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TAIWAN NATIONAL POISON CENTER SURVEY OF GLYPHOSATE - SURFACTANT HERBICIDE INGESTIONS

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ABSTRACT

Between January, 1986 and September, 1988, the Taiwan National Poison Center recorded 97 telephone consultations (49 male, 48 female) on cases of ingestion of glyphosate-surfactant herbicide concentrate containing the isopropylamine salt of glyphosate (N-phosphonomethyl glycine, CAS 1071-83-6) and a non-ionic tallow amine surfactant. Eleven of the cases resulted in fatalities, all among those attempting suicide. The average amount ingested by survivors was 120 $\pm$ 112 mL and by nonsurvivors was 263 $\pm$ 100 mL ($p \leq 0.0001$). The average age of survivors was 35 $\pm$ 15 years compared to 54 $\pm$ 11 years for fatalities ($p \leq 0.0002$). Irritation of the oral mucous membrane and gastrointestinal tract was the most frequently reported effect. Other effects recorded were pulmonary dysfunction, oliguria, metabolic acidosis, hypotension, leukocytosis and fever. Fourteen patients received either atropine or pralidoxime plus atropine despite the fact that glyphosate does not inhibit acetylcholinesterase. Thirteen percent of patients received a urine test for paraquat or treatment customarily used for paraquat ingestion, possibly reflecting similar initial presentations following ingestion of these two herbicides. Laboratory differentiation is essential if any doubt exists about which herbicide was ingested. Patients ingesting large volumes of concentrated glyphosate-surfactant herbicide formulations require close observation and supportive treatment. *(Key words: glyphosate; CAS: 1071-83-6; Round-up®; herbicides/poisoning; surface-active agents/poisoning)*

INTRODUCTION

The National Poison Center of Taiwan at the Veterans General Hospital in Taipei is a referral and telephone resource center for health professionals regarding human intoxication emergencies. Approximately 30% of its calls regarding toxic emergencies in 1987 involved agricultural chemicals compared to only 4-5% of the calls reported by the American Association of Poison Control Centers National Data Collection System for fungicides, fertilizers, insecticides, and herbicides in the same year (1). This higher percentage reflects the preferential use of insecticides and herbicides for attempted suicide in the Taiwan countryside.

Although glyphosate-surfactant herbicide (GlySH) is considered to be slightly toxic in rats in Gosselin's rating system (2), ingestion of a substantial volume of GlySH concentrate has been associated with toxicity and death in humans (3-5). The product contains the isopropylamine salt of glyphosate (41%), a nonionic tallow amine surfactant (15%) and water.

To further investigate the toxic syndrome as described by Sawada and Nagai (3), the Taiwan National Poison Center telephone consultations on ingestion cases of GlySH recorded from January 1986 through September 1988 were reviewed. This paper summarizes the findings of these 97 ingestions.

METHODS

All standard telephone consultation forms of the National Poison Center were reviewed from January, 1986 through September, 1988, to identify records of human exposure to glyphosate preparations containing a surfactant. Most of the records indicated ingestion of the brand name formulation Nien Nien Chun. Registered formulations are available under several other names, including Hao Ni Chun, Lan Da, Fukwei Chun and Mien Tswu Tsao. Nien Nien Chun is equivalent to the formulation sold under the name of Roundup® herbicide in western countries.

We eliminated records of non-oral exposures since no significant health effects have been documented following dermal or mist inhalation

exposures. Data selected for tabulation were date of report, age, sex, amount ingested, suicidal or accidental exposure, hours delay between exposure and presentation for medical care, decontamination procedures (lavage, activated charcoal, fuller's earth) and use of atropine and pralidoxime. Details of the clinical course as obtained at the time of the initial call and on subsequent follow-up were used to determine the severity of toxic effect.

Amount Ingested

Amounts of herbicide concentrate ingested are estimates obtained at the time of the first call to the National Poison center from the treating physician. He in turn relied on the history given by the patient or the family, and physical evidence such as the size of the bottle and remaining contents. For statistical purposes, we assigned a volume to descriptions of "a little" or "a spoon" (N = 5) as 5 mL and "a mouthful" (N = 23) as 25 mL (6) and a "small cup" (N = 1) as 100 mL. For reports indicating an entire or fractions of a "bottle" (N = 11), we assumed it was the intermediate, 300 mL, size of the available bottles (150 mL, 300 mL, 500 mL and 1 liter). In the remaining 52 cases, the initial estimate of amount ingested was given in milliliters. None of the fatal cases required an arbitrary assignment of volume ingested. The five cases without an initial dose estimate were excluded from any analysis of amount ingested. None of the cases had measurements of serum or urine glyphosate or surfactant content.

Criteria for Severity

The cases were assessed for severity of symptoms based on the criteria described in Table 1. Only the clinical details recorded in the Poison Center record were used for this evaluation.

Statistical Analysis

Difference in age, amount ingested, and delay in medical care between fatal and nonfatal cases were tested using the Student's t test. The Student's

TABLE 1

Criteria of Severity Classification

Asymptomatic -	no complaints or abnormality on physical or laboratory exam
Mild -	Transient symptoms localized to oral mucosa or GI tract
Moderate -	Any or all of the following: Duration of GI symptoms < 24 hours, GI bleeding, endoscopically verified esophagitis, oral ulceration, transient hypotension or oliguria, pulmonary dysfunction not requiring intubation, transient hepatic or renal damage, acid-base disturbance.
Severe -	Any or all of the following: Pulmonary dysfunction requiring intubation, renal failure requiring dialysis, hypotension requiring pressor amine treatment, cardiac arrest, coma, repeated seizures, death.

t test was also used to determine whether there was a difference in amount ingested between cases who attempted suicide and cases who accidentally ingested GlySH.

To determine what effect dose might have on severity of symptoms and fatality, two multiple regression analyses were performed. All of the above tests were done with SAS® statistical software.

ILLUSTRATIVE CASE REPORTS

Case Report 1

A 51 year-old male drank 150 mL of GlySH with suicidal intent. Vigorous vomiting ensued. Four hours after ingestion, he was treated by a

community doctor with gastric lavage, atropine, and furosemide. Seven hours after ingestion, he was transferred to Veterans General Hospital, Taipei, because of deteriorating condition. On arrival, his blood pressure was 90/70 mm Hg, pulse 138 bpm, respiratory rate 20 per minute; lung exam revealed diffuse rhonchi and wheezing. Chest x-ray revealed bilateral interstitial and alveolar infiltrates. The hemoglobin was 19.7 g/dL (197 g/L), white cell count 12,100 per mm^3, platelets 249,000 per mm^3, blood urea nitrogen 21 mg/dL (7.5 mmol/L), serum creatinine 1.5 mg/dL (133 μmol/L), aspartate aminotransferase (AST) 63 U/L (1.04 ukat/L), alanine aminotransferase (ALT) 14 U/L (0.22 ukat/L). Arterial blood gas while breathing room air revealed pH 7.31, PaO_2 27, $PaCO_2$ 35. He was intubated and ventilated with positive end expiratory pressure. Worsening hypotension occurred despite intravenous dopamine and fluids. The pulmonary infiltrates increased. Cardiac arrest occurred 18 hours after ingestion from which he was resuscitated. Twenty-four hours after ingestion the gamma glutamyl transpeptidase (GGT) was 81 U/L (1.35 ukat/L), AST 101 U/L (1.68 ukat/L), ALT 52 U/L (0.87 ukat/L), blood urea nitrogen 44 mg/dL (16.5 mmol/L), creatinine 5.0 mg/dL (442 μmol/L). His blood pressure was undetectable by cuff. He died 36 hours after ingestion (See addendum).

Case Report 2

A 77 year-old female drank approximately 200 mL of GlySH with suicidal intent. One hour after ingestion, she was reportedly asymptomatic. Twelve hours later during the night, her pulmonary function and blood pressure began to deteriorate. By the morning, her arterial blood gas showed pH 7.05, PaO_2 41, $PaCO_2$ 65. Systolic blood pressure was 50 mm Hg on dopamine and her heart rate was 62 bpm. She failed to improve and then died about 46 hours after ingestion (See addendum).

Case Report 3

A 51 year-old female drank approximately 200 mL of GlySH with suicidal intent and vomited soon after ingestion of the material. An hour

later in the emergency room, her blood pressure was 110/84 mm Hg, mental status was clear, pupils were 5 mm in diameter and bilateral expiratory wheezing was heard. Thirty minutes later, her blood pressure was 90/60 mm Hg and her pulse was 70 bpm. She was given fuller's earth, mannitol and castor oil via nasogastric tube which she vomited. Two hours after ingestion, her systolic blood pressure was 50 mm Hg, and arterial blood gas on room air showed pH 7.21, PaO_2 54, $PaCO_2$ 37. Six ampules of sodium bicarbonate and supplemental oxygen were given. Fourteen hours after ingestion, she required mechanical ventilation; her blood pressure was undetectable despite dopamine and norepinephrine administration. Her central venous pressure was 8 cm of water. Nineteen hours after ingestion, her cardiac rhythm became irregular; lidocaine was given. Death occurred shortly thereafter (See addendum).

RESULTS OF SURVEY

Ninety-eight poison center telephone consultation records reported ingestion of GlySH concentrate. One case, originally reported as GlySH but with a clinical course compatible with and urine test confirmation of paraquat poisoning, was excluded. Of the remaining 97 cases, there were 49 males and 48 females. Eighty-eight people ingested GlySH with suicidal intent, five accidentally, and four with uncertain intention. There were 11 fatalities (7 women, 4 men), all among those attempting suicide, which represented 11.3% of the 97 cases reported.

Patient Characteristics

The average age of all nonfatal cases was 35 $\pm$ 15 years (range 12-75 years) and of all fatal cases was 54 $\pm$ 11 years (range 40-77 years), $p \leq 0.0002$. The amount of GlySH ingested averaged 120 $\pm$ 112 mL (range 5-500 mL) in non-fatal cases and 263 $\pm$ 100 mL (range 150-500 mL) in fatal cases, $p \leq 0.0001$. Ingestions in those with intent of suicide but who survived averaged 131 $\pm$ 114 mL. Accidental ingestions averaged only 25 $\pm$ 22 mL

TABLE 2

Characteristics of Fatal vs Non-Fatal Ingestions of GlySH

Outcome	N	Age (yrs)*	Amount Ingested (mL)*	Treatment (hrs)‡
Fatal	11	54 ± 11	263 ± 100	2.3 ± 2.0
Survival	86	35 ± 15	120 ± 112	5.8 ± 11.5

*$p \leq 0.0002$

‡$p \leq 0.01$

and all survived. There were no differences in the mean amounts ingested by males compared to females for either fatal (262 ± 75 mL vs 264 ± 118 mL) or nonfatal (104 ± 103 mL vs 138 ± 121 mL) ingestions. Likewise, there were no differences in mean age of males compared to females for the outcome of fatality (50 ± 8 years vs 57 ± 12 years) and survival (36 ± 17 years vs 34 ± 13 years).

The average time interval between ingestion and presentation for medical care was 2.3 ± 2.0 hours in those with a fatal outcome (range 0.1 to 7 hours) compared to 5.8 ± 11.5 hours in those who survived (range 0.1 to 72 hours, $p \leq 0.01$). Table 2 compares the outcome with average amount of GlySH ingested, age, and time interval between ingestion and presentation for medical care.

Table 3 shows division of the cases by decade of age. The peak incidence of ingestion is in the 20-29 year age group (N = 31). Those younger than 20 years tended to drink smaller volumes although most were suicidally motivated.

No deaths occurred in those younger than 40 years. The mortality rate in those over the age of 40 (N = 41) was 27%. The minimum lethal dose recorded was 150 mL.

TABLE 3

Ingestions of GlySH by Decade of Age

			Mean Dose (mL) ± S.D.*	
Age (years)	N	Deaths (%)	Survivor	Fatality
< 20	9	0	35 ± 28	
20-29	31	0	129 ± 121	
30-39	16	0	186 ± 123	
40-49	17	4 (24)	77 ± 87	312 ± 144
50-59	11	3 (27)	132 ± 116	217 ± 76
60-69	7	3 (43)	127 ± 151	267 ± 58
70-79	6	1 (17)	53 ± 44	200
All	97	11 (17)	120 ± 112	263 ± 100‡

*Estimate of amount ingested was available only for 92 of 97 cases

‡$p \leq 0.0002$

Severity

Based on our criteria, 12 patients were asymptomatic, 28 had mild, 33 moderate, and 16 severe symptoms. The records of eight patients had insufficient clinical detail to permit scoring of severity. The average amounts ingested by the four symptom groups were 31 ± 31 mL, 72 ± 80 mL, 176 ± 128 mL and 216 ± 118 mL, respectively. In the first multiple regression analysis, severity of symptoms, scored from 1 to 4, was the dependent variable and age in years, sex, and dose in milliliters were the predictors. In this equation, only increasing dose was a significant predictor of increasing severity of symptoms ($p < 0.0001$), although increasing age was almost significant ($p = 0.0697$).

In the second equation, the multiple logistic regression model was fit to the binary dependent variable fatality. Again age in years, sex, and dose

TABLE 4

Dose - Fatality Relationship for GlySH*

Estimated Ingested Dose	Cases	Deaths
≤ 50 mL	27	0
50 - 99 mL	15	0
100 - 149 mL	9	0
150 - 199 mL	9	2
200 - 249 mL	10	3
250 ml +	22	6
Total	92‡	11

*p = 0.0018

‡Five cases without initial dose estimate excluded from the table

in milliliters were used as predictors. Both increasing dose (p = 0.0018) and increasing age (p = 0.00013) were significant predictors of fatality. (Table 4)

Co-Ingestion of Other Agents

Ten of the 97 cases reported a history of ingestion of another substance in addition to GlySH: ethanol (N = 8), two tablets of an unspecified hypnotic (N = 1) and an organic arsenical (N = 1). Death occurred in one of the eight ingesting ethanol plus concentrated GlySH.

Treatment and Diagnosis

All of the patients received supportive and symptomatic treatment. Ninety-five patients were admitted to the hospital overnight or longer.

Gastric lavage was performed in 61 of the 97 cases and induced emesis in two despite the high rate of spontaneous vomiting. Adsorbent was delivered to 25 patients: activated charcoal to 18, fuller's earth to six, and

bentonite to one. A saline cathartic was administered to 19 patients, and castor oil to two patients.

Atropine was administered to 14 patients. Pralidoxime (PAM) was additionally given to six of these. Glyphosate is not a cholinesterase inhibitor (7). The presence of a phosphono-group in the structure may incorrectly suggest cholinesterase inhibition.

Four of the patients who received atropine died. This may reflect either an iatrogenic atropine toxicity contributing to mortality or a more severe clinical presentation prompting the clinicians to try an antidote.

Urine or serum tests for paraquat were performed in 11 patients because of a high degree of clinical suspicion for paraquat ingestion. These were negative in all but one case. One patient who had not ingested paraquat underwent hemoperfusion because of a mistaken clinical diagnosis of paraquat poisoning.

Clinical Findings

The patients' symptoms and physical findings reported to the poison center were categorized as follows:

Mental Status

Eleven individuals were reported to exhibit abnormal states of consciousness at some time in the clinical course. The initial mental status evaluation was abnormal only in those who had co-ingested other substances or were treated with atropine except one person who was "drowsy". Mental status alteration developed later in the course of severe poisoning and may be attributable in whole or in part to hypoxia or hypotension.

Oral Membranes and Gastrointestinal Tract

Forty patients complained of oral and throat pain. Seven of the 40 exhibited oral mucosal ulceration, six reported dysphagia, three had a husky voice, and one showed excessive salivation. Since the acetylcholinesterase

TABLE 5

Endoscopy after Ingestion of GlySH

Age	Sex	Amount Ingested	Days After Ingestion	Finding
23	M	300 mL	4	Hyperemia of mucosa in mid esophagus without ulcer or erosion. Hemorrhagic gastritis (moderate) in high and mid body of stomach. Duodenum negative to 2nd portion.
75	F	125-150 mL	5	Esophagitis
17	M	40 mL	3	Moderate superficial esophagitis; mild gastritis
23	F	50 mL	Same Day	Mild gastritis
30	M	300 mL	7	Edema of stomach mucosa
18	M	25 mL	3	Gastritis
29	M	30 mL*	4	Mild antral gastritis

*Plus 1 bottle of wine

level was within normal range this may represent drooling from difficult swallowing. Reports of endoscopy were recorded in the Poison Center records of seven patients, detailed in Table 5. No full thickness mucosal injury was found; however, gastritis, esophagitis, and mucosal edema were seen. Most of these endoscopies were not performed in the acute phase following ingestion, but only after prolonged symptoms indicated the evaluation.

Forty-three patients continued to vomit after presenting for medical care; three of these had hematemesis. Twelve had diarrhea, including one passing bloody stool. Only ten complained of persistent abdominal or

epigastric pain, although more than half of all patients received antacid therapy during hospitalization, presumably for epigastric discomfort.

Pulmonary

Evidence of pulmonary involvement was found in 16 patients by abnormalities in radiograph, arterial blood gas, or physical examination. Aspiration pneumonitis was suspected in only one case. Thirteen severely affected patients required intubation and mechanical ventilation for respiratory failure; 10 died. Diffuse pulmonary damage was apparent radiographically and suggestive of non-cardiogenic pulmonary edema. Rales, rhonchi, wheezing, cyanosis, dyspnea, and cough were accompanying clinical symptoms. Mild asymptomatic hypoxemia on room air ($PaO_2 < 85$) was detected in three additional patients. Among cases categorized as severe, the initially normal pulmonary status deteriorated within the first twelve hours after admission. Intensive therapy failed to reverse the hypoxemia in fatal cases complicated by pulmonary edema.

Cardiovascular Effects

Shock was a feature recorded in nearly all severe cases of poisoning with GlySH. Blood pressure was normal on initial evaluation in 10 cases but deteriorated over the ensuing hours. In 7 additional cases, the first recorded blood pressure indicated hypotension (systolic < 80 mm Hg). In three cases, the first recorded blood pressure was elevated (diastolic $\geq$ 100). One initially hypertensive person later developed shock.

The records do not systematically document the characteristics of the electrocardiogram; thus, no assessment of arrhythmogenicity can be made. One unattended woman died suddenly; dysrhythmia cannot be excluded. In another case, ventricular dysrhythmia was documented before death. Several cardiac arrests were preceded by bradycardia. These dysrhythmias may have been precipitated by general physiologic decline and not necessarily by direct effect of the agent ingested.

Renal

Oliguria or anuria was documented in 10 patients. Only one of those seriously poisoned survived long enough to develop renal failure and undergo hemodialysis. Seven of these 10 patients also had documented hypotension, which may have caused or contributed to the decreased urine output.

Both serum creatinine and blood urea nitrogen tended to be normal or slightly elevated initially. In most cases, no serial data were available to ascertain progressive renal injury.

Two patients developed gross hematuria and two developed microscopic hematuria. Urinary tract catheterization may be responsible for lower tract injury as the source of bleeding. Prothrombin or partial thromboplastin times were not reported.

Metabolic Acidosis

Arterial blood gas measurements were recorded in 18 patients including nine of the eleven fatalities. Metabolic acidosis was seen in 14 (78%). The average initial pH measured in fatal cases was 7.18 $\pm$ 0.13 compared to 7.25 $\pm$ 0.20 for nonfatal cases. No additional data are available from this series to confirm the presence, magnitude, and etiology of metabolic acidosis in patients following significant GlySH ingestion.

Other Abnormalities

Mild temperature elevations (>37.5^{o}C) were recorded in seven patients. White blood cell counts were reported in only 14 patients and were greater than 10,000 cells per mm^3 in 11 (average 14,300, range 6,000 - 28,000 cells per mm^3). Serum acetylcholinesterase was measured in two patients and found to be in the normal range. Amylase was elevated in one patient (> 700 U/L [11.67 ukat/L]) and normal in two others.

Hepatic transaminases (AST, ALT) were recorded for 10 patients and either one or both enzyme activities were mildly elevated in four (AST up to 237 U/L, 3.95 ukat/L); ALT up to 270 U/L, 4.5 ukat/L). No serial observations were available.

DISCUSSION

GlySH is a concentrated preparation containing the isopropylamine salt of glyphosate (41%), a nonionic tallow amine surfactant (15%) and water. The dilution for use is approximately 40 fold to about 1% glyphosate salt and 0.4% surfactant. Glyphosate's toxicity to plants is dependent on a specific effect on the plants' shikimic acid metabolic pathway (8). The absence of this pathway in mammals may help explain the relatively low systemic toxicity of glyphosate (rat oral LD_{50} > 5,000 mg/kg) (9).

Mechanism of Toxicity

In previous reports, Sawada and Nagai (3,5) speculate that the surfactant in the formulated herbicide may be responsible for the clinical syndrome following massive ingestion. The comparative systemic toxicities of glyphosate and the surfactant in the rat (oral LD_{50} 5,000 mg/kg vs 1,200 mg/kg) support this theory. Tai et al. found the hypotensive effect to be due to the surfactant when the formulated product, the surfactant alone, and glyphosate alone were administered intravenously into dogs (10). This implicates the surfactant as the etiologic agent in hemodynamic abnormalities. However, the experimental conditions do not duplicate the clinical situation and must be interpreted cautiously.

In studies of the respiration of rat liver mitochondria using the oxygen electrode, Olorunsogo et al. suggested that uncoupling of oxidative phosphorylation could explain glyphosate intoxication (11). The study of Olorunsogo's data, however, reveals some unexplained inconsistencies. For example, the resting respiratory rates (State 4) were inconsistent in all the glyphosate treated rats, with the post-ADP rates higher (and more normal) than the pre-ADP rates. This phenomenon does not occur in uncoupled mitochondria. Furthermore, there is no relationship between dose of glyphosate given in the range of the sublethal to lethal doses (30-120 mg/kg) and respiratory control ratios (O_2 consumption in the presence of ADP/O_2 consumption in the absence of ADP) in isolated mitochondria. Finally, no

data on the effect of adding pure glyphosate (which is not metabolized in animals or man) on the oxidative phosphorylation of normal mitochondria were presented (12). Likewise, the clinical picture in this survey of patients ingesting up to 500 mL of a 41% glyphosate preparation is inconsistent with oxidative uncoupling. Tachypnea and tachycardia, the expected effects of poisoning with agents that uncouple oxidative phosphorylation, were not consistently seen and no cases of significant hyperpyrexia were encountered.

Clinical Syndrome

In our review, we found that ingested doses of a mouthful or more of the concentrate were capable of producing symptoms. The clinical toxic syndrome is comprised of hypotension possibly developing into shock, oral, esophageal and gastrointestinal mucosal injury, pulmonary edema, oliguria or anuria, metabolic acidosis, leukocytosis, and fever. The cause of death in most fatalities appeared to be intractable shock. It is of interest to note that in our series, death occurred only in those 40 years of age or older.

Limitations of Data

Our data have several limitations. First, the amount ingested is only an estimate derived by the treating physician at the time of the first call to the National Poison Center. We assigned an arbitrary numerical value to common measures recorded in the chart for 39 patients.

Secondly, because this was a retrospective survey, primarily of telephone consultations, the detail and scope of clinical information varies among the cases. Our findings represent a minimal occurrence of each abnormality. A higher incidence of positive findings might be revealed in a study systematically soliciting the data in current cases.

Third, the incidence of ingestion of GlySH may be underreported and the severity of toxicity overestimated by this review. Patients with less severe symptoms may not present themselves for medical care, thus biasing the data collection toward those cases with more severe reactions. On the other

hand, it is also possible, although not likely, that a patient rapidly developing severe symptoms after suicidal massive ingestion may die before care is sought. Likewise, the medical condition may not be attributed to ingestion of GlySH. Our call area is densest around the north of Taiwan in the urbanized area and decreases toward the central and south agricultural regions. Not all physicians use the National Poison Center for assistance; thus we do not know the total number of ingestions of GlySH on the island.

Lastly, there is no assurance that each case involved a GlySH ingestion since no serum or urine glyphosate analyses were available.

There apparently was a diagnostic concern in distinguishing GlySH ingestions from paraquat ingestions in a number of cases (13%). These herbicides may cause similar initial presentations - oral irritation, gastrointestinal distress, and hypotension in the setting of unimpaired mental status. One case, excluded from analysis, was confirmed in the laboratory to be due to paraquat ingestion but was originally reported as an ingestion of GlySH. We cannot judge if this situation existed in any of the other patients, but recognize this possibility of initial misclassification of exposure.

There may have been undetected co-ingestion of other toxins or possible ingestion of formulations of uncertain composition which may introduce confusion in description of the toxic syndrome. Clinical records are often inadequate to confirm the identify of the specific product.

Recommendations for Treatment

At this time, no specific treatment recommendations can be made for large volume ingestions of concentrated GlySH other than to provide intensive supportive care. Careful monitoring of the status of pulmonary, cardiovascular, and renal functions is essential. There is no proven antidote. Atropine and PAM are not indicated and may cause toxic effects when used indiscriminately.

There are no data to support or refute the benefit of steroids, hemodialysis, hemoperfusion, or forced diuresis in seriously ill patients. Hemodialysis removes glyphosate but a clinical focus on glyphosate removal

is misdirected if the surfactant is the primary toxic agent. Unpublished data (Yamashita et al.) indirectly show that the surfactant is bound by activated charcoal and thus indicate that charcoal hemoperfusion may be beneficial. However, this assumes that the surfactant does not undergo metabolism. One case report in the Japanese literature (4) describes urinary recovery of glyphosate following forced diuresis. Forced diuresis is potentially harmful because of the risk of fluid imbalance and there is no evidence that it favorably affects outcome.

Glyphosate can be detected in serum and urine by an HPLC method (13) but the assay is not widely available. Insufficient data exist to determine the clinical relevance of serum or urine glyphosate levels. No clinical assay is available to measure the surfactant at this time, or to assess specific therapies aimed at reducing absorption or increasing clearance of surfactant.

CONCLUSION

The toxic syndrome resulting from large volume ingestion of GlySH concentrate consists of mucosal and gastrointestinal irritation, hypotension, metabolic acidosis, oliguria, and pulmonary insufficiency. Effects on organs other than the gastrointestinal tract tend to occur with increasing amounts ingested. The data suggest that those over 40 years of age ingesting amounts greater than 150 mL are at the highest risk of a fatal outcome. In areas with high incidence of paraquat ingestion, a urine colorimetric test for paraquat is essential to distinguish it from GlySH to verify any suspected involvement with paraquat. Therapy for poisoning with GlySH consists of close observation and intensive supportive care.

ADDENDUM

The cultural influence of caring for the spirits of one's ancestors is seen in the custom of declaring a death at home, if possible. Ceremonial offerings, such as the burning of money, are easier to perform if the last known residence of the spirit in the body, i.e. the point of spiritual departure,

is close to the family. There are people who sneak into the hospital to burn money under the hospital bed because the family member died there. Thus, before death is declared, the family frequently requests transportation with all "life support" attached for discontinuation and declaration at home. In the opinion of the authors these requests are not made and granted until all hope is gone. It is unlikely that continued care would result in recovery. There have been deaths from ingestion of this herbicide formulation in western Europe and the United States, where the highest quality of technical care was available. Since this question might be raised in the mind of the general reader, references to this have been deleted from the case reports in the manuscript.

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