

## CASE REPORT

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# Fatalities By Ingestion of Propylene Glycol

**ABSTRACT:** Propylene glycol (PG), a widely used solvent and lubricant, is thought to have low toxicity when ingested. Three cases were identified where PG, either alone or in combination with other chemical agents, contributed to death. The decedent in whom PG was the sole agent was a 32-year-old schizophrenic man with cardiomegaly and renal impairment. The blood PG concentration was 4410 mg/L at least 9.5 h following ingestion.

**KEYWORDS:** forensic science, propylene glycol, suicide, toxins

In a review of the literature, no instances of accidental or suicidal fatalities from ingestion of PG (1,2 Propanediol, C<sub>3</sub>H<sub>8</sub>O<sub>2</sub>) were found.

Propylene glycol is a clear, colorless, odorless, sweet-tasting aliphatic alcohol with a half-life of 2–5 h in people with normal renal function. Because it is generally thought to have low toxicity, it was introduced in the 1930's as a replacement solvent for the more toxic ethylene glycol (EG). Propylene glycol is ubiquitous and has diverse applications. The industrial uses of PG are related to its heat exchange properties making it useful in antifreeze and as a synthetic lubricant in hydraulic fluids. The food industry uses PG as a plasticizer and to prevent mold and fermentation. It is also used in cosmetics as an emollient in the formulation of lotions and creams. Because PG is miscible with water, it is used as a solvent and vehicle for the administration of a large number of parenteral and oral medications that are unstable in water.

Like ethanol, PG is rapidly absorbed from the gastrointestinal tract and is distributed uniformly into total body water. Approximately 45% of absorbed PG is excreted unchanged by the kidneys. The balance is oxidized in the liver by hepatic alcohol and aldehyde dehydrogenases to lactaldehyde and methylglyoxal respectively. Further oxidation produces lactic acid, pyruvic acid and acetate. Thus, patients with hepatic or renal failure are at increased risk of toxicity.

### Materials and Method

Review of the Forensic Toxicology Laboratory database of the New York Office of Chief Medical Examiner for the period January 1, 1990 to December 31, 2003 uncovered six cases where

PG was detected. In one instance a PG-containing solution was found at the death scene (Case 1). The other decedents were found to have hyperosmolar metabolic acidosis prior to death. Analysis for EG and PG (not a routine toxicology screen) was requested in an attempt to identify the cause of the acidosis. In two cases the manner of death (MOD) was classified as suicide (Cases 1 and 2). In Case 3, the MOD was undetermined. The other three decedents were alcoholics with multiple underlying medical problems and their deaths were not thought to be related to PG. One was a 49-year-old woman whose PG concentration was only 44 mg/L in pre-mortem blood retrieved from the hospital. Blood taken at autopsy was negative for PG. The others were a 68-year-old man with a post-mortem PG concentration of 343 mg/L and a 61-year-old man with a post-mortem PG concentration of 847 mg/L. Both had received continuous infusions of Lorazepam that utilizes PG in its formulation.

Propylene glycol was identified and quantitated in biologic specimens using a method modified from Porter et al. (1). Acetonitrile, containing 1,3 propanediol as internal standard, was added to calibrators (500 mg/L, 1000 mg/L, 2000 mg/L), controls (600 mg/L, 1200 mg/L) and specimens from autopsy. After centrifugation, an aliquot of supernatant was derivatized by addition of phenylboronic acid in 2,2-dimethoxypropane. An aliquot of this reaction mixture was injected onto a Hewlett Packard 5890 or 6890 gas chromatograph equipped with a 15 m × 0.25 mm column with a 25 μm thickness 50% phenyl-, 50% methyl-polysiloxane stationary phase. The detector was either a flame ionization detector (Case 1) or a mass selective detector (MSD). For single ion monitoring on the MSD, the quantitation and identifier ions were as follows: propylene glycol phenylboronate m/z 146, 162, 104; ethylene glycol phenylboronate m/z 91, 148, 118; 1,3 propandiol phenylboronate (internal standard) m/z 104, 162, 77.

### Case Reports

Case 1—This 43-year-old man was found dead in the animal research laboratory where he worked. Two suicide notes were found near the body. He had access to multiple drugs in the laboratory including diazepam and a euthanasia solution containing PG. At

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TABLE 1—Drug concentrations in three cases of propylene glycol related death.

	Blood (mg/L)	Gastric Contents (mg/Kg)	(mg in Gastric Contents Submitted)
Case 1 Propylene Glycol	285	24210	(1810 mg in 75.5 g)
Pentobarbital	7.3	887	(66 mg in 75.5 g)
Doxylamine	0.6	1.2	(0.1 mg in 75.5 g)
Diazepam	0.5	94	(7 mg in 75.5 g)
Nordiazepam	<0.1	NDT	
Ethanol	0.10*		
Case 2 Propylene Glycol	4410	4830	(720 mg in 150.8 g)
Lidocaine	DET		
Case 3 Propylene Glycol	538	51680	(7000 mg in 135.9 g)
Ethylene Glycol	384	NDT	
Acetone	0.001*		

\* g%.

DET = detected.

NDT = not detected.

autopsy the decedent was found to have cardiac hypertrophy with left ventricular wall thickening. Autopsy blood toxicology results are presented in Table 1. The PG concentrations were 285 mg/L and 24,210 mg/Kg respectively in blood and gastric contents.

Case 2—This 32-year-old man, with a history of juvenile rheumatoid arthritis, “kidney problems,” and a long history of non-compliant paranoid schizophrenia with delusions and hallucinations, called his mother asking to be taken to the hospital because he was dying. She arrived at his apartment about an hour later to find him having trouble breathing and complaining of abdominal pain and diarrhea. On the way to the emergency room, he ate heartily, arriving one hour later. Approximately an hour and a half after arriving at the hospital, while awaiting triage, he went to the bathroom where he was found unconscious. At this time his blood pressure was 80/40 and his pulse rate was 190/min. Laboratory tests showed metabolic acidosis (pH 7.25) with an anion gap of 29.9 mEq/L and a serum osmolality of 362 mOsm/L with an osmolar gap of 50 mOsm. His blood urea nitrogen (BUN) was 90 mg/dL and his creatinine was 3.4 mg/dL. He subsequently had a cardiopulmonary arrest, was intubated and resuscitated. Later he developed acute renal failure. Based on the laboratory results, the possibility of acute poisoning with EG or methanol was considered and charcoal was administered via nasogastric tube. He died approximately 8.5 h after arriving at the emergency room. Prior to his death he had given his mother a rambling note with multiple references to his death and killing.

At autopsy he was found to have cardiomegaly (heart weight 750 g) with left ventricular wall thickening. The postmortem blood PG concentration was 4410 mg/L and the PG concentration in gastric contents was 4830 mg/Kg (Table 1). The source of PG was not definitively determined. However, the decedent’s hobby was racing model cars and he often used a product containing propylene oxide to enhance the engine’s performance.

Case 3—A 44-year-old man with a history of alcoholism and anxiety disorder with “attention seeking behavior” had an argument with his girlfriend after which he “went to his car for something.” Approximately four hours later he complained of abdominal pain and had slurred speech. After an additional four hours he was noted to have an unsteady gait and urinated on the floor. An hour later he collapsed on the floor and his girlfriend phoned for help. On arrival in the emergency room he was unconscious. He was intubated for impending respiratory failure. His blood pressure was 180/100 and his pulse rate was 110/min. Laboratory testing identified a

wide anion gap (25 mEq/L) metabolic acidosis (blood pH 6.85). In light of this, his girlfriend called her son asking him to check her boyfriend’s car. He found a half-empty bottle of antifreeze. Neither the girlfriend nor her son, however, knew when the antifreeze was opened or how much there had been in the container. A cup containing antifreeze was later found at the girlfriend’s house. The patient was maintained on supportive care but deteriorated and died approximately 36 h after collapsing. At autopsy he was found to have cardiomegaly (heart weight 640 g) with dilated ventricles. His postmortem blood had a PG concentration of 538 mg/L and an EG concentration of 384 mg/L (Table 1). Microscopically, oxalate crystals were seen in the kidney tubules.

## Discussion

We report here two cases of suicide and one case where the MOD was undetermined in which PG was detected on postmortem toxicologic analysis. In Case 1, PG was the vehicle for self-administration of a euthanasia preparation and death was related to polypharmacy, of which PG was a minor component. In Case 2, PG was the only agent detected. In Case 3, PG was detected along with EG. In Cases 2 and 3, PG or a mixture of PG and EG resulted in hyperosmolar metabolic acidosis.

Osmolality measures the number of particles in solution. The calculated osmolality does not take into account unknown solutes present under abnormal conditions, and is usually slightly lower than the measured osmolality (2). Hyperosmolality occurs in two clinical settings: decreased serum water content and increased serum concentration of unmeasured, osmotically active, low-molecular weight compounds (<150 daltons) such as PG, mannitol, ethanol, methanol, isopropyl alcohol, EG, ethyl ether, paraldehyde, and acetone. Values above 10 mmol/Kg H<sub>2</sub>O are considered abnormal (3).

Animal experiments have been conducted which showed that PG had a low toxicity and, at low doses, it is considered innocuous (4). Yu et al. (5) in a study of 22 people given PG orally, concluded that there was no clear relationship between plasma concentration and central nervous system toxicity.

Propylene glycol is a low molecular weight alcohol (76.1 daltons) with one-third the narcotic value of ethanol on a weight-for-weight basis (6). Other low molecular weight alcohols, such as methanol and isopropyl alcohol also have a milder narcotic effect than ethanol but are known to be toxic or lethal when present in high serum concentrations. Propylene glycol is metabolized to D-lactate which may accumulate primarily in the brain, and may contribute to central nervous system abnormalities including nystagmus, ataxia, seizures, depression, disorientation and stupor. It may also result in acute renal insufficiency, cardiac arrhythmias, and respiratory arrest. In large quantities PG produces narcosis which may result in death (3,6,7).

Most cases of human PG toxicity result from medication administration intravenously, orally or topically. Most of the reports in the literature are due to its delivery in conjunction with intravenous medications (6,8–14). The majority of these patients at the time of intoxication were being maintained on ventilatory support (6,8–11). In those on ventilatory support, the maximum serum PG concentration recorded was 5200 mg/L (6). Of those who were not noted to be on ventilatory support at the time of intoxication (12–14) the highest PG level recorded was in a 46-year-old man who had a “near fatal” PG intoxication from intravenous diazepam. His PG concentration was 13,000 mg/L (13). All patients survived the toxic insult. Demey et al. (15) reported on a 72-year-old woman with impaired renal function who was comatose secondary to PG

used as a medication solvent. Her plasma PG concentration was 9100 mg/L. She was in intensive care but whether or not she was on ventilatory support was not mentioned. Her condition improved following hemodialysis.

An 8-month-old male treated with PG-containing silver sulfadiazine went into cardiopulmonary arrest when his serum PG concentration was 3690 mg/L (3). Following resuscitation he was noted to have anoxic encephalopathy and was maintained on ventilatory support. While on ventilatory support his peak serum PG concentration was 10,590 mg/L. Bekeris et al. (2) reported on two patients who received topical medication containing PG. Hyperosmolarity was noted in both but PG concentrations were not mentioned. Both died of complications from burns. McKinney et al. (16) reported on two children who drank windshield cleaner containing PG. The younger boy had a maximum PG concentration of 3740 mg/L and was drowsy. The older boy, who showed minimal clinical effect, had a maximum PG concentration of 3670 mg/L. Both recovered without complications. Cate et al. (17) reported on a 58-year-old schizophrenic man with azotemic renal failure who presented with stupor. His blood PG concentration was 700 mg/L. He recovered following therapy. No source for the agent was discovered. The authors suggested that PG toxicity would be unlikely to occur in healthy adults free of renal disease unless massive amounts were ingested.

In Case 2 reported here, the source or quantity of the product consumed that resulted in a blood PG concentration of 4410 mg/L at autopsy is not known. Of interest, the decedent had access to propylene oxide which can be metabolized to PG via epoxide hydrolase (18). He died approximately 9.5 h after his mother picked him up. Since the half-life of PG is 2–5 h, this value is probably well below his peak PG concentration. The man in Case 3 died approximately 45 h after presumed ingestion of antifreeze. Postmortem blood PG and EG concentrations were 538 mg/L and 384 mg/L respectively. Of the cases referenced in this report, two people on ventilatory support had PG concentrations of 4420 mg/L and 5200 mg/L which are higher than those found in Case 2 (6,8). Two people who were not noted to be on ventilatory support also had significantly higher PG concentrations than Case 2: 9100 mg/L and 13,000 mg/L (13,15). A chronic alcoholic with acute ingestion of ethanol and antifreeze had a serum ethanol concentration of 167 mg/dL and a serum PG concentration of 4700 mg/L (19). He was discharged on hospital day 2. There is, however, a report of an 8-month-old patient who had a cardiopulmonary arrest when his PG concentration was 3690 mg/L (3).

At autopsy, Case 2 was also found to have cardiomegaly and this, along with renal impairment (BUN 90 mg/dL and creatinine 3.4 mg/dL), may have contributed to his demise.

PG is a pervasive compound with low toxicity; however, it must be included in the differential diagnosis of patients with metabolic acidosis. In rare cases it may by itself (Case 2) cause or, in combination with other chemical agents (Cases 1 and 3), contribute to death. However, the absolute lethal blood concentration of PG has certainly not been established, in this or other reports.

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