and coworkers; Case 3). Renal angiomyolipomata occur rarely in the general population but are not uncommon in patients with tuberous sclerosis.[14-16] This tumor is of special interest to urologists, since it may displace the pelves and calyces of kidneys and simulate a malignant tumor, or, when multiple and bilateral, may simulate conditions associated with polycystic kidneys.

Summary

A case of diffuse lymphangiomyoma, believed to be the thirtieth of record, is reported. Characteristic features of the disease are its predilection for women; occurrence in a localized form which is curable by complete surgical excision, or in diffuse form which progresses to death from cardiorespiratory failure; and onset with dyspnea, recurrent pleural effusions, spontaneous pneumothorax and chylous effusions in serous cavities. Pathologically it is considered to be a hamartoma, often of multifocal origin. Renal angiomyolipoma, reported in only one other instance, was present.

Treatment and prognosis are different for the localized than for the diffuse forms of the disease.

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Accidental Ingestion of Water Hemlock

Report of Two Patients with Acute and Chronic Effects

DAVID J. COSTANZA, MD
VINCENT W. HOVERSTEN, MD
San Francisco

WATER HEMLOCK is probably the most poisonous plant that grows in the United States. It is extremely toxic to livestock and to man. In two cases of severe poisoning in humans, the acute phase was manifested by convulsions, uncontrolled neuromuscular movements, respiratory distress, cardiovascular variability, and metabolic acidosis. The long-term chronic effects were electroencephalographic abnormalities and anxiety neurosis.

The toxic effects of cicutoxin in man were first recorded by Wepfer in 1679.[1] He reported several children poisoned by the Cicuta hemlock plant and noted "noncoagulation of the blood." In 1814 Stockbridge[2] reported three cases, which were the first in the United States; two of the patients died during violent convulsions. In 1911, Egdahl reviewed the literature and found reports of 47 cases in Europe and the United States.[3] The frequency of reports is now much greater and shows that cicutoxin toxicity is still a severe health hazard especially to children. Within the past two years two other reports from divergent areas of the country attest the continued danger of exposure,[4,5] and poisonings are still reported in Europe.[6] Two cases of accidental ingestion of large amounts of cicutoxin, in which the patients survived but had long-term aftereffects, are reported herein.

In 1969, five boys were hiking in the hills of

From the Marin General Hospital, Larkspur, and the Medical Service, San Francisco General Hospital, and the Department of Medicine, University of California, San Francisco.

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Reprint requests to: S. Nutter, Editorial Office, Room 4101, San Francisco General Hospital, 1001 Potrero Avenue, San Francisco CA 94110.

Marin County, California, when they became hungry and saw a plant that was similar to a known wild edible plant. Two ate several bites of the root (rhizome), which tasted like sweet wild anise, two tasted it and spat it out, and the fifth refused to taste or touch it. Approximately 20 to 30 minutes after ingestion the two boys, who were brothers, became nauseated while driving in the car. They started to salivate, had stomach cramps, and vomited repeatedly. At a nearby gasoline station both boys began to have repeated grand mal seizures. First aid was given and the police delivered the boys to the Emergency Room at Marin General Hospital.

CASE 1. A 15-year-old Caucasian boy was admitted to Marin General Hospital 31 January 1969, 30 to 45 minutes after ingestion of two or three rhizomes of the water hemlock plant, Cicuta virosa. The patient was cyanotic, had widely dilated pupils, and was in obvious respiratory distress. Blood pressure was 130/80 mm of mercury and pulse 120 beats per minute in supraventricular tachycardia. An oral pharyngeal airway was inserted. The patient began to have convulsions and 100 mg of phenobarbital and 100 mg of sodium diphenylhydantoin (Dilantin®) were given intravenously, and intravenous infusion of a solution of Ringer's lactate was started. A Foley catheter was inserted into the bladder. The cyanosis disappeared, respiration was labored, and naso-tracheal airway intubation was accomplished. A Bird Mark VII respirator was applied and respiration was continuously monitored. Blood pressure fluctuated between 80/60 and 170/90 mm of mercury and the heart rate varied from 50 to 120 beats per minute. The skin was warm and dry. The muscles were rigid and the pupils dilated widely and then constricted spontaneously. There were also periods of opisthotonos with severe rigid muscle spasms. All of these symptoms were observed repeatedly and seemed to have no relation to each other—they seemed to vary independently. Convulsions continued and pentobarbital sodium, 100 mg, was given every 30 minutes intravenously.

After lavage of the stomach, a universal antidote was instilled, and then 8 ounces of potassium permanganate 1:1000 in solution was left in the stomach for 45 minutes and withdrawn. Five percent sodium bicarbonate, 200 ml, was then instilled in the stomach and withdrawn. Convulsions continued intermittently despite treatment with pentobarbital sodium.

About an hour after admission a slight flush developed around the face and neck. Fluctuation of the pupils, clenching of teeth, severe muscle spasms and rigidity, and periodic episodes of severe opisthotonos and intermittent hemiballismic motions continued. Bilateral ankle clonus was present but Babinski and Hoffman reflexes and Wartenberg's sign were absent. The patient was restless and thrashed about. Sodium pentothal, 50 mg, was administered intravenously about 90 minutes after admission; the thrashing diminished in severity, but the convulsive disorder continued. After toxicologic consultation, 3 ml of paraldehyde was administered intravenously over a ten-minute period and the convulsions stopped. Blood pressure finally stabilized at 130 to 140/78 to 86 mm of mercury approximately two hours after admission. Maintenance doses of phenobarbital sodium, 60 mg intramuscularly every six hours, were started. Once the convulsions were controlled, the alternating bradycardia and tachycardia subsided, although the cardiovascular events were not directly correlated with the convulsive disorder. The electrocardiogram taken during the convulsive period was within normal limits, showing only sinus arrhythmia.

Laboratory data on admission were as follows: serum sodium 137, potassium 3.8, and chloride 99 mEq per liter, carbon dioxide combining power 7 mM per liter, phosphorus 2.2 mg per 100 ml, alkaline phosphatase 1.8 Bodansky units, creatinine 1.1 and blood urea nitrogen 13.0 mg per 100 ml. Bilirubin, amylase, calcium, glucose, albumin, and globulin were within the normal range. Leukocytes numbered 17,800 per cu mm with 62 percent lymphocytes, and the platelet count was normal. The prothrombin time was 15 patient seconds/12.5 control seconds on admission, but follow-up measurements were normal. The serial changes in serum glutamic oxaloacetic transaminase (SGOT), lactic dehydrogenase (LDH) and creatine phosphokinase (CPK) are summarized in Table 1.

Urinalysis revealed transient 2+ proteinuria; 5-hydroxyindoleacetic acid was normal at 3.1 mg in 12 hours.

The patient was rousable after ten hours, but not completely awake until approximately 24 hours after ingestion. He complained of soreness all over his body, particularly in the muscles of the arms and legs. He thought his mind was a little fuzzy but he was not sure about this. An

electroencephalogram was very abnormal, showing generalized excess of slowing throughout and a large amount of paroxysmal discharging, more prominent over the frontal areas and exhibiting alternating lateral predominance. A Neurologic Index of Mental Impairment (NIMI) test[7] revealed severe organic mental impairment. There was a steep rise in the levels of creatine phosphokinase and lactic dehydrogenase, which was attributed to muscle trauma secondary to convulsions and rigidity. An x-ray film on January 31 and a second electrocardiogram on February 2 showed no abnormalities. Before the patient was discharged, peeling of the skin on palms and soles was noted. The patient was discharged and Dilantin, 100 mg orally three times a day, and phenobarbital, 15 mg orally four times a day, were prescribed.

Approximately a week after discharge the patient had an acute anxiety reaction and was seen by a psychiatrist. He had hallucinations and visual flashes of white and purple and complained of a feeling of nausea when his eyes were closed. His symptoms were considered partly due to organic flashback and partly due to anxiety neurosis. Approximately three weeks after discharge the patient stopped taking the medications, against medical advice. Results of the two follow-up electroencephalograms and NIMI tests obtained on 11 February and 29 September 1969 were still very abnormal. The last NIMI test showed improvement with a score of 68 percent (normal for 12 years and older, 86 ± 7 percent), indicating mild loss of intellectual functioning for his age and grade level. The electroencephalogram on 29 September 1969 was mildly abnormal, showing pronounced improvement with only slight degeneralized and paroxysmal cerebral dysrhythmia.

CASE 2. A 14-year-old Caucasian boy was admitted to Marin General Hospital 31 January 1969 about 45 minutes after ingestion of part of one rhizome of Cicuta virosa. The patient was convulsing, cyanotic, and comatose. Blood pressure was 138/60 mm of mercury, pulse 84 beats per minute, and respirations wheezing in character between convulsions. Bowel sounds were audible without a stethoscope. The facial skin was flushed. An endotracheal tube was inserted immediately and an intravenous infusion of Ringer's lactate solution was started. The stomach was washed with 8 ounces of potassium permanganate solution 1:1000, and then a 5 percent sodium bicarbonate solution was instilled into the stomach and withdrawn. Simultaneously with the lavage, amobarbital sodium, 0.5 grams, was administered intravenously. Because of persistent convulsions, penthothal sodium, 50 mg, was given intravenously three times about 15 to 30 minutes apart. About an hour and a half after admission the blood pressure was 70/60 mm of mercury but increased spontaneously without vasopressors to 100/70 mm. Because of another convulsion, phenobarbital sodium, 120 mg, was administered intramuscularly. The wheezing and hyperactive bowel sounds ceased and the pupils became normal in size. The convulsions stopped completely about three and a half hours after admission, but the patient became very active, clenching his teeth, swinging his arms randomly, arching his back, and moving his whole body continuously. He was not responsive to commands. Intramuscular administration of paraldehyde, 3 ml, and another dose of phenobarbital sodium, 120 mg, did not appear to affect the hyperactivity. Therefore, diazepam (Valium®) was administered both intravenously (5 mg) and intramuscularly (5 mg). (By differing the regimen from that followed in Case 1, it was hoped to determine the best means of controlling the recurrent convulsions.) Repeated doses of Valium appeared to control the excessive activity in about 30 minutes. Eight hours after admission

TABLE 1.—*Laboratory Data Obtained on Admission and Subsequently in Both Patients*

	Date (1969)						
Constituent (unit)	*1/31-7:00 pm*	*2/1*	*2/2*	*2/3*	*2/4*	*2/11*	*2/12*
CASE No. 1							
SGOT (normal 50 units)	60	..	180	..	266	30	..
LDH (normal 200 units)	570	..	590	..	720	380	..
Creatine phosphokinase (normal 30 units)	103	..	1200	..	2400	38	..
CASE No. 2							
SGOT (normal 50 units)	106	18	..	1180	1060	..	40
LDH (normal 200 units)	700	1060	..	1870	1290	..	..
Creatine phosphokinase (normal 30 units)	99	128	..	2380	4000	..	56

the patient continued to have intermittent prominent flushing of the face and body, but a 12-hour urine test revealed a normal level of 5-hydroxyindoleacetic acid.

Laboratory data on admission were as follows: serum sodium 144, potassium 4.1 and chloride 104 mEq per liter, carbon dioxide combining power 7 mM per liter, phosphorus 2.7 mg per 100 ml, alkaline phosphatase 3.0 Bodansky units, creatinine 1.5 and blood urea nitrogen 13 mg per 100 ml, and amylase 375 Somogyi units per 100 ml. Glucose, calcium, bilirubin, albumin, and globulin were all within normal limits. Leukocytes numbered 21,000 per cu mm with 58 percent lymphocytes, and the platelet count was within normal limits. The leukocyte count returned to normal by the fifth day. Serial changes in SGOT, LDH, and CPK are summarized in Table 1.

About 30 hours after admission the patient wakened enough to ask what had happened. His muscles were very sore and the skin on his face was scaling almost as if he had been sunburned. Both conditions lasted for several days. On the second hospital day his temperature rose from normal levels to 39.4°C (103°F) and rhonchi were heard in his chest. The chest roentgenogram was clear but Hemophilus parainfluenza was cultured from the throat. Tetracycline therapy, 500 mg four times a day, was carried out until all evidence of infection disappeared. On 4 February 1969 an electroencephalogram showed prominent variable slowing throughout, with irritative features, and a NIMI test revealed decided intellectual impairment. Although still weak, the patient was discharged February 13. At this time both the creatine phosphokinase and serum glutamic oxaloacetic transaminase levels were still a little above the normal range. With the exception of occasional nightmares, no specific psychiatric problems occurred after discharge but an electroencephalogram taken 27 February 1969 was still abnormal although the NIMI test taken at the same time was within normal limits.

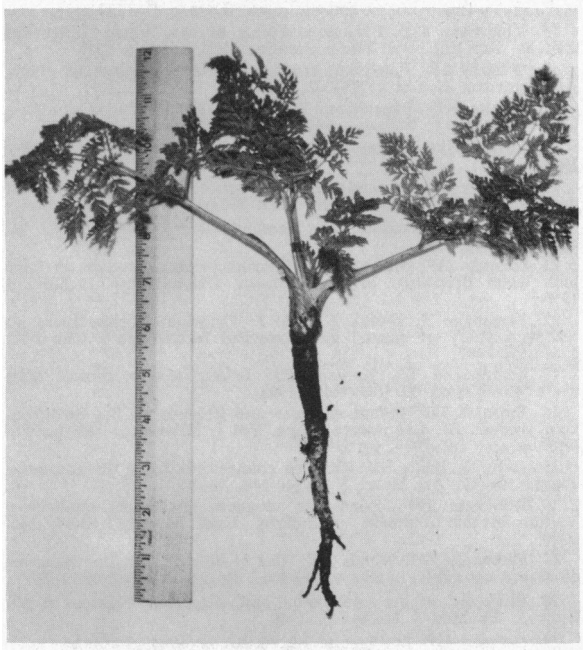

Figure 1.—Young Cicuta virosa plant, showing compound leaves and fleshy root. This species grows 8 to 10 feet high.

Discussion

Water hemlock, cow bane, five-finger root, "snake weed," "wild carrot," or Cicuta virosa (Cicuta maculata, Cicuta vagans) is of the botanical family Umbelliferae. It is a perennial plant with large compound leaves and clusters of fleshy roots (Figure 1) and is related to the parsley family. The plants are usually found in marshy ground around ponds or ditches. They may be mistaken for wild parsnips, artichokes, celery, sweet potatoes, and, in our case, sweet anise.[8-16]

Cicutoxin (an unsaturated aliphatic alcohol) is the toxic component of Cicuta virosa and is found in all parts of the plant, but the greatest concentration is in the root stock or rhizome. The usual lethal dose in an adult is one rhizome,[17] although whistles made from the hollow stems of the plant have caused deaths in children.[18] A piece of root the size of a walnut has been known to kill a cow, and a single root has been known to kill a horse.[3]

Usually nausea, salivation, emesis, and tremors develop within 30 to 60 minutes after ingestion. Abdominal cramps and projectile and violent vomiting occur, and severe convulsions ensue.[8,14,19,20] Death results from exhaustion and respiratory paralysis. Retrograde amnesia has been reported to be not uncommon upon recovery,[14,17] but so far as could be determined serial electroencephalograms and tests of mental function have not been reported heretofore.

Clinically we observed previously reported toxic reactions: salivation, nausea, projectile vomiting, abdominal cramps, restlessness, rigidity, opisthotonus, convulsions of severe and violent nature, widely dilated pupils, trismus, and retrograde amnesia. Additional physiologic effects that have not been reported elsewhere were hemiballismic type

motion, localized flushing, and subsequent peeling of facial skin and of palms and soles. The pronounced and varied reactions of the cardiovascular system observed in the two cases herein reported, including bradycardia, tachycardia, hypotension and hypertension, agree with clinical observations of Egdahl[3] and Statton[8] and the pharmacologic studies of this toxin by Grundy and Howarth.[21] In addition, Withers et al[5] reported no detectable pulse and demonstrated hypotensive effects in dogs when 95 percent ethyl alcohol extract of hemlock root was administered intravenously.

Of the abnormal laboratory data, the very low bicarbonate level probably resulted from metabolic acidosis and was possibly accentuated by respiratory alkalosis, although plasma pH was not determined. The high creatine phosphokinase levels reflected the severe muscle rigors, rigidity, and convulsions[22] and the lactic dehydrogenase levels also revealed a moderate elevation of LDH isoenzyme fraction 5, suggesting liver or skeletal muscle damage.[23,24] We believe that the persistence of these levels was attributable to severe muscle involvement in the convulsions, although we cannot be certain that direct muscle toxicity was not present. Elevated enzyme levels after convulsions are well known and they have been observed after convulsive shock therapy.[24] The increased prothrombin time in Case No. 1 is unexplained but may be due to liver involvement. Proteinuria was transient and may have been a nonspecific reaction of the toxin.

We found that Valium was more effective than paraldehyde or barbiturates in controlling the severe uncoordinated muscular movements of the acute phase. We were not able to evaluate or compare these drugs adequately with regard to their effectiveness in controlling seizures, but both were effective.[26-30] It was a relief to know that we had drugs to control these seizures and movements which were the wildest and longest convulsions in the experience of those on the medical and nursing staff attending these patients.

We conclude on the basis of the abnormal follow-up electroencephalograms and NIMI tests and the psychiatric evaluation that the toxic effects on the psyche and cerebrum were not transient. Chronic cerebral and psychiatric effects have not been reported heretofore. During the early convalescent period, one patient (Case 1) had dreams, fears, a feeling of non-wellbeing, attacks of acute anxiety, and visual phenomena. The electroencephalograms, NIMI tests, and clinical observations indicated severe organic mental impairment that persisted for several months.

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The Fairfax Police Department responded promptly to the emergency and gave excellent first aid. Professor Lincoln Constance of the Department of Botany, University of California, Berkeley, California identified the plant and rhizome, after the California Highway Patrol had swiftly taken them to him.

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