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Plant Poisoning

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Each year over 100,000 exposures to toxic plants are reported to poison centers around the country [1]. Most of these exposures are of minimal toxicity largely because of the fact that they involve pediatric ingestions, which are of low quantity. The more serious poisonings usually involve adults who have mistaken a plant as edible or have deliberately ingested the raw plant or tea made from the plant to derive perceived medicinal or toxic properties. Plants have been used since the times of antiquity for various reasons, such as hallucinogens, abortifacients, and antiarthritics. The plants within this manuscript have been chosen because they have been documented to cause fatalities or account for emergency medicine visits.

There is a poor correlation between taxonomy and toxicity. Members of the same family may have different toxic effects or sometimes, no toxicity at all. Not infrequently, a single plant may contain several different toxins. In this discussion, plants are grouped by their toxins rather than on the basis of their taxonomy.

Plant identification is often a daunting task. If a specimen is available, local nurseries may be of help in identification. Poison centers are usually a good starting point in the identification of plants and management of their ingestion. Most centers have botanical consultants and other resources that are of assistance in the event of plant exposures. As discussed in this article, there are few antidotes for plant exposures. With the exception of the plants containing the cardiac glycosides and those that have cholinergic and anticholinergic presentations, treatment is usually supportive.

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Toxalbumins (ricin, abrin)

Ricinus communis (castor bean) has had commercial importance as the source of castor oil, which has been used as a laxative and machine lubricant. Castor beans are generally the size of a peanut, mottled gray to brown in color. They, like the seeds of *Abrus precatorium*, are often used to make necklaces and bracelets. In several countries, castor beans are used medicinally as cathartics, emetics, and for the treatment of leprosy and syphilis. Although the castor bean was known to be poisonous for centuries, its major toxic component, ricin, was not isolated until 1905 [2]. *Ricinus*, *Abrus*, and *Jatropha* spp differ somewhat in appearance and taxonomy but contain toxins that are structurally and functionally similar. Ricin and abrin are generally considered to be the most potent (by weight) of plant toxins, though the plants containing them no longer account for major morbidity or mortality [3]. This is probably because most exposures are oral and, therefore, of much lower toxicity than the exceedingly rare parenteral exposure. Ricin has recently been on the news because of its association with terrorist activity, including in London (2001), South Carolina (2003), and Washington (2004).

Plants

Plants that contain toxalbumins are: *R communis* (castor bean, castor oil plant, palma cristi) (Fig. 1), *Abrus precatorius* (jequirty, roseary pea, prayer bean, crab's eye, mieniemienie, indian bead, Seminole bead, weather plant) (Fig. 2), and *Jatropha curcas* (coral plants, physic nuts, barbados nuts).

Fig. 1. *Ricinus communis* (castor bean).

Fig. 2. *Ricinus communis*/*abrus precartonius* (castor bean/jequirty pea).

Also, suspected plants are: *Hura crepitans*, *Robinia pseudoacacia*, *Momordica charantia*, and some species of *Sophora* [4].

Location

R communis is found throughout the southern United States but may be grown as an ornamental in the northern states. *Jatropha* and *Abrus* species have a more limited tropical range. Both may be found in Florida.

Toxic parts

All parts of the plant are toxic, especially the seeds. There is general agreement that if these seeds are left with the husk intact (unchewed), toxicity will not occur as they pass through the gastrointestinal tract.

Description

R communis (see Fig. 1) grows to 5 to 15 feet at maturity and has a palmate leaf. Seeds grow in clusters near the top of the plant and are covered with a spiney husk (see Fig. 2). *Jatropha* spp has a similar appearance. *Abrus precatorius* grows as a vine with compound leaves and tendrils. The seeds measure 0.3 cm by 0.8 cm and are scarlet with a black "eye" (see Fig. 2).

Mechanism of toxicity

Toxalbumins are proteins that bind to carbohydrates. Olsnes and colleagues [5] identified the molecular structure of both ricin and abrin in

1974. Both compounds consist of two peptide chains that are cross-linked by two disulfide bonds. The B chain, or "haptomer," binds to galactose containing receptors on the cell surface. The A chain, or "effectomer," then penetrates the cell and is transported into the cytoplasm to the ribosomes where it interrupts protein synthesis (Fig. 3). Wheat germ and barley have a similar "ribosome-inactivating protein," but due to their lack of a cell-penetrating B chain, they are not cytotoxic [6]. The cytotoxic properties of these compounds are being explored as a means of suppressing tumor cell growth [7] and in research to determine binding sites within nuclei [6]. Ricin, when parenterally administered to animals, has been shown to increase cardiac output, cause hemorrhage and necrosis of the heart, induce vasospasm of coronary arteries [8], and depress systolic and diastolic cardiac function [9]. Because these effects were demonstrated with purified toxin, other constituents of the seeds may contribute to the clinical picture. *R communis* seeds also contain a hemaglutinin, which does not appear to cause hemolysis when administered by the oral route [5].

Clinical presentation (oral)

The toxicity of castor bean is largely dependent upon the route of administration. By far the most common exposure is by way of the oral route. The most consistent presentation is that of gastrointestinal upset. In a review of 103 case reports from 1900 to 1985, Challoner and McCarron [10] found the signs and symptoms listed in Table 1.

Clinical presentation (parenteral)

Ricin, when administered by the parenteral route, is considerably more toxic as exemplified in animal studies. A case report by Knight [11] in 1979

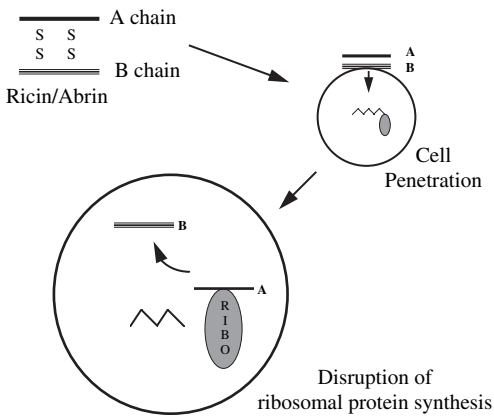


Fig. 3. The B chain of ricin attaches to the cell wall. Once inside, the A chain attaches to the ribosome and disrupts protein synthesis.

Table 1
Relative frequency of the signs and symptoms associated with castor bean poisoning

Symptoms/signs	Patients reporting (%)
Vomiting	84%
Diarrhea	83%
Dehydration	35%
Shock	27%
Abdominal pain	13%
Abnormal kidney function tests	9%
Leg cramps	6%
Abnormal liver function tests	5%
Acrocyanosis	5%
Hematuria	5%
Miosis	3%
Gastrointestinal bleeding	3%
Hemolysis	3%

seemed to confirm the parenteral toxicity of this compound. The case report is based upon a coroner's inquest, and premortem details are incomplete. A 49-year-old Bulgarian broadcaster was brought to a London hospital after being jabbed in the posterior thigh with an umbrella while standing on a street corner. His initial complaint was fever and malaise. A circular area of inflammation with a central punctate lesion of 2 mm diameter was noted on his posterior thigh. The following day, his white blood cell count was 33,000 per cm^3, and a tentative diagnosis of sepsis was made. He died on the third day. Postmortem examination revealed a platinum-iridium sphere beneath the puncture wound. It had been cross-drilled allowing for a volume of 0.28 cm^3. Based upon that information and the clinical course of an experimental animal injected with ricin, the diagnosis of ricin poisoning was made by a Government Chemical Defense official at Porter Down. No confirmation of the toxin could be made. In later years, however, circumstantial evidence seemed to support the claim. A more recent case of parenteral poisoning was reported by Fine and colleagues [12], which bears resemblance to the case reported by Knight. A 36-year-old chemist injected approximately 2 mg/kg ricin intramuscularly. The patient initially suffered from headache and rigors. His heart rate was 120, and blood pressure was 140/80 on admission. Two 3-cm erythematous patches marked the injection sites. His white blood cell count, amylase, aspartate aminotransferase, and alanine aminotransferase were mildly elevated. He remained intermittently febrile for 8 days and was released in good health after 10 days. Thus, parenteral injection of ricin in humans is not well documented, although its toxicity is thought to be severe. The clinical presentation of an oral exposure should not be confused with that of the potentially fatal parenteral exposure.

A precatorius (jequirty pea) seems to cause gastrointestinal irritation. The mechanism of action of abrin is similar to that of ricin. Clinical reports indicate that, like castor bean, gastrointestinal irritation is the most frequent

presentation associated with ingestion [13]. Reports of fatalities are from literature dating from the 1950s or earlier.

Jatropa seed has been reported to cause vomiting (64%), abdominal pain (52%), muscle twitching, nausea, salivation, and sweating. In the Phillipines, where *Jatropa* spp exposures are common, 98% of patients in one study were discharged in 24 to 48 hours with only supportive care [14]. *Jatropha* spp are grown as ornamental plants in the southern United States.

Allergic reactions

Several anaphylactic reactions to castor bean have been reported [15,16] in castor oil workers and in nonindustrial settings. Because several of these cases were reported in the distant past, they may serve to confuse the true clinical picture of castor bean ingestion.

Laboratory studies

There are currently no clinically useful determinations for ricin or abrin. Electrolyte status, complete blood cell count, liver function [17], and creatine phosphokinase should be monitored.

Management of oral exposures

Since the early 1900s, warnings have persisted about the potential lethality of castor beans [18]. Medical literature has perpetuated the idea that, if chewed, a single bean may kill a child, and perhaps as few as 8 beans could prove fatal to an adult. Rauber and Heard [19,20] reviewed medical literature from circa 1900 to 1984. Of 751 exposures to castor bean, there were 14 deaths for an overall mortality rate of 1.8%. Challoner and McCarron [10] reviewed a portion of those data and some more recent cases and established an overall mortality of 3.4% with only 1 death occurring since 1950. A review of the reported deaths indicates that the treatment, which in the early 1900s included oubain, cocaine, camphor, 20% fructose, digitalis, and strychnine, might have contributed to the mortality. Other fatalities seem to have been due to inadequate or no rehydration [16,20]. Based upon available information, the management of asymptomatic nonsuicidal patients who have consumed only a few seeds (*R communis, A precatorius, Jatropha* spp) should consist of oral administration of activated charcoal and close home monitoring. Hospital admission is indicated for patients who have developed symptoms or for asymptomatic patients who cannot be closely watched at home. Symptomatic patients should be given activated charcoal. The dose of activated charcoal is 50 to 100 g in 8 ounces of tap water for adults and 1 gm/kg or 25 to 50 g in 4 ounces of water for children. Aggressive fluid resuscitation and other supportive care is the mainstay of management of the more serious exposures. Cathartics are not indicated, and extracorporeal elimination is of no benefit.

Management of parenteral exposures

At present, there are insufficient data to make specific recommendations beyond supportive care. No antidote exists for oral or parenteral exposures. A vaccine to ricin has recently been developed and is currently undergoing clinical studies because of the concern regarding use by terrorists.

Cicutoxin

The first reports of toxic effects from *Cicuta* spp occurred in 1697. Stockbridge [21] reported the first case of poisoning in the United States in 1814. In a review of deaths reported to poison centers between 1986 and 1996, Krenzelok and colleagues [3] found reports of 19 deaths. Of these, *Cicuta* spp accounted for more than any other plant. Exposure to *Cicuta* and *Oenanthe* spp may be accidental as in most pediatric cases, but more commonly, the fatal cases involve misidentification of the plant as a foodstuff or as a hallucinogen.

Plants

Plants containing cicutoxin are: *Cicuta maculata* (water hemlock), *Cicuta douglasii* (western water hemlock), and *Oenanthe crocata* (hemlock water dropwort) (Figs. 4–6).

Fig. 4. *Circuta* spp flower (water hemlock).

Fig. 5. *Cicuta* spp root (water hemlock).

Location

Water hemlock grows in the eastern half of the United States and Canada. *C douglasii* (western water hemlock) grows in the western United States. *O crocata* is considered to be a European plant, but is reported to have been transplanted into the Washington, DC area [22]. These plants are found in or immediately adjacent to water. They are most frequently encountered in lakes or streams, but may be found in marshy areas.

*Description (*Cicuta *spp)*

These plants are generally found growing out of the water or close enough for their roots to make contact with the water. Both varieties form a low-growing bush that may be 3 to 4 feet tall. Stems are hollow and have a carrot-like odor. Flowers, which occur during the summer months, are small and white in flat-topped clusters or "umbels." Leaves of the eastern variety are sharply toothed like the western water hemlock, but *C maculata* has a longer, thinner leaf. *C douglasii* produces a more ovate leaf. Both plants have thick whitish roots which, when sliced sagitally, possess transverse stripes. The stripes may form small chambers late in the growing season. The roots have been mistaken for wild carrots. They are 5 to 6 in long, white, and, when cut, have a strong carrot-like odor.

Fig. 6. *Cicuta* spp (water hemlock).

Although the roots are characterized as having transverse chambers, they are frequently solid. Roots of *Oenanthe* spp are also said to secrete a yellowish sap when cross-sectioned [23]. Water hemlock bears a striking resemblance to other "umbellifores," which are nontoxic. *Heracleum lanatum* (cow parsnip) and *Daucus carota* (Queen Anne's lace) may be distinguished by their location and physical differences in the stem. Mistaking a toxic member of the Apiaceae family for a nontoxic one has been a fatal error for several foragers over the years [24–27]. Almost yearly, one to two deaths are reported to poison centers in the United States due to the ingestion of these plants.

Toxic parts

All parts of the plants are toxic, especially the roots.

Mechanism of toxicity

Though nausea and vomiting are considered to be the most consistent findings, seizure activity followed by cardiac arrest is the common sequence in fatal exposures [28]. An exact mechanism for the proconvulsant activity of cicutoxin has not been determined. Starreveld and Hope [29] suggested that seizure activity might be due to cholinergic overstimulation of the reticular formation or basal ganglia. Nelson and colleagues [30] performed a series of experiments in mice to explore the efficacy of anticholinergic agents in the prevention of cicutoxin-induced seizures. They found that

anticholinergic agents failed to protect the animals, whereas pretreatment with cholinergic agents did not appear to lower seizure threshold.

By 1979, a more appealing theory for cicutoxin's proconvulsant activity had arisen. Carlton and colleagues [31] suggested that cicutoxin (Fig. 7) is structurally similar to picrotoxin, an indirect antagonist at $GABA_A$ receptors. GABA receptors serve as ion channels to allow the passage of chloride ions into the neuron (Fig. 8). This hyperpolarizes the neuron moving it away from its threshold for firing. Many anticonvulsants, such as the benzodiazepines and barbiturates, act as indirect agonists at the GABA receptor. By preventing the action of GABA, picrotoxin hyperpolarizes the neuron, moving it closer to its threshold for firing. If cicutoxin acts on the GABA receptor at the picrotoxin site, seizure activity would be expected as it is with picrotoxin. This would also be consistent with Nelson's findings that seizures were better controlled in animals treated with diazepam or barbiturates than with other agents [30,32].

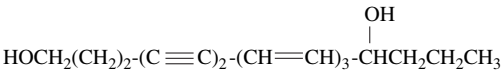
Clinical presentation

Case reports of *Cicuta* spp [24,28,29,33–35] and *Oenanthe* spp [23,36–39] ingestions are similar in presentation. Ingestion is followed by nausea, vomiting, and diaphoresis. Although these signs and symptoms have led some authors to speculate about increased cholinergic activity as the mechanism for seizure activity [29], the frequent reports of mydriasis [33–35] detract from this theory. The initial convulsion often occurs within the first hour. Repeated convulsions with intermittent lethargy ensue for the next several hours. Fatalities usually occur within 10 hours and are almost invariably associated with repeated seizure activity. *O crocata* poisoning has been estimated to be 70% fatal in one small series [38].

Rhabdomyolysis and renal failure have been reported [31]. Although some toxins may cause rhabdomyolysis directly, the presence of prolonged seizure activity that was reported in this patient may be the etiology.

Laboratory studies

Although clinically useful means of determining cicutoxin or oenanthotoxin are not available, methods of identification are described by King and colleagues [37] for the latter. These methods included ultraviolet absorption; thin-layer chromatography; high-pressure liquid chromatography; and mass spectrometry, which may be useful for later confirmation of exposure.



Cicutoxin

Fig. 7. Structure of cicutoxin.

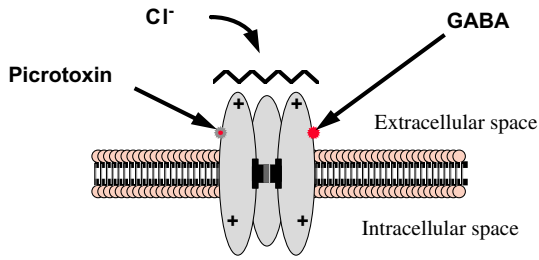


Fig. 8. When picrotoxin attaches to the GABA receptor, the chloride ionophore closes preventing hyperpolarization of the interior of the neuron.

Management

Asymptomatic patients should be given activated charcoal and observed for 4 hours postingestion. If no symptoms occur, they may be released. The dose of activated charcoal is 50 to 100 g in 8 ounces of tap water for adults and 1 gm/kg or 25 to 50 g in 4 ounces of water for children. Activated charcoal should not be given to a comatose patient until the patient's airway is protected.

Symptomatic patients frequently arrive after seizures have occurred. The patient's airway should be secured first. Diazepam or phenobarbital are most appropriate for seizure control and should be used aggressively. Phenytoin has no clear role in management of cicutoxin-induced seizures. Because of vomiting, and occasionally diarrhea, fluid replacement is often required. Creatine phosphokinase should be monitored because of the possibility of rhabdomyolysis. In addition to maintaining urine output, urine alkalinization may be of benefit in patients who have rhabdomyolysis [40]. Hemodialysis plus charcoal hemoperfusion has been performed in one case [41]; however clearance of cicutoxin was not measured, and the favorable outcome is consistent with many of the cases managed without extracoporeal elimination [34]. At this time, hemodialysis/hemoperfusion have not been shown to be beneficial. Seizure control and supportive care are the mainstay of therapy.

Cardiac glycosides

The medicinal properties of the cardiac glycosides were known to the ancient Egyptians as well as the Romans who used it as an emetic, heart tonic, and diuretic [42]. In 1785, William Withering published *An Account of the Foxglove and Some of Its Medical Uses: With Practical Remarks on Dropsy and Other Diseases* thus popularizing its use. In 1890, Sir Thomas Fraser introduced *Strophanthus* and its digitalis-like effects. Worldwide, these plants have been used as abortifacients, and in the treatment of leprosy, venereal disease, malaria, and as a suicide agent [43]. More than 200 naturally occurring cardiac glycosides have been identified to date. *Digitalis* spp ingestion is seldom reported. *Convallaria majalis* (lily of the valley)

exposures are associated with minimal morbidity and, in a recent review of 10 years of data from regional poison centers, have had no associated mortality [41]. Of the many plants containing cardiac glycosides, *Nerium oleander* is responsible for the greatest number of toxic exposures each year [44]. For that reason, this discussion is focused on that plant.

Plants

Plants containing cardiac glycosides are: *Digitalis purpurea*, *D lanata* (foxglove) (Fig. 9); *N oleander* (oleander) (Fig. 10); *Strophanthus gratus* (oubain); *Thevetia peruviana* spp (yellow oleander) (Fig. 11); *Convallaria majalis* (lily of the valley) (Fig. 12); and *Urginea maritima*, *U. indica* (squill). Other plants thought to contain cardiac glycosides: *Asclepias* (milkweed); *Calotropis* (crown flower) [45]; *Euonymus europaeus* (spindle tree); *Cheiranthus*, *Erysimum* (wall flower); and *Hellaborus niger* (henbane).

Location

Oleander is native to the Mediterranean and Asia, but thrives in both tropical and subtropical areas around the world. In the United States, where it is planted as an ornamental, it can be found from the Southeast to the Southwest. It may be grown in northern states, but does not survive freezing

Fig. 9. *Digitalis purpurea* (foxglove).

Fig. 10. *Nerium oleander* (oleander).

Fig. 11. *Thevia peruviana* (yellow oleander).

Fig. 12. *Convalleria majalis* (lily of the valley).

conditions. *Digitalis* spp and *Convallaria majalis* may be found throughout North America.

Description

N oleander is a shrub that may grow to 30 feet in some locations. The leaves are usually 6 in long and 1 in wide. The leaves are leathery with a smooth margin and overall lanceolate shape. Flowers of *N oleander* are red, white, or pink. Leaves of *Thevetia peruviana* are smaller but similar in shape, and they are yellow/orange.

Toxic parts

All parts of the plant are toxic. Seeds are said to contain more glycoside than other parts of the plant.

Mechanism of toxicity

Oleandrin (*N. oleander*) and thevetin (*T peruviana*) are structurally similar to digitoxin (Fig. 13). Because of this and the similarity of clinical presentation, the three are considered to act in similar fashion. The toxin attaches to the α subunit of the Na^+/K^+-ATPase pump to inhibit its action. Because this pump exchanges intracellular sodium ions for extracellular potassium ions, inhibition leads to an overall increase in intracellular sodium ions. Rises in intracellular sodium concentration result in secondary rises in intracellular calcium levels, explaining the positive inotropic effect of

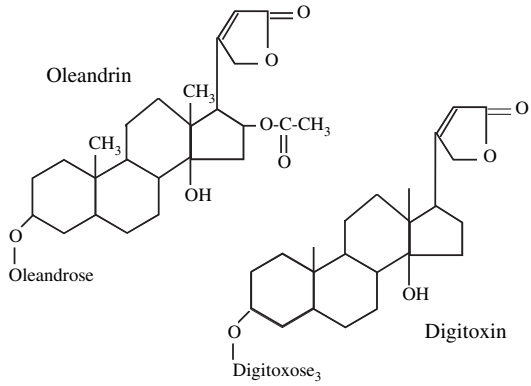


Fig. 13. Structures of oleandrin and digitoxin.

cardiac glycosides. In toxic amounts, the rises in intracellular sodium and calcium depolarize the cell after repolarization to cause late afterdepolarizations and increased automaticity typical of cardiac glycoside poisoning. Depolarization of baroreceptors innervated by the ninth cranial nerve triggers afferent reflexes, which increase vagal tone and produce bradycardia and heart blocks [46]. Severe poisoning results in hyperkalemia as the ability to pump potassium into the muscle is curtailed.

Clinical presentation

Gastrointestinal irritation is common with ingestion of *N. oleander or T peruviana*. The latter was studied as a potential antiarrhythmic agent in the 1930s, but was not marketed because it caused more gastrointestinal irritation than digitalis [47]. Saravanapavananthan and colleagues [48] reviewed 170 cases of *T peruviana* ingestion and found that vomiting was the most common presenting complaint (68.2%). Other symptoms are shown in Table 2.

Electrocardiographic effects have occurred in up to 61.8% of patients in one study (Table 3) [48].

PR prolongation, QT shortening, P- or T-wave flattening may occur [49]. Hyperkalemia occurs in more serious poisonings [49–51]. Central nervous system (CNS) depression may occur as a direct effect of the toxin [51],

Table 2
Relative frequency of signs and symptoms associated with oleander poisoning

Symptom	%
Dizziness	35.9
Diarrhea	38.0
Abdominal pain	5.9
Pain/numbness in tongue, throat, lips	4.1
No symptoms	12.9

Table 3
Relative frequency of dysrhythmias associated with oleander poisoning

Electrocardiographic change	%
AV block	52.4
Bradycardia	49.5
T-wave changes	35.2
ST depression	23.8
Ventricular ectopy	6.6
Atrial ectopy	2.8

but is frequently associated with bradycardia and hypotension. Death has been reported [48,49].

Laboratory studies

Osterloh and colleagues [50] described cross-reactivity of oleander glycosides on radioimmunoassay for digoxin. The test may serve as confirmation of the presence of cardiac glycosides; however, clinical symptoms are more indicative of toxicity. Postmortem serum concentrations are known to increase and do not predict the premortem levels [49].

Management

In general, management of cardiac glycoside toxicity from plants is the same as for digitalis toxicity. Airway control and other basic life support measures are the first concern. Gastric decontamination with activated charcoal should follow those measures. The dose of activated charcoal is 50 to 100 g in 8 ounces of tap water for adults and 1 gm/kg or 25 to 50 g in 4 ounces of water for children. Hyperkalemia may be treated with such agents as insulin and dextrose infusions, nebulized albuterol, and/or sodium bicarbonate infusion. Ventricular tachyarrhythmias may be managed with lidocaine, and bradyrythmias may respond to atropine or ventricular pacing.

Large doses of Fab-antidigoxin antibodies correct both rhythm and hyperkalemia in dogs poisoned by oleander [52]. Shumaik and colleagues [53] reported the use of digoxin-specific Fab fragments in the treatment of a 37-year-old man who had ingested *N oleander* leaves. Other reports of their use have supported those findings [51,54]. Indications for Fab fragments are shown in Box 1.

Grayanotoxins

Rhododendrons and azaleas were introduced into Europe from Asia in the mid-1700's to early 1800's. Both are parts of the 500 to 1000 natural species with numerous hybrids. Exact species identification can be difficult. The toxic components of this genus vary, and their presence in a given plant is difficult to predict. Although ingestion of leaves, flowers, nectar, or the use

Box 1. Indications for Fab fragments

1. Hyperkalemia (K+>5.5 mEq/L)
2. Refractory ventricular dysrhythmias
3. Hemodynamically significant bradydysrhythmia unresponsive to atropine
4. Severely symptomatic elderly patients should be treated aggressively with Fab fragments

of the leaves in the production of tea will produce toxicity, most poisonings result from consuming honey made from nectar of these plants. Honey poisonings are less common today, because honey from several different sources is combined before marketing. The earliest description of poisoning by these plants appears in the Anabasis, a description of the unsuccessful military expedition of Cyrus the Younger to overthrow Artaxerxes II (401–400 BC). The following is an account of the incident that took place in what is now northeastern Turkey on the coast of the Black Sea:

> The number of bee hives was extraordinary, and all of the soldiers that ate of the honey combs lost their senses, vomited, and were affected with purging, and none of them was able to stand upright; such as had eaten only a little were like men greatly intoxicated, and such as had eaten much were like mad men and some like persons at the point of death. They lay upon the ground, in consequence, in great numbers, as if there had been a defeat; and there was general dejection. The next day, no one of them was found dead; and they recovered their senses about the same hour they had lost them on the preceding day.

Several other recent accounts of the toxicity of "mad honey" are available [55].

Plants

Plants containing grayanotoxins are: *Rhododendron* spp (rhododendrons, azaleas), *Kalmia angustifolia (sheep laurel), Kalmia latifolia* (mountain laurel), and *Pieris* spp (Andromeda). Grayanotoxin I may also be found in honey made from the nectar of these plants (Fig. 14).

Location

Native to the temperate parts of the world, they are grown widely as ornamentals. *R occidentale*, *R macrophyllum*, and *R albiflorum* are of special interest on the West coast in the production of honey. Reports of contaminated honey have also occurred in the East where rhododendrons as well as *Kalmia latifolia* (mountain laurel) and *K angustifolia* (sheep laurel) may serve as a source of grayanotoxin.

Fig. 14. *Rhododendron* spp (rhododendron).

Description

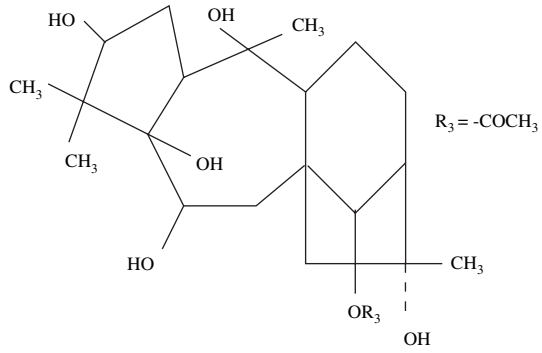
Leaves are evergreen, oblong, leathery, and have a smooth margin. They appear in whorls about the branch. Because of the many species, the leaf size is variable but generally ranges from 1 to 5 in. The flowers are white to pink (rhododendrons), and white, pink, magenta, crimson, or orange (azaleas).

Toxic parts

The entire plant is toxic.

Mechanism of toxicity

In 1955, it was discovered that the members of the Ericaceae family contained structurally similar compounds that were responsible for their toxicity. These compounds, which were formerly known as andromedotoxin, acetylandromedol, and rhodotoxin, are now termed *Grayanotoxin I* (Fig. 15) [56]. Grayanotoxin II and III are toxic derivatives of Grayanotoxin I. Animal studies initially indicated that these toxins were capable of producing respiratory depression, bradycardia, hypotension, and seizure activity [57]. Subsequent studies in squid axons have shown that Grayanotoxin I acts by attaching to the sodium channels of cell membranes and changing both open and closed channels to a modified open state. This increases sodium conductance dramatically and leads to cellular depolarization [58,59]. It seems that a single molecule of grayanotoxin is sufficient to activate a sodium channel [60]. This effect is thought to explain, in part, the CNS and cardiac



Grayanotoxin I

Fig. 15. Structure of grayanotoxin I.

manifestations of grayanotoxin poisoning. Masutani and colleagues [61] noted in their study of grayanotoxin effects on frog skeletal muscle, that grayanotoxin seems to contain four hydroxyl groups essential for its biologic activity. These are also present in veratridine (false and white hellebore), batrachotoxin (poison dart frog), and aconitine (monkshood).

The rises in intracellular sodium concentrations in the heart, baroreceptor cells, and brain cells mimic the effects of cardiac glycosides to produce increased automaticity, enhanced vagal tone (heart blocks, bradyrhythmias, and so forth), and CNS changes. Because Na+/K+-ATPase is not inhibited, hyperkalemia is notably absent.

Clinical presentation

Although most exposures are of little consequence [62], serious cardiotoxicity has been reported. Vomiting, loss of consciousness, and seizure were observed in a 27-year-old female who had ingested 75 mL of honey she had purchased in Turkey. She was hypotensive and bradycardic. Her only laboratory abnormality was a mild leukocytosis. Dysrhythmias included sinus node arrest, AV-escape beats, second-degree AV block, and intraventricular conduction block. The patient recovered after insertion of a cardiac pacemaker [63].

Laboratory studies

Thin-layer chromatography has been used to identify these compounds [64].

Management

Initial management should include the administration of activated charcoal if the ingestion has occurred within the last 2 hours. The dose of

activated charcoal is 50 to 100 g in 8 ounces of tap water for adults and 1 gm/kg or 25 to 50 g in 4 ounces of water for children. Supportive care is usually sufficient for management; however, bradycardia may be treated with atropine or cardiac pacemaker. Although experimental agents, such as tetrodotoxin [65], have been used to reverse the effects of Grayanotoxin I, no clinically available antidote exists. Lidocaine or other sodium channel–blocking antiarrhythmics (group I) would seem appropriate for ventricular arrhythmias.

Veratrum alkaloids

Veratrum alkaloids are found in the various species of *Veratrum* and *Zigadenus* found throughout the United States and in parts of Canada. Historically these plants have been used as sources of medicines and insecticide. Their toxicity was noted in sneezing powders, made from pulverized roots of these plants. Inhalation or ingestion has resulted in several signs and symptoms including hypotension or bradydysrhythmia. Teratogenicity in farm animals, particularly sheep, has been widely reported.

Plants

Plants containing veratrum alkaloids are: *Veratrum album* (white hellebore) (Fig. 16), *V californicum* (corn lily, skunk cabbage), *V viride* (false hellebore), and *Zigadenus* spp (death camus) (Fig. 17) [66,67].

Fig. 16. *Veratrum* spp (false hellabore).

Fig. 17. *Zigadenus* spp (death camus).

Location

V viride is found in Canada and the eastern United States from New England to Georgia. Related species are found in western United States (*V californicum*), Alaska and Europe (*V album*), and Asia (*V japonicum*) [68]. False hellebore tends to grow in low-lying, swampy areas, whereas white hellebore is found in alpine meadows [56].

Description

Veratrum plants are tall (2–7 feet) perennial herbs. Broad, longitudinally plicated leaves are spirally arranged on a stout stem. White to yellowish green pedicellate flowers line the terminal 30 to 60 cm of the stem. These plants also contain a highly seeded fruit [56].

Zigadenus spp is a genus of the lily family. It is found throughout the United States and Canada. Flowers are pale yellow, pink, or white. The leaves are long, thin, and grass-like. The root is a bulb that is similar in appearance to and often mistaken for wild onion. *Zigadenus*, however, lacks an onion-like odor [66,69].

Toxic parts

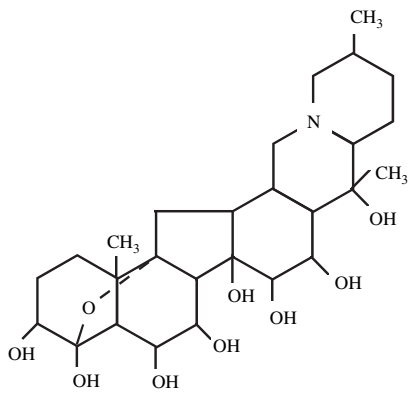
The entire plant contains toxic veratrum alkaloids; however, the bulb and flowers most commonly cause poisoning. Fruit seeds and leaves rarely cause human toxicity.

Mechanism of toxicity

The veratrum alkaloids, which are chemically similar to steroids, include protoveratrines (Fig. 18), veratridine, and jervine [68]. These agents were introduced in the 1950s as antihypertensive agents; however, they were found to have a narrow therapeutic index and their use was discontinued [68,70]. Of these steroidal alkaloids, veratridine is the most potent [60]. The primary activity of these compounds is to attach to voltage-sensitive sodium channels in conductive cells and increase sodium permeability raising intracellular sodium concentration–like grayantoxins. Veratrine affects only a limited number of the sodium channels, but those affected reactivate 1000 times more slowly than the unaffected channels (ie, slow recovery). These alkaloids also appear to block inactivation of sodium channels and change the activation threshold of the sodium channels so that some remain open even at their resting potential [60]. Again, the rise in intracellular sodium concentrations leads to increased automaticity, enhanced vagal tone without hyperkalemia, and occasional neurotoxicity. High doses given to animals result in cardiac arrest [71].

Clinical presentation

Poisoning with veratrum alkaloids most typically occurs after accidental ingestion of the plant secondary to confusion with an edible species [68]. Toxicity also results from inhalation of sneezing powders prepared from pulverized white hellebore root [72]. Nausea and vomiting are most commonly seen after ingestion of the veratrum alkaloids. Clinically significant bradycardia and hypotension are also generally seen. Other reported toxic effects have included abdominal pain and distention, salivation, respiratory depression, yellow or green scotomata, paresthesias, increased muscle tone,



Protoverine

Fig. 18. Structure of protoverine.

rigors, and rarely, seizures [68,70,72–74]. Various electrocardiographic changes have also been reported with veratrum poisoning. Marinov and colleagues [75] reported a characteristic electrocardiographic pattern in 10 of 12 patients poisoned with *V album* that included PR and QT interval shortening, ST segment depression, T-wave morphology changes, and bundle branch block. Quatrehomme and colleagues [76] noted nausea and vomiting followed by hypotension. In contrast to Marinov's observations, Quatrehomme and colleagues reported QT prolongation.

Characteristic facial deformities (cyclopia, cleft lip and palate, microphthalmia) and limb defects (bowed fibulae, shortened tibia, excessive flexure of the knees) occur in offspring of pregnant sheep who ingest plants containing veratrum alkaloids. Jervine and other steroidal alkaloids found in the *Veratrum* spp are responsible for these birth defects [77].

Laboratory studies

There is no clinically useful laboratory study to confirm veratrum alkaloid exposure.

Management

Initial management should include the administration of activated charcoal if the ingestion has occurred within the last 2 hours. The dose of activated charcoal is 50 to 100 g in 8 ounces of tap water for adults and 1 gm/kg or 25 to 50 g in 4 ounces of water for children. Bradycardia usually responds to atropine administration. Hypotension may or may not respond to the atropine. Crystalloid fluids or vasopressors, such as dopamine, have been used to support blood pressure. Symptoms generally resolve in 24 to 48 hours or less, and deaths are rare [68].

Aconitine

Members of this genus grow throughout the world. Exposures are commonly associated with the overzealous consumption of herbal preparations containing aconitine. Though several fatal poisonings have been reported, aconitine is still readily available at many nutrition or herbal medicine stores.

Plants

Plants containing aconitine are: *Aconitum napellus* (monkshood) (Fig. 19), *A vulparia* (Wolfsbane). Several species are also used in herbal preparations including *A carmichaeli* (''chuanwu'') and *A kusnezoffii* (''caowu'') [78]. The latter two appear to account for more fatalities than ingestion of monk's hood. *Delphinium* spp (Larkspur) have similar toxicity [79].

Fig. 19. *Aconitum napellus* (monkshood).

Location

A napellus and *A vulparia* grow in meadow areas of the mountainous areas from Arizona into Canada. *Aconitum* spp are cultivated as perennial ornamentals. *Delphinium* spp are found throughout the United States and Canada where they are also grown as ornamentals.

Description

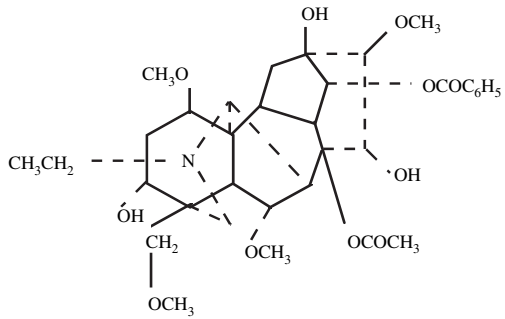
Plants grow to 3 to 4 feet. The leaves are palmately divided into five lobes, which are divided into narrow segments. Flowers, which are dark blue to purple or purple and white, are composed of five petal-like sepals, one of which covers the top of the flower. The latter forms a hood-like structure over the flower, hence the name. These plants, though perennial, dry up and appear dead soon after the onset of summer heat.

Toxic parts

All parts are toxic (roots, flowers, leaves, stems) [80].

Mechanism of toxicity

Like grayanotoxins and veratrum alkaloids, aconitine affects its toxicity through action on sodium channels. Aconitine (Fig. 20) seems to increase sodium entry into muscle, nerve, baroreceptors, and Purkinje fibers to produce a positive inotropic effect, enhanced vagal tone, neurotoxicity, and increased



Aconitine

Fig. 20. Structure of aconitine.

automaticity and torsade de pointes [81]. During late repolarization of the Purkinje fiber (late phase 4), aconitine attaches to a limited number of the sodium channels and increases Na^+ influx [71,82,83] causing *late* (or delayed) afterdepolarizations (Fig. 21) and increased automaticity (eg, premature ventricular beats). However, aconitine-induced sodium accumulation may also lead to *early* afterdepolarization during late phase 2 or early phase 3 of the action potential (Fig. 22). These early afterdepolarizations produce lengthening of the QT interval and are thought to explain reports of torsade de pointes in patients poisoned with aconite [82–85]. Bifascicular ventricular tachycardia, a dysrhythmia most frequently associated with digitalis toxicity, has also be reported in patients poisoned with aconite [86].

Clinical presentation

Most case reports of aconitine poisoning have come from ingestion of herbs containing aconitine [78,87]. Following exposure, onset of symptoms

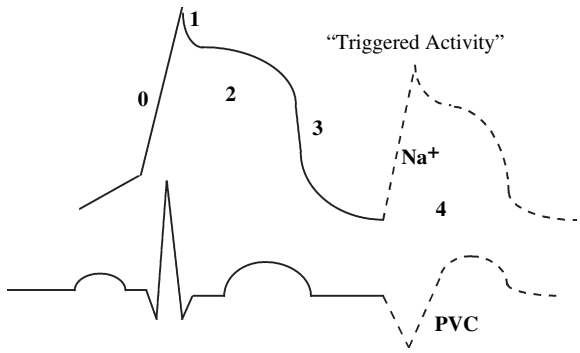


Fig. 21. Delayed afterdepolarizations (DAD) formation. Increasing sodium concentration in phase 4 leads to refiring of the Purkinje cell and DADs. These are manifest as premature ventricular contractions.

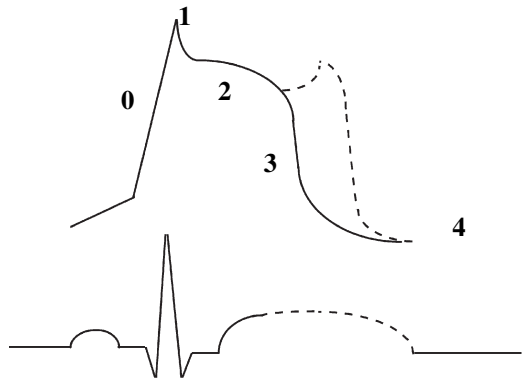


Fig. 22. Early afterdepolarization (EAD) formation frequently occurs when positive ions such as K + are held within the cell. The cell re-fires in late phase 2 or early phase three. When this occurs, an EAD is produced and results in QT prolongation, and sometimes, torsade de pointes.

has been reported in one series of cases to occur between 3 minutes to 2 hours, with a median of 30 minutes [85]. Symptoms may persist for 30 hours [88]. Neurologic complaints include initial visual impairment, dizziness, limb paresthesias, weakness [89], and ataxia [80]. Coma may follow. Chest discomfort, dyspnea, tachycardia, and diaphoresis may also occur [89]. Hyperglycemia, hypokalemia, bradycardia (with hypotension), atrial and nodal ectopic beats, supraventricular tachycardia, bundle branch block, intermittent bigeminy, ventricular tachycardia, ventricular fibrillation, and asystole have been reported [80,82,89,90]. Death is usually due to ventricular arrhythmia [89,91]. Ingestion of delphinium root has also resulted in ventricular dysrhythmias and cardiac arrest [79,89,91].

Laboratory studies

The presence of aconitine has been demonstrated by high-performance liquid chromatography at autopsy [91].

Management

Neurologic complaints require supportive care. The paramount concern is management of lethal arrhythmias. Ventricular tachycardia has failed to respond to several antiarrhythmic agents, including lidocaine, disopyramide, bretylium, amiodarone, potassium, and phenytoin. Tai and colleagues [86] reported successful use of flecainide following lidocaine failure in a single case. Yeih and colleagues [92] reported successful use of amiodarone following lidocaine failure in a case report. No antiarrhythmic agents have demonstrated clear superiority. In animal studies, Adaniya and colleagues [82]

demonstrated the ability of magnesium to suppress early afterdepolarizations and polymorphic ventricular tachycardia. Although some authors [93] differentiate between polymorphic ventricular tachycardia and torsade de pointes, Adaniya and colleagues [82] seem to use the two terms interchangeably.

Nicotine and related compounds

Pyridine/piperidine alkaloids including nicotine, coniine, anabasine, cystisine, arecoline, lobeline, and many others have a similar mechanism of action. Plants containing these alkaloids are widely distributed today, but are thought to have originated in South America. *Nicotiana rustica*, which contains up to 18% nicotine, is thought to have been the first tobacco export from the New World. Much more potent than *N tabacum* (0.5%–9% nicotine), it is still smoked in Turkey and serves as a source for commercial nicotine production [94]. *N tabacum* is planted throughout the Southeast as the source of cigar and cigarette tobacco. Because the toxicity of smoked tobacco has been widely discussed elsewhere, only dermal and gastrointestinal absorption are addressed in this article. Small quantities of nicotine are also found in plants from the family Solanaceae such as tomatoes, potatoes, and eggplant. This is of little consequence in terms of poisoning [95,96]. Several of the *Nicotiana* and *Lobelia* species are cultivated as flowering plants. Of the uncultivated plants in this group, *N glauca* (tree tobacco) and *Conium maculatum* (poison hemlock) are the most common sources of poisoning.

Plants

Nicotine

Plants containing nicotine are: *N tabacum* (tobacco), *N glauca* (tree tobacco) (Fig. 23), *N trigonophylla* (desert tobacco), and *N attenuata* (coyote tobacco).

Conine

Conium maculatum (poison hemlock) contains conine (Figs. 24 and 25).

Lobeline, lobelamine

Plants containing lobeline/iobelamine are: *Lobelia inflata* (indian tobacco), *L cardinalis*, and other species.

Other plants with nicotine or related compounds: *Aethusa cynaprium* (fool's parsley) contains coniine. *Laburnum anagyroides* (golden chain tree), *Sophora secundiflora* (mescal bush bean), *S tomentosa* (necklace pod *Sophora*), *and Gymnocladus dioicus* (Kentucky coffee bean) all contain cystisine. *Areca catechu* (betel palm/betel nut) contains arecoline [94].

Fig. 23. *Nicotiana glauca* (tree tobacco).

Location

Conium maculatum

Poison hemlock grows throughout the United States and southern Canada except in desert regions. It is frequently found along roadways or railroads.

Nicotiana glauca

Tree tobacco is common from the Southeast to the Southwest, where it may grow to 10 feet or higher. It will grow in the desert but is commonly found along ditches in those areas. Where water is more plentiful, it has a wider range.

Description

Conium maculatum

This biennial may reach 10 feet in height. The leaves are pinately divided three to four times and have a fern-like appearance similar to parsley, for which it is sometimes mistaken. The flower is umbrella-shaped and strikingly similar to that of *Daucus carota* (Queen Anne's lace) or *Cicuta* spp (water hemlock). The stem is hollow and has red to purple speckles along

Fig. 24. *Conium maculatum* flowers (poison hemlock).

its length. The crushed stems are said to smell like mouse urine; however, that observation is extremely subjective and should not be used to identify the plant. Its taproot is occasionally mistaken for parsnip. This plant is reputed to be the source of poison used in the execution of Socrates [32].

Fig. 25. *Conium maculatum* leaves and stem (poison hemlock).

Nicotiana glauca

Early growth has a shrub-like appearance and may be mistaken for collard greens due to the grayish cast of the green leaves. The leaves are oval with a smooth margin with a rubbery texture and grow up to 6 in in length. The flowers are approximately 2 in long by 1/2 in wide, bright yellow, with a tubular shape.

Toxic parts

All parts of both plants are poisonous. The seeds and roots of *C maculatum* are especially toxic.

Mechanism of toxicity

Nicotine, coniine (Fig. 26), anabasine, lobeline, and related pyridine/piperidine alkaloids cause similar toxicity. Their primary action is activation and then blockade of nicotinic acetylcholine receptors. Activation of nicotinic receptors in the cortex, thalamus, interpeduncular nucleus, and other locations in the central nervous system account for coma and seizures. Nicotine has been shown to enhance fast excitatory neural transmission in the CNS by triggering presynaptic cholinergic receptors, which increase presynaptic calcium and stimulate both cholinergic and glutaminergic transmission [97]. Nicotinic receptor activation facilitates the release of many neurotransmitters, including acetylcholine, norepinephrine, dopamine, serotonin, beta-endorphins, and others.

Activation of nicotinic receptors at autonomic ganglia produce varied effects in the sympathetic and parasympathetic nervous system. These most commonly include nausea, vomiting, diarrhea, bradycardia, tachycardia, and miosis [98]. Nicotine alkaloids act as depolarizing neuromuscular blocking agents and produce fasciculations and paralysis.

Clinical presentation

Ingestion or dermal exposure to nicotine and related compounds can result in any or all of the signs and symptoms listed in Box 2.

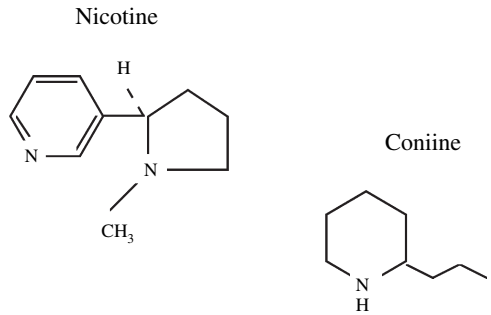


Fig. 26. Structure of nicotine and coniine.

Box 2. Muscarinic and nicotinic effects of nicotine and related compounds

Muscarinic
Salivation
Lacrimation
Urination
Gastrointestinal cramping
Emesis
Miosis
Bronchospasm
Bradycardia

Nicotinic
Weakness
Fasciculations
Paralysis
Tachycardia
Coma
Seizures

Though rare, severe poisonings do occur [99], one of the more commonly reported poisonings results from the ingestion of cigarettes. The ingestion of a single cigarette (up to 2.0 mg nicotine absorbed) is enough to cause symptoms in a small child. Smolinske and colleagues [100] reported three severely poisoned children who had ingested a minimum of 1.4 mg/kg. Twenty-five asymptomatic children ingested less than 1 mg/kg. Curry and colleagues [101] reported nine cases of ingestion of *N glauca*, which had been mistaken for collard and turnip greens. Three fatalities occurred. Symptoms included leg cramps, paresthesias, dizziness, and headache. Onset was within 1 hour, and resolution in the surviving patients ranged from 3 hours to several hours. Mellick and colleagues [102] reported two cases of *N glauca* ingestion resulting in neuromuscular blockade and eventual complete recovery. Frank and colleagues [103] reported a *C maculatum* ingestion in a 4-year-old, which resulted in miosis, vomiting, and coma. The onset of symptoms was 30 minutes after ingestion with resolution in approximately 9 hours. Drummer and colleagues [96] reported three fatalities from *C maculatum*. Foster and colleagues [104] reported the accidental ingestion of *C maculatum* by a 14-year-old child that resulted in respiratory failure, asphyxia, and eventual death. Another child who ingested a smaller amount of the same *C maculatum* plant had symptoms of nausea, malaise, and tingling of the extremities and survived. The 2002 American Association of Poison Control Center Annual Report describes a 13-year-old child that

developed ascending paralysis, had a seizure, and then died after ingestion of *C maculatum* that was mistaken for parsley [105].

Green tobacco sickness commonly occurs in the tobacco-growing states. Workers handling leaves can absorb nicotine through the skin. It occurs almost exclusively in workers who are cropping leaves from the plant [98]. Symptoms comprise nausea, vomiting, diarrhea, diaphoresis, and weakness, which usually resolve with symptomatic treatment.

The use of betel quid, which is popular in India, Southeast Asia, and the East Indies [94], has been reported in people who have immigrated to the United States from those countries. The quid is a betel nut wrapped in a betel vine leaf and smeared with a paste of burnt lime [106]. It contains arecoline and several other cholinergic pyridine alkaloids.

Rhabdomyolysis has been reported from the ingestion of *C maculatum*, although the reports are somewhat confusing in that "hemlock poisoning" is attributed to exposure to both *Cicuta* and *Conium* species [107,108].

Laboratory studies

Nicotine and conine and other alkaloids may be measured in urine by various methods, including gas chromatography [109], mass spectrometry [96], and thin-layer chromatography [110].

Management

Activated charcoal should be administered for ingestions that have occurred in the previous 2 hours. The dose of activated charcoal is 50 to 100 g in 8 ounces of tap water for adults and 1 gm/kg or 25 to 50 g in 4 ounces of water for children. In patients who have dermal exposure, as in the case of green tobacco sickness, the skin should be thoroughly washed with soap and water. Atropine may be used to block muscarinic symptoms, such as bronchospasm, vomiting, diarrhea, or bradycardia. There is no standard dose in this situation, and the amount given should be titrated to reverse muscarinic symptoms without inducing anticholinergic toxicity. Convulsions are best treated with benzodiazepines or barbiturates. Nicotinic symptoms such as weakness, fasciculations, or paralysis cannot be reversed, but supportive care is generally sufficient to manage the patient, with some patients requiring ventilatory support. There are no clinically useful antidotes for the nicotinic effects. Patients should be monitored for rhabdomyolysis and its subsequent renal impairment. Due to the usual rapid onset of symptoms, patients who present and remain asymptomatic and who are not suicidal may be released after 4 hours of observation.

Anticholinergics

Several plants and mushrooms exhibit anticholinergic properties. The best known of these are the members of the Solanaceae family. Of the

anticholinergic plants, the genera *Atropa*, *Datura*, and *Hyoscyamus* produce hyoscyamine (atropine). Other members of this group produce scopolamine. The members of both groups are listed, but for the sake of this discussion, *Datura* spp is the primary focus, because they account for more hospitalizations than the other plants.

The first recorded *Datura* poisoning occurred in 1676 during the Bacon Rebellion when soldiers under Captain John Smith made a salad of *Datura stramonium* leaves and began to hallucinate. The name "Jamestown weed" was given to this plant, and its name has been corrupted over the years to "Jimson weed."

Plants

Plants that have anticholinergic properties are: *Atropa bella-donna* (deadly nightshade), *Datura metaloides* (sacred datura) (Figs. 27 and 28), *D stramonium* (Jimson weed) (Fig. 29), *D arborea* (trumpet lily), *D candida*, *D suaveolens* (angel trumpet), other *Datura* spp, *Hyoscyamus niger* (henbane), *Lycium barbarum* (matrimony vine) and *Mandragora officinarum* (mandrake) (Figs. 27–29).

Location

Datura metaloides is a perennial southwestern plant that grows well in desert areas. *D stramonium* grows as an annual on recently disturbed

Fig. 27. *Datura metaloides* (sacred datura seeds).

Fig. 28. *Datura metaloides* (sacred datura).

ground throughout the United States. It is frequently found in soybean fields.

Description

D meteloides

D meteloides is a stout bushy plant with thick stems. The large leaves are oval with wavy edges. The foliage has a pungent odor. Seeds are found in

Fig. 29. *Datuna stramonium* (jimson weed).

spiney pods approximately 1.5 in long. The flowers are 6 to 8 in long and white with purple edges.

D stramonium

Similar to *D metaloides*, Jimson weed has a dark purple stem and is a taller plant.

Toxic parts

The entire plant is toxic. The flowers, fruits, and seeds are especially toxic.

Mechanism of toxicity

The members of the genus *Datura* contain varying amounts of hyoscyamine (atropine) and scopalamine (Fig. 30). Young plants tend to contain mostly scopalamine, but as they mature, hyoscyamine predominates. The toxicity of these compounds results from competitive blockade of acetylcholine at peripheral and central muscarinic receptors.

Clinical presentation

Onset of symptoms is usually within 30 to 60 minutes of ingestion and may last for 24 to 48 hours. Both central and peripheral syndromes may be seen. Levy [111] described 27 cases in which every patient had altered mental status and mydriasis.

Central anticholinergic syndrome

Central nervous system excitation often manifests as agitation and hallucinations. CNS depression and coma may follow. Hallucinations are generally visual but may be auditory. Speech has a characteristic mumbling quality and is often incomprehensible. Patients frequently answer questions with appropriate one-word answers, but if prompted (and able) to speak in

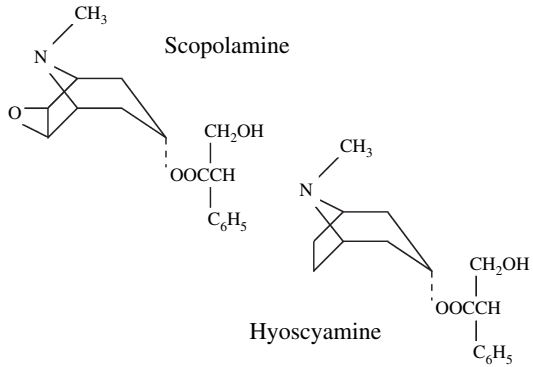


Fig. 30. Structures of scopolomine and hyoscyamine.

sentences, the fragmented speech pattern becomes obvious. Undressing behavior is not uncommon.

Peripheral anticholinergic syndrome

Tachycardia and mydriasis are common findings. Flushed skin may be more difficult to detect. Fever is occasionally noted. Bowel sounds may be depressed or absent, but usually persist. Bladder motility may be decreased as well. Although dry mucous membranes may be associated with hyperventilation, dry axillae in association with the other signs indicates anticholinergic poisoning and helps distinguish it from increased adrenergic activity.

Datura accounts for many admissions to critical care units each year. Although children are occasionally poisoned, the most frequent exposure occurs in patients who have ingested seeds or a tea brewed from the seeds in an attempt to induce hallucinations. Death is rare and may result more as the result of impaired judgment than direct toxicity. A few death reports do seem to indicate potentially fatal toxicity in high-dose exposures [112,113]. Petechial hemorrhages of the endocardium and hyperemia and edema of the lungs were reported in both cases.

Laboratory studies

Atropine may be detected by radioimmunoassay, gas chromatography/mass spectrometry, thin-layer chromatography [114], and liquid chromatography. Scopolamine has been analyzed in plasma and urine by radioreceptor assay and gas chromatography/mass spectrometry [109].

Management

Decontamination is best accomplished with the administration activated charcoal if the ingestion has occurred within the previous 2 hours. The dose of activated charcoal is 50 to 100 g in 8 ounces of tap water for adults and 1 gm/kg or 25 to 50 g in 4 ounces of water for children. Tachycardia rarely requires treatment. Patients should be monitored for urine output and bladder distention. A nasogastric tube should be inserted in patients who have decreased gut motility. Hypotension should be treated with intravenous isotonic fluids. Dopamine may be used if hypotension persists after the patient's intravascular volume has been restored, but this is unusual. The combination of impaired diaphoresis with agitation may lead to severe hyperthermia, which must be aggressively treated with sedation/paralysis and active cooling. Rhabdomyolysis is common and explains renal failure and other complications seen in severe *Datura* toxicity. Because of their anticholinergic activity, phenothiazines and diphenhydramine should be avoided. Haloperidol does not seem to be effective for resolution of central anticholinergic effects [115]. Benzodiazepines are, on the other hand, effective in the treatment of agitation.

Several authors have advocated the use of intravenous physostigmine for patients who have central anticholinergic effects [111,115,116]. Physostigmine inhibits acetylcholinesterase, thus increasing the amount of acetylcholine available to the muscarinic receptors. While benzodiazepines may be used to sedate agitated patients, physostigmine may restore the patient's level of consciousness to its baseline. It is particularly helpful in differentiating anticholinergic poisoning from other causes of altered mental status. It should not be used unless peripheral anticholinergic signs accompany a clinical picture of central anticholinergic poisoning. Seizure activity, bradycardia, heart blocks, and asystole have followed use of physostigmine [117,118]. Because of the potential for greater risks than benefits, consultation with a poison center or medical toxicologist regarding administration of physostigmine for anticholinergic plant ingestion is recommended before use.

Saponin glycosides

Phytolacca americana (pokeweed) contains several potentially toxic compounds. Saponin glycosides, which play a defensive role for these plants, account for gastrointestinal injury and are found in other species that are listed below. In addition to these glycosides, *P americana* also contains proteins that have mitogenic, hemaglutinin [119], and antiviral [120] properties.

Plants

Plants containing saponin glycosides are: *P americana* and synonym, *Phytolacca decandra* (pokeweed, poke, pigeonberry, inkberry, pocan, garget redwood, cancer-root, jalap, scoke, American nightshade) (Fig. 31).

Other plants containing saponin glycosides are: *Glycyrrhiza glabra* (Licorice), *Panax ginseng* (Ginseng), *Hedera helix* (English ivy), and *Aleurites* spp (Tung tree).

Location

It is found throughout the eastern half of the United States from the southern states into Canada. It has been introduced into some parts of the Southwest [69].

Description

Phytolacca americana grows up to 9 feet tall by late summer. It tends to grow in areas of partial sunlight where the ground is untended. The leaves are eliptic-lanceolate and 6 to 12 in in length with alternating attachment. The stems and stalks are red. The white flowers are 1/4 in in clusters. The berries grow to 1/4 in diameter by fall when they are deep purple. They

Fig. 31. *Phytolacca americana* (pokeberry).

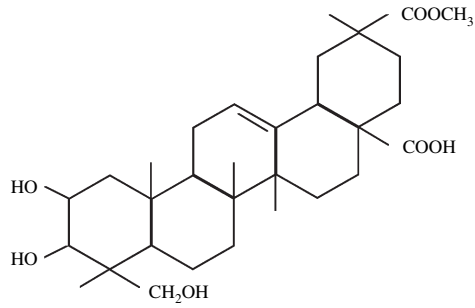
are found in clusters of 20 to 30 berries. The root is large, tan with a rough surface, and has multiple branches.

Toxic parts

All parts of the plant, especially the roots, are toxic.

Mechanism of toxicity

The toxic components of pokeweed are triterpene saponins, which include phytolaccatoxin, phytolaccagenin (Fig. 32), and a proteinaceous mitogen



Phytolaccagenin

Fig. 32. Structure of phytolaccagenin.

[121]. Phytolaccatoxin, phytolaccagenin, and saponin glycosides produce gastrointestinal irritation, which causes vomiting and diarrhea with a foaming or "soapy" consistency. In 1964, Farnes and colleagues [122] reported the mitogenic properties of pokeweed. In 1966, Barker and colleagues [123] reported several children who had varying exposure to *P americana*. Those who had ingested pokeberries or who had abrasions or scratches on their hands when they handled the berries developed increased numbers of circulating plasmablasts and proplasmacytes as well as mature plasma cells for up to 2 weeks following the exposure. They subsequently reported eosinophilia, thrombocytopenia, and abnormal platelet morphology in similarly exposed children [124]. Waxdal [119] isolated five separate proteins designated Pa-1 through Pa-5, which had varying amounts of mitogenic activity. Pa-1 was the most mitogenic and was also the most potent hemaglutinin. These proteins are thought to account for the mitogenic properties of pokeweed on both thymus-dependent (T) cells and thymus independent (B) lymphocytes. A pokeweed antiviral protein has also been reported. This protein seems to remove an adenine residue from RNA of eukaryotic ribosomes interfering with protein synthesis. It has been found to inhibit herpes simplex infection of certain cell lines and repress human immunodeficiency virus 1 replication in T cells at concentrations that do not inhibit cellular protein synthesis [120]. The utility of these findings remains under study.

Clinical presentation

Exposure to pokeweed is frequently reported [26,117,125]. The leaves are prepared as a salad; berries are used for teas [121], and roots have been mistaken for horseradish [126], parsnips, or other vegetables. Various parts of the plant are used as herbal medications for rheumatism, antihelmenths, emetics, laxatives, and for the treatment of a host of other maladies. The most frequent route of exposure is oral, but plasmacytosis has been noted after berries have come into contact with broken skin [123,124,127].

Ingestion of pokeleaves as a salad has been a common source of gastroenteritis. The traditional preparation is of poke salad involves "parboiling" the immature leaves. Parboiling is a process of boiling the leaves in water, discarding the water, reboiling the leaves, and rinsing them after the second boiling. This however is sometimes insufficient to remove the toxins [128].

Nausea, vomiting, and stomach cramps were reported in over 80% of patients in one report [128]. Lower-dose exposure to berries may only result in mild diarrhea and may be delayed up to 12 hours after exposure [129]. Loss of consciousness has been reported after ingestion of pokeberry tea. This was accompanied by salivation, vomiting, urinary incontinence, and hypotension, suggesting it may have been due to a vasovagal event [130]. Heme positive stools have also been observed [126,131]. Cardiac effects have included hypotension, bradycardia, tachycardia, and Mobitz type I heart block [132], which was felt by the authors to represent a vagal effect. The

dysrhythmia occurred during an episode of extreme nausea and resolved when the patient was treated with promethazine. Roberge and colleagues [133] also reported ventricular fibrillation in a single patient who had heart disease. The authors felt that the ischemic changes on her electrocardiogram (precordial ST–T-wave depression, Q waves in leads II and III) were most likely related to her accelerated heart rate and dysrhythmia because saponin glycosides are not thought to be directly cardiotoxic. Other signs of poisoning include an initial burning in the mouth and throat, diaphoresis, and generalized weakness. Visual disturbances and coma have also been reported, although these may be related to hypotension [130]. Although most reports of death are from the distant past, there has been one recent report in the American Association of Poison Control Centers Annual Report data. In the 2000 American Association of Poison Control Centers Annual Report, there is a case of an 18-year-old that accidentally ingested a *P americana* root. The individual had emesis 90 minutes after the ingestion and ventricular fibrillation leading to death approximately 2 hours after the exposure [134]. Hematopoetic effects resolve in a matter of weeks [123,124].

Laboratory studies

Specific tests for *Phytolacca* derived toxins are not clinically useful. Diagnosis is based on history and, when possible, plant identification. Electrocardiographic findings are nonspecific. Complete blood cell count may occasionally show atypical lymphocytes, plasma cells, thrombocytopenia, or eosinophilia a few days after exposure [123,124].

Management

Supportive care is the mainstay of therapy. Gastric decontamination may be accomplished with the administration of activated charcoal if ingestion has been within 2 hours of presentation. The dose of activated charcoal is 50 to 100 g in 8 ounces of tap water for adults and 1 gm/kg or 25 to 50 g in 4 ounces of water for children. Nausea and vomiting may be treated antiemetics. Hypotension, which may result from gastrointestinal losses or vagal stimulation, should be treated initially with fluids. Dysrhythmias should be treated in the usual fashion, although resolution of hypovolemia and vagal stimulation are presumably sufficient to treat abnormal cardiac rhythms [132,133].

Catechol phenols (urushiol) and noncatechol phenols (resorcinol)

Urushiol and noncatechol phenols like resorcinol are oleoresins found in plants of the family Anacardiaceae (72 genera of flowering plants bearing fruits that are drupes) [135,136]. The oleoresins elicit an allergic skin reaction on contact in higher primates including human [137–140]. Historically,

urushiol-based lacquers, which were used to produce traditional lacquerwares in Japan approximately 7000 BC, were made from the sap of the lacquer tree (*Rhus verniciflua*). The name urushiol is derived from the Japanese word *urushi*, denoting the sap (kiurushi) of the lacquer tree [141]. Plants of the family Anacardiaceae cause more allergic contact dermatitis than all other plant families combined [139,140]. Toxicodendron, a genus of this family, comprises the most allergic members in North America including poison ivy, poison oak, and poison sumac [138,142–148]. The main allergens in toxicodendrons are catechols-like urushiol (1,2–dihydroxybenzene) (Fig. 33) [149–151]. Urushiol oleoresin is a slightly yellow liquid that avidly binds to skin. On exposure to oxygen, it turns dark brown within 10 minutes and black by 24 hours [152]. The cashew nut tree (*anacardium occidentale*), mango (*mangifera indica*), and the Brazilian pepper tree (*schinus terebinthifolius*), common throughout the tropics, are also implicated, albeit less frequently, in allergic contact dermatitis in the United States [132,148,153]. The main allergens in those trees are noncatechol phenols like resorcinols (1,3–dihydroxybenzene) (Fig. 34). Urushiol, a catechol, possesses greater allergenicity than noncatechol phenols [154]. Urushiol-induced contact dermatitis affects approximately 10 to 50 million Americans per year. Outdoor activities and occupations (agriculture, forestry, and firefighting) expose individuals to a significant risk of contracting Toxicodendron dermatitis with consequent lost-time injuries and treatment cost [155,156].

Plants

There are two species of poison ivy (*Toxicodendron radicans and Toxicodendron rydbergii*) and poison oak (*Toxicodendron diversilobum and Toxicodendron toxicarium*) and one species of poison sumac (*Toxicodendron vernix*) that are common to North America (Figs. 35 and 36) [139,157].

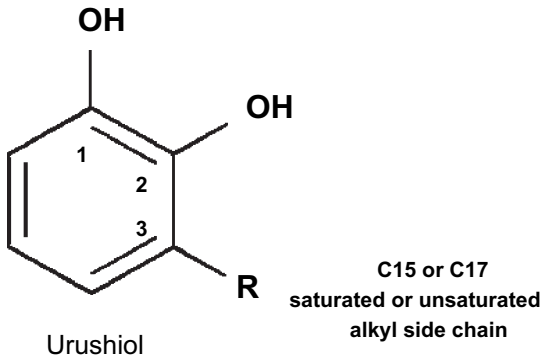


Fig. 33. Structure of urushiol.

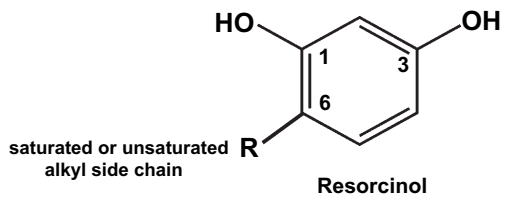


Fig. 34. Structure of resorcinol.

Location

Toxicodendron radicans (common or Eastern poison ivy) is found in the Eastern half of the United States and southern Canada. It grows as weeds (along roads, trails and streams) or shrub-like. It also climbs as a woody vine. *Toxicodendron rydbergii* (Northern or Western poison ivy) is found in the Western half of the United States (except California) and in northern border states. It grows as nonclimbing shrubs. *Toxicodendron diversilobum* (Western poison oak) is found in the Pacific coast of the United States. It grows as a shrub and climbing woody vine. *Toxicodendron toxicarium* (Eastern poison oak) is found in the southeastern United States. It grows in sandy soils as a shrub but can also climb. Toxicodendron vernix (poison sumac) is found in the eastern third of the United States. It grows as a bush in damp and swampy areas [139,148,157].

Fig. 35. *Toxicodendron* spp (poison oak).

Fig. 36. *Toxicodendron* spp (poison ivy).

Toxic parts

The urushiol oil in all Toxicodendron species is found in the stems, roots, leaves, and skin of its fruits. Usually a break in the plant skin is required for plants to release the urushiol. Urushiol is nonvolatile and dries up quickly retaining its antigenic potential. When the oil is transferred to the human skin, as little as 2 mg is sufficient to cause dermatitis in the sensitized individual. Toxicodendrons undergo seasonal variations. In the fall, the leaves turn red and accumulate higher concentration of urushiol. In the winter and fall, as the leaves dry up, the nonleaf remaining parts of the plant retain its urushiol content and thus remain a significant potential contact hazard [139,148,157].

Description

Toxicodendron plants are ubiquitous throughout North America. They are rarely found above 5000 feet elevation. They have pinnately or alternate compound leaves, possessing three or more leaflets. The plants show a wide spectrum of variation in appearance. They grow as woody creeping or climbing vines, shrubs, or trees. A single plant can have leaves with smooth, toothed, or lobed edges. Flowers and fruit arise uniquely in an axillary position in the angle between the leaf and twig. The leaf stalk leaves a characteristic ''V''-shaped scar after it falls off. The green fruits turn off-white as

they ripen. Poison ivy and poison oak grow along roads, trails, or streams. They possess three (sometimes five) leaflets per leaf giving rise to the adage, "leaves of three, let them be." Poison ivy leaves are 3 to 12 cm long and classically have pointed tips and are ovate (widest point below the center). It can grow as a shrub up to 4 feet, as a creeping vine (4–10 in high) or climbing vine. It reproduces by creeping rootstocks or by seeds. Virginia creeper (*Parthenocissus quinquefolia*) belongs to the grape family and is nontoxic. It has a similar appearance and growth habitat and often grows together with poison ivy. Poison oak leaves are 3 to 15 cm long and usually have round ends. Western poison oak grows as a dense shrub in open sunlight or as a climbing vine in shaded areas. Eastern poison oak grows as an erect shrub up to 3 feet tall. Poison oak reproduces by creeping rootstocks or by seeds. Poison sumac contains leaves that are pinnate, are 25 to 50 cm long, and have 7 to 13 leaflets. It grows as a woody bush up to 3 m tall. Poison sumac grows exclusively in wet and flooded soils [139,147,148,157–160].

Mechanism of toxicity

Urushiol molecules consist of catechols (1,2–dihyroxybenzene) substituted at position 3 with an alkyl side chain that has 15 or 17 carbon atoms (see Fig. 33). The alkyl group may be saturated or unsaturated. The urushiol oleoresin is a variable mixture of the saturated and unsaturated urushiol molecules depending on the toxicodendrons species. Poison ivy and poison sumac contain mostly C15 alkyl side chains (pentadecylcatechols), but poison oak contains mostly catechols with C17 side chains (heptadecylcatechols). Catechols and their alkyl side chains are immunologically inert on their own. However, combining them to produce urushiol converts them into potent immune sensitizers. The allergenicity of the particular urushiol resin is dependent on the degree of unsaturation of the alkyl chain at position 3 of the catechol. Placement at position 6 induces tolerance [136,137,161–166]. Urushiol-induced allergic contact dermatitis is mediated by a T-lymphocyte–mediated delayed type IV hypersensitivity reaction [136,167–174]. On initial skin contact, urushiol catechols bind and penetrate the skin. They are converted to quinine intermediates (hapten) that bind to host proteins on Langerhans cells (antigen-presenting cells) in the epidermis and become antigens. As a result, cytokines are released by keratinocytes, Langerhans cells, and macrophages in the skin. The cytokines in turn activate Langerhans cells to take-up and process the antigens and emigrate to regional lymph nodes. The Langerhans cells mature into dendritic cells that process and re-express the antigens on their surface for presentation to naïve T cells in the regional lymph node. Upon antigen presentation, T cells with receptors specific to the antigen get activated and clonally expanded to produce urushiol-specific effector and memory T lymphocytes. Urushiol-specific T lymphocytes recirculate in the periphery where it may contact the antigen again. This is the

induction phase of allergic contact hypersensitivity pathogenesis, which confers the naïve host "sensitization" to urushiol [174]. After subsequent contact with urushiol, antigen-specific memory and effector (clonal) T cells are activated in the skin with the induction of their inflammatory cytokines. This elicits a cell-mediated cytotoxic immune response that ultimately produces the clinical manifestation of contact dermatitis: erythema, edema, vesicles, pain, and pruritis. This elicitation phase of allergic contact hypersensitivity pathogenesis not only is urushiol-specific, but also dose-dependent (ie, the severity of the inflammatory response is proportional to the amount and duration of exposure) [175–177].

Clinical presentation

Over 70% of the United States population reacts to poison ivy allergens after patch testing. But, only 50% reacts to plants in their habitat. In areas where toxicodendron plants are less common, the prevalence is approximately 20%. Tolerance is conferred in approximately 10% to 15%. Peak frequency for sensitization occurs between 8 and 14 years of age. Genetic susceptibility has been demonstrated. Break in the plant skin is required to release urushiol. Therefore, lightly brushing against uninjured leaves is benign. Urushiol may be spread by contaminated clothing, pets, sawdust, lacquered furniture, or smoke aerosols. Urushiol-containing smoke aerosols can cause severe dermatitis and respiratory tract inflammation, especially in forest firefighters [178]. After contact with urushiol, a sensitized individual typically develops an erythematous pruritic eruption within 2 days (4–96 hours) of the exposure. However, dermatitis may occur up to 3 weeks after primary contact or within hours of secondary contact. Streaks of erythema and edematous papules typically precede vesicles and bullae. If the urushiol load is lower, only erythematous edematous reaction may be seen. However, significant exposure will produce bullae, edema, and severe pain. Vesicle and bulla fluid contain no urushiol as demonstrated by patch testing, and thus it does not propagate the rash. Variation in skin thickness (especially stratum corneum) and urushiol load at various body parts likely cause variable time appearance of clinical manifestations. In addition, contact with dormant urushiol on fingernails, pets, and inanimate objects may cause symptoms to appear within few weeks after the initial exposure. Without treatment, the dermatitis lasts approximately 3 weeks. More severe reactions especially in susceptible individuals take longer to resolve and can last up to 6 weeks [138–140,142–148,179–181]. In "black-spot poison ivy dermatitis," an uncommon manifestation of toxicodendron exposure, urushiol acts as both an irritant and allergen [182,183]. Oxidized resin can be found on the skin, resulting in a black discoloration. This results in an acute irritant contact dermatitis that is superimposed on an acute allergic contact dermatitis [184]. This form of dermatitis is uncommon because most people wash off

the resin as soon as it is noted. Uncommon complications of toxicodendron exposure include erythema multiforme [185–187] and nephritis [188], thought to be immune complex–mediated. Hyperpigmentation following urushiol-induced dermatitis occurs more commonly in dark skin. Secondary polymicrobial bacterial infections have been reported in urushiol-induced dermatitis [189,190]. Though less commonly reported than skin and inhalation exposures, ingestions of toxicodendron plants do occur. A syndrome of systemic contact dermatitis with skin manifestations of inflammation has been described following both intentional and unintentional toxicodendron ingestions [191,192].

Laboratory studies

The black spot test maybe used in the field to identify urushiol-containing plants [152]. Urushiol turns dark brown within 10 minutes of exposure to oxygen and black by 24 hours. Patch testing is used to diagnose delayed allergic reactions such as contact dermatitis. An allergen, in this case urushiol oleoresin, is applied to a patch, which is then placed on the skin. Patch testing for toxicodendron allergy has limited clinical utility. Only 50% of individuals who have positive skin patch test actually react to poison ivy in the field. Furthermore, patch testing with urushiol oleoresin carries a 10% to 20% risk of sensitizing an individual to the oleoresin. Therefore, patch testing is not recommended for diagnostic purposes [193–195].

Management

Urushiol oil is degraded in water. The oleoresin can be removed in a significant amount only if it is washed off as soon as the exposure to the toxicodendron is recognized. After 10 minutes, only 50% can be removed; after 15 minutes, only 25%; after 30 minutes, only 10%; and after 60 minutes, none of the urushiol can be removed [195]. Postexposure decontamination products have shown some effectiveness in reducing the dermatitis if applied to the skin within 2 hours of exposure.Vesicles, bullae, and weepy lesions are best treated with lukewarm baths, wet-to-dry soaks, or mild shake lotions (calamine). An astringent such as Burow's solution (aluminum subacetate) works well to cool and dry the weeping lesions. Topical antihistamines, anesthetics, and antibiotics should be avoided to prevent sensitization. Topical steroids are more effective if applied in the early stages of the erythema and pruritis before the appearance of vesicles. Steroid topicals with moderate potency are recommended. Abrupt discontinuation can cause a rebound inflammation. Immunosuppressive topical treatment with tacrolimus (inhibits T-cell activation in skin) has been shown to be a safer and effective alternative to topical corticosteroids in atopic dermatitis [195a]. However, its effectiveness in urushiol-induced dermatitis has not been studied. Systemic corticosteroids are effective when indicated. It is recommended in moderate to severe urushiol-induced dermatitis. Doses are usually 1 to 2 mg/kg per

day, slowly tapered over 2 to 3 weeks. If the corticosteroid course is short, then rebound dermatitis is likely to follow [145,146,148,160,180,195].

Prevention

Urushiol penetrates latex but not vinyl gloves. Hyposensitiztion strategies for Anacardiaceae sensitized individuals have not been effective [148,161, 195–198]. Barrier creams like ivy-block (an organoclay compound, 5% quaternium-18 bentonite lotion) have been tested and shown to be effective [199,200]. This product has been approved by the US Food and Drug Administration for prevention of Toxicodendron dermatitis.

Oxalates

There are many plants that contain oxalates. The oxalates contained in plants are found in two different forms insoluble oxalates, usually calcium oxalate, or soluble oxalates or oxalic acid. One family of oxalate-containing plants is the Aracea family, which comprises over 109 genera [201]. *Dieffenbachia* is one genus within the Aracea family that is of particular historical significance. *Diffenbachia* species have been used for their toxic effects for hundreds of years. They have acquired the common name of ''dumb cane'' and ''mother-in-law's tongue'' secondary to their local irritative effect when chewed [202]. In the Caribbean, *Diffenbachia* spp were used to punish slaves by rubbing the plant stalks on their tongues, resulting in mucosal swelling, pain, and the inability to talk [202]. They were used in a similar manner on the same islands to sabotage crime witnesses, rendering them unable to testify in court [202]. Several plants, including spinach and rhubarb, that contain soluble oxalates are common to the human diet and are not well known for toxic effects.

Plants

A list of more common oxalate-containing plants includes: *Dieffenbachia* spp (dumb cane, mother-in-law's tongue) (Fig. 37), *Philodendron* spp, *Caladium* spp, *Colocasia* spp (elephant's ear, taro), *Arisaema* spp (jack-in-the-pulpit), *Rheum rhabarbarum* (rhubarb), and *Spinacea oleracea* (spinach).

Locations

Dieffenbachia spp, *Philodendron* spp, *Colocasia* spp, and *Caladium* spp can all be found in the tropical regions of the Americas. They are all now common ornamental houseplants in the United States. Both the *Rheum* and *Spinacea* spp originated in Asia but now are cultivated in commercial and residential gardens in the United States.

Fig. 37. *Diffenbachia* spp (dumbcane).

Toxic parts

Dieffenbachia spp, *Philodendron* spp, *Colocasia* spp, *Caladium* spp, and *Arisaema* spp: all parts are toxic except the tubers of *Colocasia esculenta*. Rhubarb's leaf blades are toxic. Spinach has leaves that contain soluble calcium oxalates.

Description

Dieffenbachia spp are shrubby plants with large oval-shaped leaves. Leaves may be completely green or green with ivory mottling. *Philodendron* spp have climbing vines with triangular or heart-shaped leaves, which are green, red, or white in color. *Caladium* spp are stemless with multicolored (green, red, and white) heart-shaped leaves. *Colocasia* have large heart-shaped leaves that may grow up to 65 cm in size. Rhubarb has a thick reddish leaf stalk and large fan-shaped leaves. Spinach has oval-shaped leaves that grow in a rosette formation.

Mechanism of toxicity

The plants that contain insoluble oxalates have a different form of toxicity than the plants that contain soluble oxalates. Insoluble oxalate is in the form of calcium oxalate that forms needle-shaped crystals or raphides. In certain plants, such as the *Dieffenbachia* spp, these raphides are

contained in oval-shaped cells called idioblasts. The idioblast cells have an opening on both ends of the cell. When mechanical force is applied to the idioblasts, the rahpides fire out of the cell and are propelled a distance of 2 to 3 cell lengths. The mechanical force of these calcium oxalate crystals causes local cell damage [202–204]. There is also evidence that there may be some other toxic component within the idioblasts. Research has failed to identify the exact nature of this other toxic substance; however theories include a proteinaceous substance, a substance with a proteolytic property, or a substance that affects bradykinin activity [203,204].

Soluble oxalates, or oxalic acids, produce its toxicity in a different manner. Oxalic acid can bind with ionized calcium leading to systemic hypocalcemia. Hypocalcemia has been documented by this method in livestock, but has not been well documented in humans. Oxalic acid can also bind with calcium in the urine, leading to nephrolithiasis. Nephrolithiasis by this mechanism is thought to be more common in people who have a diet high in oxalic acid–containing foods and whose gastrointestinal tract absorbs more oxalic acid [205–207].

Clinical presentation

Most exposures to calcium oxalate–containing plants result in no effects. The Pittsburgh Poison Center did a retrospective review of *Dieffenbachia* and *Philodendron* exposures called to their center over a 2-year period. There were a total of 188 exposures with 4 resulting in local oral symptoms that were either self-limited or resolved with minimal treatment [208]. The clinical effects of calcium oxalate–containing plants are the results of local irritation. Swelling, pain, and oral ulcers can occur as a consequence of chewing or eating these plants [209,210]. An irritant contact dermatitis can occur after handling plants with calcium containing raphides [201,211]. *Philodendron* spp can cause an allergic contact dermatitis in susceptible individuals. Chemosis, tearing, and pain has been reported after ocular exposure to the juice of *Dieffenbachia* spp [212].

Ingestion of plants containing soluble oxalates can theoretically lead to hypocalcemia leading to tremor, tetany, and seizures. This clinical scenario has not been well documented in humans, and an older case reports that attributes death to this plant overlooks confounding factors that may have caused or contributed to the death [213]. An older publication warns about the dangers of rhubarb toxicity, but fails to cite references [214]. Chronic ingestion of soluble oxalates can lead to an increase in nephrolithiasis and associated symptoms [205–207].

There are three case reports in the literature that attribute severe toxicity and/or death to *Dieffenbachia* or *Philodendron* species. The following two cases involve patients who have significant periods of time outside of the hospital between the exposure and serious outcome. These nonobserved time periods allow for possible confounding variables and thus difficulty in

concluding the relationship between the plant and the outcome. The only reported death was from an 11-month-old boy who died from cardiac arrest 17 days after he was found chewing on a *Philodendron* plant. The child had original symptoms consistent with local oral mucosa irritation and was admitted to the hospital. His condition improved after 5 days and he was discharged from the medical facility. Fifteen days after the ingestion, he was readmitted to the hospital, and an endoscopy on day 16 showed esophageal erosions and an esophageal stricture. The child died of cardiac arrest in the hospital on day 17. The reporting physicians concluded that his cardiac arrest was caused by vagotonia related to his esophageal injury [215]. There is a report of a 12-year-old child that had an aortoesophageal fistula as a complication of esophagitis caused by the intentional ingestion of a *Dieffenbachia* leaf. The child had an initial endoscopy that showed grade 2 esophagitis of the entire esophagus. After a 2-week hospitalization, the child was discharged home on nasogastric tube feeds. Five weeks after the ingestion, the child had an endoscopy that showed improvement of the esophagitis. Two days after the endoscopy, the patient had an acute gastrointestinal bleed. The child required emergent surgery and was found to have an aortoesophageal fistula [216].

A 69-year-old man suffered from airway edema and glossitis requiring emergency tracheostomy approximately 1 hour after oral exposure to a *Dieffenbachia* plant. The man had mistaken the plant for sugar cane. The patient was treated with methylprednisolone, albuterol, and diphenhydramine, and his condition resolved after 3 days [204].

Laboratory studies and imaging

There are no readily available tests to confirm oxalate–containing plant exposure. Electrolyte status and calcium levels may be useful in a patient who is symptomatic and has ingested a large amount of soluble oxalates. A patient who has obvious oral burns and symptoms of dysphagia should undergo endoscopy. A patient who has ocular symptoms should undergo slit-lamp examination.

Management

Treatment for calcium oxalate–containing plants consists of symptomatic care. For oral exposure with local pain, systemic pain medications or viscous lidocaine may be beneficial. Local oral edema may respond to an H2-antagonist such as diphenhydramine. Oral edema along with airway compromise should be treated aggressively with systemic steroids, an H2-antagonist, and consideration of endotracheal intubation or tracheostomy if necessary. In the one reported case in the literature with severe airway compromise, the patient was also treated with nebulized albuterol and

racemic epinephrine, both with unclear results [204]. Patients who have significant oral symptoms, oral lesions, and/or dysphagia should be considered for endoscopy.

Contact dermatitis from raphide-containing plants may respond to topical or systemic steroids. Symptomatic care with an H2-antagonist may also be beneficial. Corneal irritation from raphide-containing plants may be treated with a cycloplegic or steroidal eye drop [212].

Summary

Patients who have exposures to potentially toxic plants frequent emergency departments. It is important for health care providers to realize that most of these exposures are of minimal toxicity. The more serious poisonings usually involve adults who have either mistaken the plant as edible or have deliberately ingested the plant to derive perceived medicinal or toxic properties. There are multiple potential mechanisms of toxicity following plant exposure. Health care providers should be aware of the plants endogenous to their region.

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