of tissue. However, the mucosa, complete with microvilli, was strikingly preserved, resulting in a textbook-like histological picture (Fig. 5). Superficial necrosis of the hepatic capsule and the immediately underlying liver tissue was evident. The liver was otherwise unremarkable. The kidneys were normal except for numerous red blood cells within the renal tubules.

Subsequent investigation at the scene yielded the 16-oz soft drink glass bottle from which he drank a clear heavy liquid which gave off vapor. The decedent was known to have previously worked at a fiberglass furniture factory which utilized Cadox M-50, a solution of approxi-

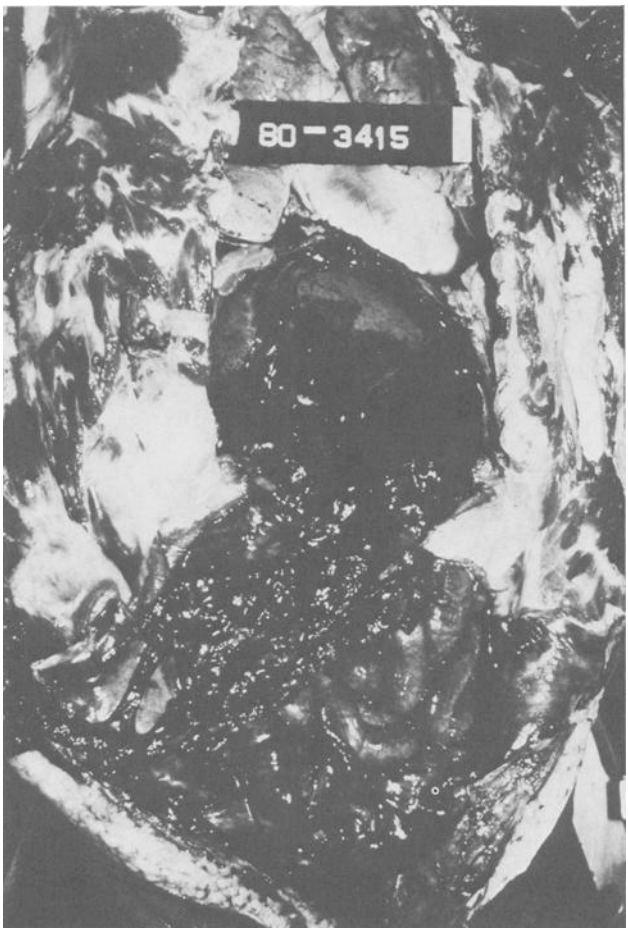

FIG. 2—*Abdominal cavity with black necrotic stomach and superficial necrosis of other organs.*

mately 50% MEKP and 50% dimethyl phthalate. The substance in the bottle has the same appearance and specific gravity of a sample of Cadox M-50 from the factory. Thorough police scene investigation did not reveal any other sources of toxins. The gastric pH of 5.0 obtained shortly after admission helped mitigate against ingestion of a lye or acid. An industrial consultant[4] has stated that MEKP can be tested for in the laboratory by assaying percentage of active oxygen using a colorimetric reaction with aqueous potassium iodide [*10*]. Whether or not this procedure would work in specimens obtained from the living victim is uncertain since rapid breakdown of MEKP may preclude testing. Since the parent moiety, methyl ethyl ketone (MEK), is present in 1/10 of 1%, assay for MEK may be attempted by high pressure liquid chromatography; however, the small concentrations of MEK may preclude detection. Another substance which can be tested for by high pressure liquid chromatography is dimethyl phthalate. Dimethyl phthalate, an insect repellant, is about 50% of the Cadox M-50 solution and thus may be detected.

In the case at hand, the specimens submitted by the Emergency Room for toxicological

[4]Bill Schmidt, personal communication, Research Department, KZO Chemie America, McCook, IL.

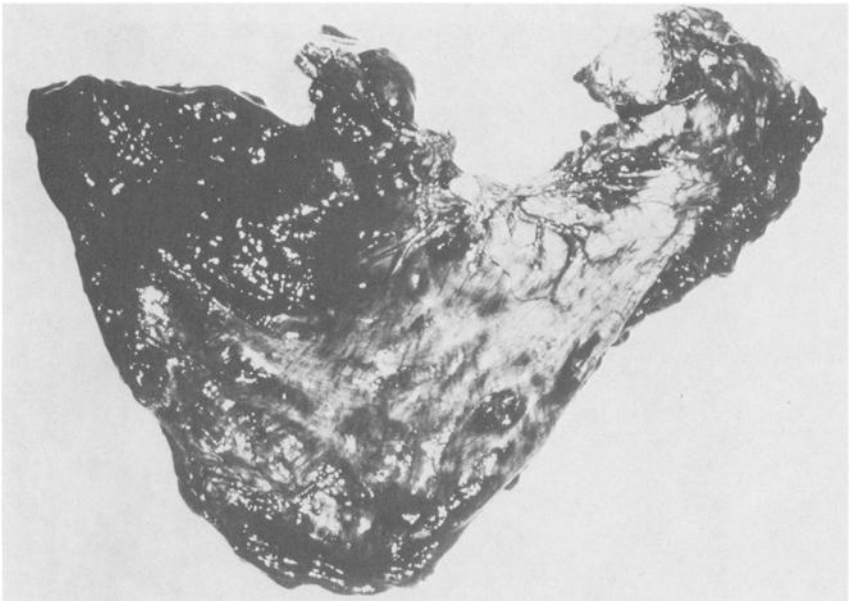

FIG. 3—*Black necrotic stomach.*

screening were gastric lavage (presented as a clear watery fluid), urine, and blood. The clinical suspicion was that of a possible drug overdose or the ingestion of a foreign substance or both. Routine toxicological screening involved (1) blood volatile quantitation (gas liquid chromatography), (2) blood drug screen (ultraviolet spectrophotometry and gas liquid chromatography), (3) urine drug screen (enzymatic immunoassay), (4) gastric drug screens (ultraviolet spectrophotometry), and (5) urine heavy metal evaluation (Reinsch test). The toxicological screening did not reveal any of the usual drugs of abuse. Heavy metals were negative as well as gastric lavage screening.

Discussion

Evidence for suicide was clearly present not only in terms of suicidal ideation but, in addition, the characteristics of MEKP are such that accidental ingestion is uncommon. Because of its instability, the substance is sometimes stored in refrigerators where food and drink are kept. It may then be mistaken for water or soda especially if maintained in unlabeled or poorly marked bottles, but is generally recognized as something different after drinking a very small amount. Other reported incidents of toxicity and death are presented in Table 2.

The same properties which make MEKP useful in industry probably account for its destructive effect when ingested. The substance is an organic peroxide which exists in solution as a mixture of peroxide species [*1*]. Peroxides are highly reactive, producing free radicals which may oxidize vulnerable and saturated fatty acids and certain amino acids. These processes of lipid peroxidation and protein denaturization affect not only the cytoplasmic processes but also produce increased membrane permeability and ionic gradient disturbances [*11*].

Previous toxicological studies on MEKP by Floyd and Stokinger [*12*] failed to reveal specific pathological changes attributed to either intraperitoneal or oral administration of MEKP to rats. Intraperitoneal injection resulted in 80% mortality under acute high dose (80 mg/kg) in four of five rats tested. Although the LD_{50} for oral administration to rats was found to be 484 mg/kg, mortality was 100% under chronic sublethal oral administration dosage (1/5 LD_{50}).

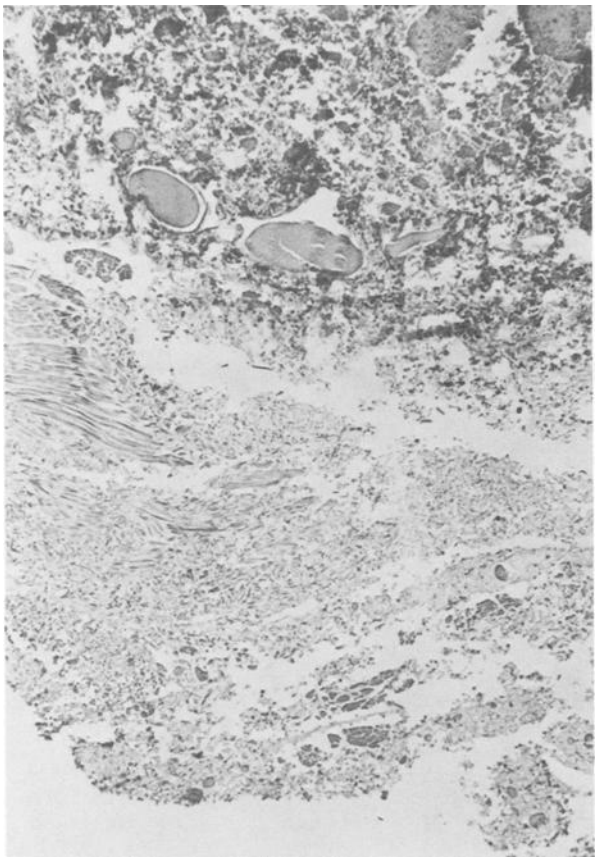

FIG. 4—*Microscopic view of stomach. Note congested submucosal capillary remnants, necrotic muscular layer, and destruction of submucosa* (top of photograph).

It is difficult to correlate our pathological findings with the lack of such in the Stokinger study because of the great difference in concentrations administered. Stokinger used a 5% MEKP concentration; our sample was a 50% concentration. The lowest published toxic dose (TD_{LO}) is reported to be 480 mg/kg for oral toxicity in humans [5]. It seems likely that the necrosis that we observed is explainable by the mechanism stated above.

The findings of corrosive effect on the gastrointestinal (GI) tract by this organic peroxide has certainly been reported by different authors as well as other complications (Table 2). It also seems likely that the same mechanisms contributed to hemolysis. Gastrointestinal necrosis and its associated complications were very significant in this case; however, the profound and relatively unresponsive acidosis was probably also a factor in this patient's death. Dimethyl phthalate, an insect repellant, has a low toxicity rating (two) as reported in *Clinical Toxicology of Commercial Products* [2, p. II-205] and is not corrosive to mucous membranes; thus, this chemical would not be expected to have significantly contributed to the clinical course or the autopsy findings. Methyl ethyl ketone is in such minute concentration (0.1%) in the Cadox M-50 solution that it also would not be expected to cause injury.

The incidental findings of subdural and subarachnoid blood extravasation as well as the other intracranial lesions possibly reflected terminal disseminated intravascular coagulation and hypoxia. Certainly, the victim's original problem did not stem from this intracranial bleed.

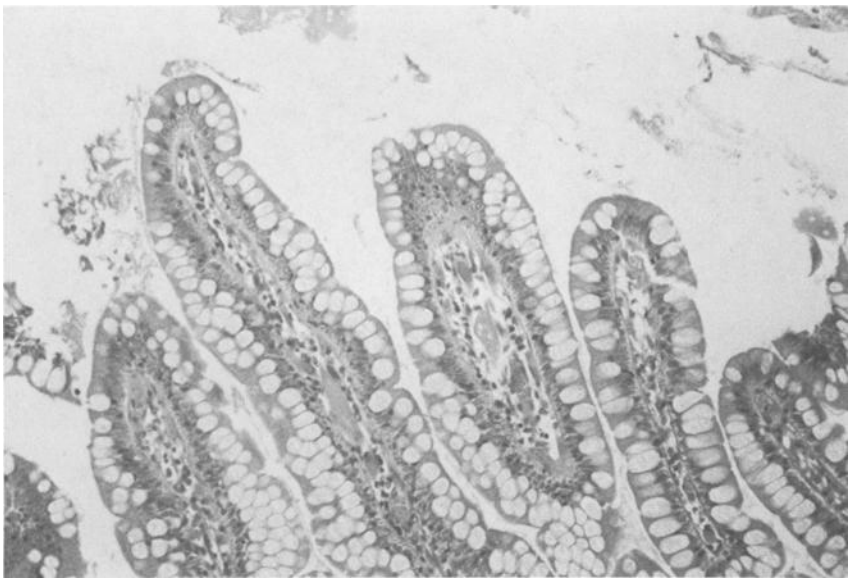

FIG. 5—*Striking preservation of small intestinal mucosa.*

TABLE 1—*Four incidents related to MEKP from 1974 to the present.*

Age	Sex	Incident	Injury	Fatality
19 months	F	playing with catalyst (MEKP) of liquid plastic hobby kit at home	small burns of lips and esophagus resulting in hospitalization	no
58 years	M	flash fire at home while applying MEKP to kitchen floor for application of polyurethane coating	2nd and 3rd degree burns on leg and right arm resulting in hospitalization	no
50 years	M	explosion while placing MEKP in metal container at work	burns	no
55 years	M	accidental ingestion of MEKP	...	yes

Furthermore, there is no evidence of trauma or preexisting natural disease to account for this hemorrhage.

One notable aspect of this case is the remarkable preservation of the small intestinal mucosa. Irregardless of the expected corrosive effect of the ingested chemical, one would expect to find some degree of autolysis simply because of postmortem change since the autopsy was performed 20 1/2 h after death. The body was, however, refrigerated in the interim. It is unclear to us why we see this preservation. We suggest the possibility that some breakdown product of methyl ethyl ketone peroxide may act as a fixative.

Although MEKP ingestion is not common, it is evident that it has a tremendous destructive potential. In the absence of evidence at the scene, one might need a high index of suspicion to identify this chemical, for example, a work history involving the fiberglass industry. We describe a clinical history and pathological findings that appear typical of ingestion of MEKP.

TABLE 2—*Other reported incidents of toxicity and death.*

Ref	Circumstance of Ingestion	Amount Ingested	Fatality	Prominent Clinical/Autopsy Findings
6	A 34-year-old Eskimo longshoreman ingested P-102 Catalyst® (60% MEKP 40% dimethyl phthalate) on a "dare" during a drinking spree	60 mL	no	pharyngitis vomiting dysphagia epigastric pain subsequent stricture of esophagus
7	A 46-year-old Hawaiian man suicidally ingested Norox (60% MEKP and cyclohexone peroxides in dimethyl phthalate) (survival time 27 days)	50 mL	yes	gastritis esophagitis intestinal bleed pneumonia
8	A 57-year-old white man ingested a mixture of 60% MEKP and 40% dimethyl phthalate in a suicide attempt	unknown	no	gastritis esophagitis pneumonia toxic myocarditis
...	A 41-year-old Haitian man suicidally ingested Cadox M-50 (survival time 12 h)	unknown	yes	pharyngitis esophageal necrosis gastric necrosis with perforation

We also raise a question concerning an interesting observation and its possible relationship to methyl ethyl ketone peroxide and its metabolic byproducts.

Acknowledgment

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