Poisons of Plant Origin

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CONTENTS

1 INTRODUCTION

We share our world with a vast number of plant species. Species of seed plants alone number around 400 000 (Govaerts, 2001). Plants are adapted to many different environments and growing conditions that, in turn, are related to the production and/or accumulation of a multitude of biologically active compounds, also referred to as phytochemicals, that make it possible for plants to thrive under different environmental and competitive conditions. Examples include compounds produced to deter herbivores of various kinds, from large mammals to insects, compounds to defend against infection by bacteria, fungi and parasites, as well as compounds that increase success in competing for resources against other plants. Some biologically active compounds are accumulated to provide a store of nutrients or to facilitate specialized physiological processes, or may simply reflect the relative abundance of chemicals in the plant's environment. The diversity of biologically active phytochemicals is a valuable resource, both as nutrients and as compounds that have health benefits when consumed in moderate quantities. Many important classes of pharmaceuticals were originally derived from plants, or are extracted directly from plants. Traditional herbal medicines, derived directly from plant tissues or crude extracts, are the mainstay of healthcare in many parts of the world, especially where access to modern healthcare is limited (Kofi, 2005), while persisting to varying degrees in societies with the most advanced healthcare systems (Bent and Ko, 2004).

Since biologically active compounds are so commonly encountered in plants, it is not surprising that some plants, under conditions of sufficient exposure and phytochemical absorption, have the ability to cause toxicity. As with most other toxicants, the dose required to produce toxicity varies tremendously between compounds, routes of exposure and with the susceptibility of the individual.

The relative importance of plant toxicities is illustrated by the fact that human exposures to plants that are perceived as poisonous, and reported to Poison Control Centers in the United States, comprised 2.7% of total reported exposures to toxicants in 2006. This represents over 64 000 incidents (Bronstein *et al*., 2007). The 25 most frequently reported poisonous-plant exposures in the United States from 1987 to 2006 are listed in **Figure 1**. These reports indicate the relative importance of popular, decorative garden and house plants in a predominantly urban, Western society, like the United States. Due to cultivation in nurseries and wide distribution to gardens and homes, where growing conditions can be controlled, exposure to these plants is no longer correlated with their original distributions under natural conditions, and exposures can be expected in almost any urban environment. In societies where naturally occurring, local vegetation is commonly used in traditional medicine and as a food source, the most frequent poisonous-plant exposures are likely to reflect local abundance and use of plants. An ominous development in recent years has been the speed and efficiency of distribution of potentially hazardous food ingredients, which may be contaminated with poisonous plant material (Prakash *et al*., 1999). A recent example is an Australian recall of

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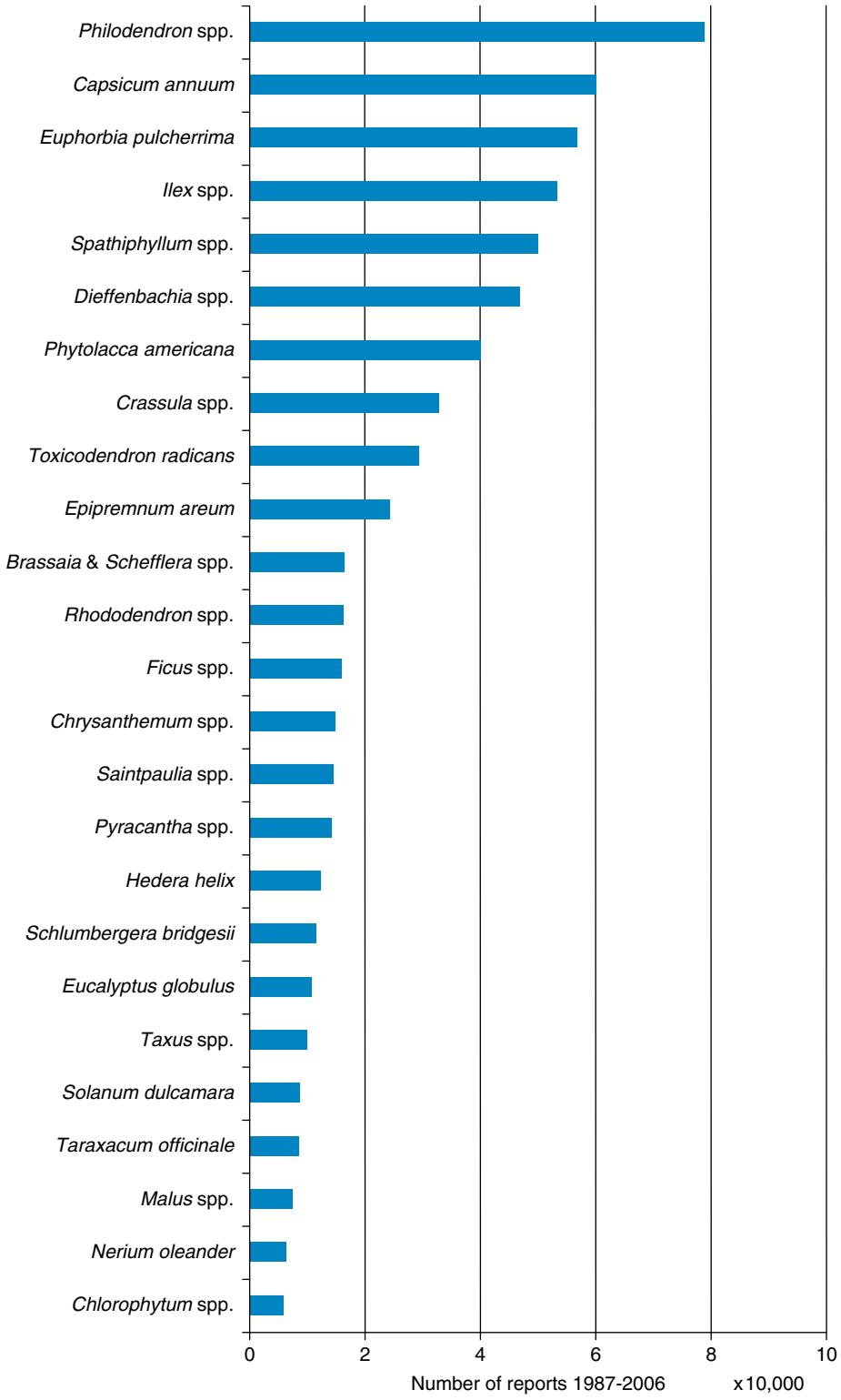

Figure 1 The 25 most frequent poisonous plant exposures reported to United States Poison Control Centers from 1987 to 2006. (Bronstein *et al.*, 2007; Lai *et al.*, 2006; Litovitz *et al.*, 1988; 1989; 1990; 1991; 1992; 1993; 1994; 1995; 1996; 1997; 1998; 1999; 2000; 2001; 2002; Watson *et al.*, 2003; 2004; 2005.)

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vegetarian crackers in January 2008 that were manufactured using cyanogenic glycoside-containing cassava as an ingredient (SADH, 2008). Rapid and massive distribution of processed and poorly recognizable hazardous food ingredients of plant origin presents a difficult challenge.

Fortunately, the majority of poisonous plant exposures do not result in toxicity. Most plant toxins, with some notable exceptions, produce severe toxicity or lethal effects only at relatively high doses, and exposures to highly toxic doses are uncommon under normal conditions. Our interactions with plants are therefore mostly harmless, even when we are exposed to potentially poisonous plants. It is only when exposed to plant species of exceptional toxic potential, or when the route of exposure and dose leads to ample absorption of toxic compounds, that we see toxic effects. This represents a problem in its own right, however, because it may lull us into disregarding as trivial those rare exposures that may lead to severe toxicity or death (Nelson *et al*., 2006). For this reason, it is important that healthcare professionals have a basic knowledge of the most important and harmful poisonous plants.

Correct identification of a poisonous plant may be crucial in the treatment of patients where significant exposure took place and/or the patient is experiencing symptoms of poisoning. One of the common pitfalls when dealing with plant exposures is the incorrect identification of the plant, based on common names and other assumptions made by nonexperts. The identity of a plant should not be based only on a common name, but should at least be consistent with detailed descriptions of the physical characteristics of the plant. Ideally, the plant should be identified by experts, such as botanists familiar with the plant, based on a properly collected and prepared physical example of the plant, or by direct comparison with herbarium specimens. Where timely submission of plant samples to an expert or herbarium is impractical, plant material should be preserved in a plant press or a substitute, such as a large, heavy book. Whenever possible, reproductive parts, including flowers, fruits and seeds should be included, as well as detailed descriptions of the plant's location and growth form. When rapid identification is needed, references on poisonous plants containing detailed descriptions and pictures are available (Frohne and Pfänder, 2005; Nelson *et al*., 2006; Gloster, 2004), and should be consulted when necessary in the absence of expert opinion. Although online sources should be interpreted with caution, searches for plant images using services such as Google Image Search™ often produce multiple images of the most common and important poisonous plants that can be helpful in attempts to rapidly obtain a probable identification based on prominent morphological characteristics. Comprehensive, reliable online sources are available that can be consulted for additional information that are useful for identification. Some sources are more relevant to specific parts of the world, such as the United States Department of Agriculture (USDA) Plants Database in North America (USDA, 2008), while others have a global coverage, such as the electronic Plant Information Centre (Royal Botanic Gardens, Kew, 2008). Poison centres and other poisoning information services are readily available in many parts of the world, and are often able to give sound advice on plant identification, plant poisoning diagnoses and case management.

The information that follows below is mostly limited to poisons of plant origin that are considered to be important because they are associated with common or serious toxicity. However, discussions of some plants are included that are only mildly toxic and very rarely cause poisoning, but which are often perceived as harmful by the general public and result in frequent enquiries to Poison Control Centers and other healthcare professionals. Plants are discussed as groups that share specific or closely related toxic compounds or that share specific toxicity syndromes. Descriptions include the most prominent families and/or genera associated with poisoning, the toxic agents and their mechanisms of action, risk factors, toxicity syndrome descriptions and suggested management strategies. Where available, frequently used common names for families and genera are included, but it should be noted that common names are often regional, the same name may be used to describe more than one plant and a specific plant may be known by various names.

Finally, plant poisoning is a dynamic field. The distribution of potentially poisonous plants and plant products change over time as people make use of distant sources of food ingredients, which may contain unfamiliar contaminants, as new species and varieties become popular as decorative plants, and as biologically active plants and plant products, used as traditional medicines or mind-altering drugs in one part of the world, become known and used/abused in other parts of the world where the traditional knowledge of preparation methods, dosages and risks are unknown. New information on active constituents and mechanisms of action often change how we approach diagnoses and treatment. Healthcare professionals need to keep abreast of new plant-poisoning hazards and developments in treatment to be in the best possible position to give sound advice and intervene successfully in cases of plant poisoning.

2 ANTICHOLINERGIC ALKALOIDS

2.1 Plants

Anticholinergic alkaloids are mostly associated with members of the Solanaceae (potato) family, including

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Atropa spp. (belladonna), *Brugmansia* spp., *Datura* spp. (Jimsonweed), *Hyoscyamus* spp. (henbane), *Solandra* spp. (chalice vine) and *Solanum* spp. (nightshade). These plants are typically forbs and small shrubs found in most habitats around the world. They are also commonly cultivated for use in gardens.

2.2 Toxic Agent and Mechanism

Anticholinergic alkaloids, also known as tropane alkaloids, include atropine, hyoscyamine, hyoscine and scopolamine. All plant parts are toxic, but alkaloid concentrations are especially high in green plant parts and unripe fruit (Knight and Walter, 2001). Alkaloids are resistant to breakdown and may persist as contaminants in foods, even following extensive processing into secondary products (Perharic, 2005; Lee, 2007). The tropane alkaloids competitively antagonize the effects of acetylcholine on muscarinic receptors in the central and parasympathetic nervous systems.

2.3 Risk Factors

One of the most common sources of anticholinergic alkaloid poisoning is the abuse of *Datura* spp. (Jimsonweed) seeds as mind-altering drugs, either by ingestion or inhalation (Guharoy and Barajas, 1991; Soneral and Connor, 2005). Variations in the alkaloid levels of individual plants make its use as a mind-altering drug hazardous, even for experienced users. Poisoning may also result from mistaken identification when gathering 'edible' wild leafy greens and berries. This is of particular concern where wild leafy greens are common in the diet. Indiscriminate harvesting and consumption of apparently edible berries, such as those on *Atropa belladonna* is associated with poisoning, mostly in children, where these plants are cultivated as garden subjects. Contaminated flour has been associated with mass outbreaks of poisoning (Perharic, 2005). *Atropa belladonna* poisoning is one of only a handful of plant poisonings where secondary poisoning has been described from eating the meat of animals that grazed on the plant, or from ingesting contaminated honey (Lee, 2007).

2.4 Toxicity Syndrome

Suppression of the parasympathetic nervous system leads to an apparent overexpression of the sympathetic system. Classically, the clinical syndrome has been described as 'blind as a bat', due to ciliary body and iris muscle paralysis that leads to mydriasis and cycloplegia, 'dry as a bone', due to suppression of salivation resulting in a profound dry mouth sensation, 'red as a beet', due to flushing of the skin, 'hot as a hare', due to effects on temperature regulation leading to hyperthermia, and 'mad as a hen', due to central nervous system effects that include visual hallucinations, agitation, impaired judgment and risk-taking behaviour, delirium, seizures and coma (Spina and Taddei, 2007; Lee, 2007). Death may result from respiratory or cardiac arrest. Signs appear from 30 minutes to four hours following ingestion and may last from several hours to several days.

2.5 Management

Initiate supportive and symptomatic treatment. Sedation with a benzodiazepine may be of benefit. Physostigmine by slow intravenous injection ($1–2\,mg\,kg^{-1}$ in adults; $0.02\,mg\,kg^{-1}$ in children) is an antidote. Note that the duration of alkaloid activity can be longer than the antidote activity and may require repeated administration of the antidote (Nelson *et al*., 2006).

3 CARDIAC GLYCOSIDES

3.1 Plants

Cardiac glycosides are produced by a wide range of flowering plants including both monocotyledons and dicotyledons, with growth forms ranging from bulbs to shrubs and small trees. Plants include members of the Apocynaceae (dogbane) family, including *Acokanthera spp.* (poison arrow plant), *Adenium* spp. (desert rose), *Nerium oleander* (oleander), *Pentalinon luteum* (hammock viper's tail), *Strophanthus* spp. and *Thevetia* spp.; the Asclepiadaceae (milkweed) family, including *Asclepias* spp. (milkweed), *Calotropis* spp. and *Cryptostegia* spp. (rubbervine); the Crassulaceae (orpine) family, including *Cotyledon* spp. (pig's ear), *Kalanchoe* spp. (neverdie) and *Tylecodon* spp.; the Hyacinthaceae (hyacinth) family, including *Bowiea volubilis* (climbing onion), *Urginea/Drimia* spp. (snake's head) and *Ornithogalum* spp. (star of Bethlehem); the Iridaceae (iris) family, including *Homeria* spp. and *Moraea* spp. (tulip); the Liliaceae (lily) family, including *Convallaria* spp. (lily of the valley) and *Scilla/Merwilla* spp. (squill); the Melianthaceae (melianthus) family, including *Melianthus* spp. (honey flower); the Ranunculaceae (buttercup) family, including *Adonis* spp. (pheasant's eye) and *Helleborus* spp. (hellebore); the Santalaceae (sandalwood) family, including *Thesium* spp. (flaxleaf); and the Scrophulariaceae (figwort)

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family, including *Digitalis* spp. (foxglove). Although most of these species have specific habitat requirements that restrict their distribution under natural conditions, many produce attractive flowers and foliage that make them popular as garden subjects and contribute to their availability all over the world. Examples of commonly cultivated plants grown for their showy flowers include *Digitalis purpurea* (foxglove) and *Ornithogalum umbellatum* (grass lily). *Nerium oleander* (oleander) and *Thevetia peruviana* (yellow oleander) are popular in many parts of the world as a hardy hedge plants.

3.2 Toxic Agent and Mechanism

Glycosides consist of two parts: sugars, referred to as the glycone portion of the molecules, are bonded via glycosidic bonds to nonsugar moieties, referred to as the aglycone portion. The aglycones of cardiac glycosides are steroid derivatives and are responsible for the toxic effects (Kellerman *et al*., 2005). Generally, all plant parts are considered toxic.

Cardiac glycosides inhibit Na^+/K^+-ATPase, which causes intracellular Na^+ accumulation, followed by Ca^{2+} accumulation (McDonough *et al*., 2002). These changes result in increased cardiac muscle inotropy and bradycardia. Increased vagal tone contributes to a slowing of the heart rate. As the dose increases, the heart muscle becomes more excitable and the heart becomes susceptible to dysrhythmias of various types, including frequent premature ventricular beats, bradycardia, paroxysmal atrial tachycardia with block, junctional tachycardia and bidirectional ventricular tachycardia (Ma *et al*., 2001). Na^+/K^+-ATPase inhibition also affects other smooth muscle tissue, such as the vascular system, where vasoconstriction occurs in the atrial and venous systems, and in the digestive tract smooth muscle, where excessive smooth muscle contraction is induced.

3.3 Risk Factors

Cardiac-glycoside-containing plants and extracts are commonly prescribed in traditional medicine for a variety of indications and as tonics, but in particular for the treatment of heart failure. Toxicity often results from the uncontrolled use of these plants as medicines, especially when the users have limited experience and training in the safe use of these potent medicines (McVann *et al*., 1992; Tracqui *et al*., 1997). The common use of cardiac-glycoside-containing plants as garden subjects places people at risk (Cheung *et al*., 1989). Cardiac-glycoside-containing plants are occasionally used to commit murder and suicide (Tracqui *et al*., 1997; Driggers *et al*., 1989).

3.4 Toxicity Syndrome

Plant-associated cardiac-glycoside poisoning closely resembles poisoning due to digitalis overdose (Tracqui *et al*., 1997). The most obvious initial clinical signs of cardiac-glycoside toxicity are abdominal pain, nausea and vomiting. Headache, dizziness, blurred vision and dyschromatopsia (disturbance of colour vision) may also occur. After an initial bradycardia, the pulse becomes rapid and weak. Various heart dysrhythmias are discernable by electrocardiography. Hyperkalaemia may be seen in severely affected patients. Other typical signs associated with severe toxicity include weakness, muscle tremors, paresis, dyspnoea, cardiogenic shock, convulsions and coma.

3.5 Management

Consider consulting a Poison Control Center. Prompt administration of activated charcoal is of benefit, but standard decontamination and supportive treatment on its own is often not adequate in severe cases involving life-threatening dysrhythmias, cardiogenic shock and hyperkalaemia (Eddleston, 2003). Digoxin-specific antibody fragments (Digibind™) are available as an antidote. Although it was developed specifically for digoxin, there is sufficient crossreaction with other cardiac glycosides for the drug to be useful in the treatment of cardiac-glycoside poisoning in general (McMillin *et al*., 2002). The initial dose in adults and children should be 400 mg intravenously. Additional doses may be needed, depending on the response to treatment.

4 CYANOGENIC GLYCOSIDES

4.1 Plants

Cyanogenic glycosides are produced by a wide variety of flowering plants as a means of defence against herbivores (Gleadow and Woodrow, 2002). Toxic species include members of the Caprifoliaceae (honeysuckle) family, including *Sambucus* spp. (elderberry); the Caricaceae (papaya) family, including *Carica papaya* (papaya); the Euphorbiaceae (spurge) family, including *Manihot esculenta* (cassava); the Fabaceae (legumes), including *Lotus* spp. (trefoil), *Phaseolus* spp. (tepary bean) and *Trifolium* spp. (clover); the Hydrangeaceae (hydrangea) family, including *Hydrangea* spp.; the Juncaginaceae

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(arrow-grass) family, including *Triglochin* spp. (arrow-grass); the Poaceae (grasses), including *Sorghum* spp. and *Zea mays* (maize/corn) and the Rosaceae (rose) family, including *Eriobotrya japonica* (loquat), *Malus* spp. (crab apple) and *Prunus* spp. (plums, prunes, cherries, peaches, apricots and almonds).

4.2 Toxic Agent and Mechanism

Cyanogenic glycosides may be found in most plant parts in affected plant species, but concentrations tend to be highest in the seeds of the Rosaceae, while high concentrations in the grasses are mostly found in young or resprouting plants. Intact cyanogenic glycosides are not toxic. Toxicity occurs when cyanide in the form of HCN (hydrocyanic acid), also referred to as prussic acid, is released from its glycoside form by a process of hydrolyses. Enzymes that are able to hydrolyse cyanogenic glycosides are often present in plant tissues, but are sequestered in different cell compartments and only cause HCN release when plant tissues are damaged. HCN release can also be facilitated by digestive-tract enzymes (Knight and Walter, 2001). This may be a rapid or slow process depending on conditions in the digestive tract. After release, HCN is readily absorbed. It inhibits cytochrome oxidase, which blocks cellular respiration and causes tissue anoxia. Rapid death may result from the failure of organs that are dependent on continuous and relatively efficient oxygen-dependent energy production, such as the brain and the heart. Exposure to toxic doses during pregnancy may lead to teratogenic effects (Frakes *et al*., 1985).

4.3 Risk Factors

The cyanogenic glycoside concentrations in certain plant species, especially the grasses such as *Sorghum halepense* (Johnsongrass) and other sorghum species vary depending on their growth stage. Grazing animals are often at risk if the plants are consumed during their early growth phase, or as plants regrow after a severe frost or mowing, when cyanogenic glycoside concentrations are high (Knight and Walter, 2001). High soil nitrogen content tends to promote cyanogenic glycoside accumulation in plant tissues. The flesh of ripe fruits often does not contain cyanogenic glycosides, even if concentrations in the seeds or leaves are hazardous. Human exposure to toxic levels of cyanogenic glycosides is comparatively rare because people typically do not consume large quantities of those plant parts that are hazardous. Food preparation, such as cooking, further reduces the risk. An exception to this general rule is poisoning by varieties of *Manihot esculenta* (cassava), which accumulate high cyanogenic glycoside concentrations. Cassava poisoning is a common occurrence in regions where home-prepared cassava roots and leaves are a staple food, such as rural areas of central Africa. The cyanogenic glycoside content of cassava can be reduced to safe levels by adequate preparation, which should include extended soaking in water and thorough cooking. When these steps are omitted or deficient, poisoning may occur (Ngudi *et al*., 2003; Tylleskar *et al*., 1992). Another occasional source of human poisoning is the ingestion of large quantities of raw apple seeds or pit kernels from *Prunus* species such as *Prunus armeniaca* (apricot). Note that the amount of seeds or kernels that people consume as part of a normal diet is usually not hazardous. Poisoning typically occurs only when unusually large amounts are ingested.

4.4 Toxicity Syndrome

Cyanogenic glycoside toxicity is often delayed for a variable length of time, up to several hours, because of the time required for glycoside breakdown and cyanide release in the digestive tract. Typical early signs of acute toxicity are nausea, vomiting and abdominal pain. The patient may sweat and complain of headache, disorientation, vertigo, faintness or a burning sensation in the mouth and throat. Signs of hypoxia appear and may include exercise intolerance, tachypnoea and tachycardia. The lack of oxygen uptake in tissues leads to oxygen buildup in venous blood, causing venous blood to become highly oxygenated, similar to arterial blood, and bright red in colour. Compensatory anaerobic energy production leads to lactic acidosis. Signs of hypoxia become progressively worse. Terminal signs may include convulsions, respiratory depression, bradycardia, cardiogenic shock, lung oedema, paralysis and coma (Yen *et al*., 1995; Holland and Kozlowski, 1986).

4.5 Management

When poisoning is suspected, the rapid progression of cyanide poisoning makes it imperative that treatment with an appropriate antidote should be given promptly, even when confirmatory tests are unavailable, as antidote therapy is often essential to survival. The antidote of choice in human poisoning is hydrocobalamin, which is typically packaged in concentrated, stable lyophilized powder form and must be reconstituted before use using suitable diluents such as 0.9% NaCl, lactated Ringer's solution or 5% dextrose solution. The adult dose is 5 g hydrocobalamin by slow intravenous injection (over 15 minutes). If needed, the dose may be repeated for a total of 10 g. Alternative treatments include breaking

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a nitrite pearl and holding it under the patient's nose for 30 seconds each minute. Sodium nitrite may be administered intravenously (the adult dose is 10 ml of a 3% solution). This should be followed by intravenous administration of sodium thiosulfate (the adult dose is 50 ml of a 25% solution). Although it has been used successfully (Mannaioni *et al*., 2002), the safety of combining hydrocobalamin with other treatments has not been established. Antidote therapy should be combined with appropriate supportive care.

5 PLANT-INDUCED DERMATITIS

5.1 Plants

Skin effects due to contact with plants are commonly reported to poison-control centers (Nelson *et al*., 2006). Among the 25 most reported toxic-plant exposures in the United States (**Figure 1**), eight are associated with dermal toxicity including *Crassula* spp. (jade plant), *Toxicodendron* spp. (poison oak/poison ivy), *Schefflera* spp. (umbrella tree), *Ficus* spp. (fig), *Chrysanthemum morifolium* (florist's daisy), *Hedera helix* (English ivy), *Eucalyptus* spp. (blue gum) and *Taraxacum officinale* (dandelion). Many, if not most, plants have the potential to induce allergic contact dermatitis, usually following repeated exposure. A listing of all the plants that have been associated with contact dermatitis is, therefore, impractical and it is prudent to assume that any plant has the potential to induce allergic contact dermatitis in susceptible individuals.

5.2 Toxic Agent and Mechanism

Phytotoxins may affect the skin through a variety of mechanisms, including physicochemical disruption of specific cellular processes, mechanical and/or chemical irritation, allergies and phototoxicities. Although the aetiologies differ, the skin's response to acute insult from plant toxins or mechanical injury from plant structures is most often an inflammatory response of varying severity and extent. Reactions to allergens, such as urushiol found in *Toxicodendron* spp. and a wide variety of macromolecules found on or in the tissues of most plants, are variable, depending on the degree, frequency and duration of exposure, and on the allergenic potential of the molecule(s) involved. Persistence of the allergen in the skin may also be an important factor. Type IV hypersensitivity, also referred to as allergic contact dermatitis, is the most common allergic reaction in the skin, but other types of hypersensitivities are possible (Nelson *et al*., 2006). Exposure to light is a prerequisite for the development of dermatitis associated with phototoxicity (Greeson *et al*., 2001), because it depends on the absorption of photons by phototoxic compounds, and the release of the absorbed energy to surrounding tissues in the form of higher-energy particles. Mechanical damage to skin resulting from barbs, thorns, calcium oxalate raphides, commonly found in species of the Araceae family, or stinging trichomes, such as those found in nettles (*Urtica* spp.), is often accompanied by the deposition of irritant compounds that may intensify pain and induce pruritis (Nelson *et al*., 2006).

5.3 Risk Factors

Most cases of plant-associated dermatitis are due to allergic reactions and require prior sensitization in susceptible individuals. Plants, however, vary widely in their potential to induce allergic reactions, as well as the severity and duration of reactions. *Toxicodendron* spp., for example, have a relatively high potential for inducing severe reactions with 50–70% of the general population being susceptible (Tanner, 2000), while reactions to other commonly implicated plants, such as species of *Taraxacum, Eucalyptus* and *Hedera* are usually less severe. There is tremendous variability between individuals' general susceptibility to plant allergies and the plants to which they react, which is likely to be influenced by inheritable traits. Minor exposures, such as lightly brushing against leaves, may induce a severe reaction to *Toxicodendron* spp., while repeated, intimate exposure is often required for reactions to be induced by other species, such as *Chrysanthemum morifolium*, which typically induce allergies in nursery workers who handle the plant. Even with intimate, repeated exposure to unprotected skin, however, the incidence of sensitivity is much lower compared to Toxicodendron sensitivity and appears to be variable between different population groups, being less common in Asian populations (Tanner, 2000). The part of the plant and its cooked or raw status can make a difference. Some individuals, for example, experience dermatitis if they handle uncooked, peeled potatoes, while cooked potatoes or other potato plant parts do not induce dermatitis. The importance of repeated exposure is also demonstrated by the increased incidence of sensitivity to onions in some subpopulations. Onions more commonly cause chronic hand eczema in older, frequently exposed women who handle onions during food preparation, compared to other sections of the population (Cabanillas *et al*., 2006). Phototoxic effects may occur with repeated, high-dose use of herbal remedies containing St. John's wort (*Hypericum perforatum*) (Jacobson *et al*., 2001). Ironically, though, topical St. John's wort treatment has also been shown to be of benefit in the treatment of atopic dermatitis (Schempp *et al*., 2003).

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5.4 Toxicity Syndrome

The symptoms resulting from different aetiologies most commonly presents as an inflammatory response of varying severity. The overlap between the symptoms associated with various aetiologies makes the differentiation between specific aetiologies, based on lesions and symptoms, challenging. Allergic reactions to plants that result in dermal inflammation is arguably the most common aetiology of plant-associated contact dermatitis, because many different plant species have the potential to induce allergies in susceptible individuals; and because some of the plants that have a high potential for inducing contact allergies, such as *Toxicodendron* spp. are widespread and hard to avoid when entering habitats where the plants are common. Exposures in sensitive individuals typically presents as a rash or eczema on exposed skin, which may include redness, itching, swelling, blistering and pain. The development of lesions related to Type IV hypersensitivity may take hours to days to fully develop, and symptoms may persist for several days up to two weeks. Secondary infection may result in the formation of pustules and purulent exudates. The severity of lesions associated with allergic contact dermatitis is often not proportional to the level of exposure, but rather depends on the level of sensitization in the individual. Pain and dermatitis due to plant-derived chemical and/or mechanical irritants, from exposures to plants such as stinging nettles and capsicum preparations, do not require prior exposure and sensitization. Reactions to these plants and plant-derived products are rapid and the severity is proportional to the level of exposure. Since exposure to light is a prerequisite for phototoxic effects, only sunlight-exposed skin is typically affected. Lesions tend to be more severe on skin surfaces that receive more light exposure, such as the face and hands, and light-skinned individuals are more susceptible. In some instances, photosensitivity may be linked to plant-associated allergic contact dermatitis, a situation that is more commonly encountered in older individuals (Frain-Bell and Johnson, 1979).

5.5 Management

Avoidance is the simplest and most effective approach to allergic dermatitis-inducing plants. Species that are commonly implicated in serious contact dermatitis, such as *Toxicodendron* spp., should be eradicated from areas where contact is expected to be frequent and difficult to avoid. Effective herbicides, registered for this purpose, are available. Hand-pulling by nonsusceptible individuals and repeated grazing by goats and sheep may also be effective. Burning is not an effective control method and urushiol may be carried in smoke, potentially leading to skin and respiratory reactions in smoke-exposed individuals (Nelson, 2000). If avoidance or eradication is not practical, physical protection of exposed skin using clothing or barrier creams is necessary. Barrier creams containing 5% quaternium-18 bentonite are effective in preventing contact dermatitis if properly applied (Scott *et al*., 2002). Sensitive individuals should also be alerted to the fact that second-hand exposure via pets or clothing may be hazardous. Some individuals are allergic to multiple plant species, making identification of particular species that must be avoided challenging. In such cases, attempts should be made to associate the appearance of symptoms with visits to specific areas or habitats. If associations can be made, identified areas or habitats should be avoided or appropriate precautions taken.

Early skin decontamination may be effective in preventing or reducing the symptoms of exposure to plant-associated contact allergens. This can be achieved by gently rinsing the skin with copious amounts of water. The addition of soap or the use of mild solvents, such as isopropyl alcohol, may help in allergen removal from the skin, but care should be taken not to damage the skin surface. Treatment is aimed at symptom alleviation and may involve the use of corticosteroids, analgesics, anti-inflammatory drugs or antihistamines. An important aim in treatment is to prevent itching and scratching, which leads to secondary skin damage and infections. Corticosteroids are the mainstay of the treatment of severe allergic contact dermatitis because they counter lymphocyte proliferation and cytokine production. Topical medications, such as medicated creams and ointments, are preferred if they are effective. Systemic corticosteroids may be needed if topical treatment is ineffective, usually with good results (Mark and Slavin, 2006). Lesions may become infected with bacteria, requiring systemic antibiotic treatment. Pain and dermatitis associated with direct irritants can be controlled with analgesics and anti-inflammatory drugs. If done shortly after exposure, gentle washing with copious amounts of warm, soapy water may be effective in removing irritating substances from the skin. Avoid deep scrubbing that may cause damage to the stratum corneum. Avoidance of sunlight is essential to control symptoms associated with phototoxicity. Additional alleviation of symptoms may be obtained by using analgesics and anti-inflammatory drugs as needed.

6 GASTROINTESTINAL IRRITANTS/STIMULANTS

6.1 Plants

A wide variety of plants affect the gastrointestinal tract (GIT). Commonly implicated genera and their principle toxins include: *Euphorbia* (spurges), containing diterpene esters; *Alocasia*, *Arum*, *Colocasia*, *Philodendron*, *Dieffenbachia*, *Schlefflera*, *Spathiphyllum* and related

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Araceae genera, as well as *Brassaia* (umbrella tree), *Caryota* (fishtail palm) and *Parthenocissus* (creeper) containing calcium oxalate raphides; *Daphne* (paradise plant) *Senna* and *Wisteria*, containing glycosides; *Phytolacca* (pokeweed), containing triterpenes; and *Ranunculus* (buttercup), containing protoanemonin. Some plants may be associated with GIT upset only when ingested in high quantities or at specific growth stages, while being safe under other conditions. Examples include the ingestion of greening or sprouting potatoes, unripe fruit or large quantities of dried fruit.

6.2 Toxic Agent and Mechanism

The mechanisms of action of most plants that affect the GIT have not been well defined, but can be classified into two broad categories: nonspecific irritant effects and specific receptor activity leading to GIT effects. Irritants are found in many plants and may be associated with specific growth phases or plant parts, such as unripe fruits. Irritants stimulate GIT smooth-muscle contraction directly and/or induce an acute inflammatory response, typically associated with increased fluid secretion into the GIT lumen. Severe irritation may lead to ulceration. calcium oxalate raphides leads to local tissue damage in the upper GIT associated with severe inflammation, enhanced by proinflammatory compounds associated with the raphides. Plants have evolved a variety of specialized strategies for effectively delivering raphides, including the formation of needle-shaped crystals, and pressurized crystal idioblasts that forcibly expel raphides into tissues upon contact (Franceschi and Nakata, 2005). Stimulation of cholinergic receptors appears to be a major specific mechanism of inducing increased GIT smooth-muscle contraction due to plant toxins (Nelson *et al*., 2006). GIT peristaltic and secretory control, however, depends on a complex system of balanced responses and multiple receptor ligands (Grider, 2004), offering many potential toxicity targets.

6.3 Risk Factors

Due to the relatively common occurrence of irritants in plants, indiscriminate ingestion or chewing on unfamiliar plants often leads to GIT upset. This is especially relevant to young children who often chew on indoor plants. Gathering and eating wild plants is a risk when the collectors are unfamiliar with the plants they collect, particularly when plants are gathered in early growth stages before the development of flowers and fruits. Poorly controlled production and use of herbal remedies intended for the treatment of constipation can be hazardous due to lack of consistency in active compound concentrations and dose formulations. Even when herbal remedies are appropriately formulated and produced, popular perceptions of herbal medicines as 'natural, safer' alternatives to other chemical laxatives, occasionally lead to ingestion of large doses that cause severe, long-lasting diarrhoea.

6.4 Toxicity Syndrome

The first signs of GIT irritant exposure are generally nausea and vomiting. Other typical irritant effects include hypersecretion and smooth-muscle contraction, which leads to diarrhoea, and abdominal pain associated with cramping. Severe gastric irritation or ulceration may lead to blood products appearing in the vomitus, which may have a 'coffee-granule' appearance. Diarrhoea can range widely in severity and appearance. Young children are particularly vulnerable to electrolyte loss and dehydration.

6.5 Management

The management of plant poisoning involving gastrointestinal symptoms is nonspecific, and aimed at symptom alleviation and countering the consequences of fluid and electrolyte loss. Vomiting can often be controlled with drugs such as metoclopramide. The treatment of diarrhoea depends on severity and should be aimed at the control of water and electrolyte loss and its replacement. The use of antidiarrhoeal drugs, such as loperamide, is generally not recommended (Nelson *et al*., 2006). Rehydration and electrolyte replacement therapy may include oral rehydration or intravenous fluids, depending on the need. Since GIT upset is often one of the first effects seen in poisoning cases that eventually include systemic toxicity, the potential for the gastrointestinal effects being part of a more widespread, systemic toxicity should always be considered (Nelson *et al*., 2006).

7 ION-CHANNEL ACTIVATORS/INHIBITORS

7.1 Plants

Many members of genera in the Ericaceae (heath) family have effects on ion channels, including *Rhododendron* spp. (azalea), *Kalmia* spp. (laurel), *Lyonia* spp. (staggerbush), *Leucothoe* spp. (doghobble) and *Pieris* spp. (fetterbush). Other affected families are the Ranunculaceae (buttercup) family, including *Aconitum* spp. (monkshood); the Liliaceae (lily) family, including *Zigadenus* spp. (deathcamus), *Schoenocaulon* spp. (feathershank) and *Veratrum* spp. (false hellebore); and the Taxaceae (yew) family, including *Taxus* spp. (yew).

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7.2 Toxic Agent and Mechanism

Depending on the plant and predominant active compound, various ion channels may be activated or inhibited. One of the most common mechanisms for toxicity is sodium-channel activation, typical of plants in the heath family, containing grayanotoxins. Excessive influx of sodium causes persistent depolarization of neurons and other conductive tissues such as cardiac muscle cells (Nelson *et al*., 2006). Taxine-derived alkaloids, of which several have been identified, are found in *Taxus* spp. (yew) (Wilson *et al*., 2001). Taxines are calcium- and sodium-channel antagonists. Indirect evidence suggests that taxine toxicity is largely attributable to its calcium-channel blocking effects (Wilson *et al*., 2007). Taxine-B induces increased AV (atrioventricular) conduction time and QRS duration in cardiac muscle. Intestinal effects observed in experimental animals included contraction of the duodenum and ileum and inhibition of peristalsis (Wilson *et al*., 2007).

7.3 Risk Factors

Consumption of honey derived from bees harvesting nectar from *Rhododendron* species, sometimes referred to as 'mad honey' is an important risk factor because grayanotoxins are present in nectar and remain active after nectar processing into honey (Koca and Koca, 2007). Consumption of Rhododendron flowers or nectar in other forms, such as wine, juice or as an ingredient in cakes may also be associated with poisoning (Lee *et al*., 2007).

Yew trees and shrubs are hardy, evergreen and produce attractive, bright red fruit. Their widespread and popular use as garden subjects makes them easily accessible for most people. Eating the flesh of the fruit, a bright red aril with a pleasant, sweet taste is, fortunately, not associated with poisoning (Nelson *et al*., 2006; Pietsch *et al*., 2007). Indiscriminate ingestion of seeds with the fruit's flesh, or chewing on twigs and leaves can, however, be hazardous. Yews are also commonly implicated in animal poisoning when animals gain access to garden waste (Wilson *et al*., 2007). A number of web sites dealing with suicides mention yew as a classical method for committing suicide (Pietsch *et al*., 2007). This may partly explain its relatively common use in suicide.

7.4 Toxicity Syndrome

Excessive sodium-channel activation on neurons leads to a variety of effects associated with the central nervous system, including nausea and vomiting, disorientation and seizures. Peripheral effects include paresthesia, excessive perspiration, hypersalivation and muscle weakness, fasciculation and paralysis. Cardiac effects may include hypotension and dysrhythmias ranging from mild bradycardia to complete heart blocks (Gunduz *et al*., 2008; Koca and Koca, 2007; Nelson *et al*., 2006; Lee *et al*., 2007). Taxus poisoning is associated with initial dizziness, dry mouth and mydriasis, followed by nausea and vomiting, abdominal cramping and pain, tachycardia followed by bradycardia, hyperkalaemia, convulsions and respiratory paralysis (Pietsch *et al*., 2007; Nelson *et al*., 2006).

7.5 Management

Life-threatening cardiac effects associated with sodium-channel activation can be countered with rapid saline infusion and atropine (Gunduz *et al*., 2008). Severe hypotension can be counteracted with norepinephrine (noradrenaline). The use of sodium-channel blocking agents, such as lidocaine and amiodarone, makes sense in terms of their mechanism of action, but superior outcomes using these drugs have not been proven (Nelson *et al*., 2006). Specific antidotes for taxus poisoning are not available. Treatment is based on decontamination, such as gastric lavage and activated charcoal, and symptomatic treatment to counteract cardiac dysrhythmias.

8 MICROTUBULE POLYMERIZATION INHIBITORS

8.1 Plants

Plants that inhibit microtubule polymerization include members of the Apocynaceae (dogbane) family, including *Catharanthus* spp. (periwinkle); the Liliaceae (lily) family, including *Colchicum* spp. (crocus) and *Gloriosa* spp. (flame lily); and the Berberidaceae (barberry) family, including *Podophyllum* spp. (mayapple).

8.2 Toxic Agent and Mechanism

Toxic alkaloids that inhibit microtubule polymerization include some of the most well-known antitumour drugs, such as vincristine and related dimeric alkaloids derived from *Catharanthus roseus* (Madagascar periwinkle) (Barnett *et al*., 1978). These compounds destabilize microtubules, which leads to mitotic arrest and, at sufficient exposure levels, cell death (Groth-Pedersen *et al*., 2007). The effects are more pronounced in rapidly dividing cells, which makes it useful for the treatment of tumours, but also affects rapidly dividing normal cells,

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such as bone marrow, intestinal epithelium and hair follicles. At high doses or following prolonged exposures, organs with relatively rapid cell turnover rates, such as the liver and pancreas can be affected (Brvar *et al*., 2004). It also affects peripheral nerve function and reduces the number of intraepidermal nerve fibres (Siau *et al*., 2006).

8.3 Risk Factors

The leaves of some toxic members of the Liliaceae, such as *Colchicum autumnale* (autumn crocus), may be confused with that of *Allium ursium* (wild garlic) and is a cause of poisoning in individuals that gather wild herbs for use in food (Hermanns-Clausen, 2005).

8.4 Toxicity Syndrome

Initial signs of acute poisoning usually involve the GIT and include nausea, vomiting and diarrhoea (Brvar *et al*., 2004). Ulcerations in the mouth and gastrointestinal necrosis are also possible (Nelson *et al*., 2006). Subsequent effects potentially include failure of various organ systems, including the heart, liver and pancreas. Bone-marrow suppression leads to pancytopenia (Brvar *et al*., 2004). Acute clinical signs may include colic, hepatosplenomegaly and jaundice, while more chronic exposure may lead to cirrhosis or ascitis following hepatic venous occlusion (Nelson *et al*., 2006).

8.5 Management

There are no specific treatments available. Supportive treatments for liver failure, immune suppression and other manifestations of poisoning should be instituted to alleviate symptoms and promote tissue repair. Severe liver failure may be irreversible and successful treatment could require liver transplant (Nelson *et al*., 2006).

9 NICOTINIC ALKALOIDS

9.1 Plants

Nicotinic alkaloids are found in a wide range of plants, including members of the Apiaceae (carrot) family, including *Conium maculatum* (poison hemlock); Berberidaceae (barberry family), including *Caulophyllum* spp. (cohosh); Campanulaceae family, including *Hippobroma* spp. and *Lobelia* spp.; Fabaceae (pea) family, including *Baptisia* spp. (wild indigo), *Gymnocladus* spp. (coffee tree), *Laburnum* spp. and *Sophora* spp. (necklacepod); Ranunculaceae (buttercup family), including *Delphinium* spp. (larkspur), and Solanaceae (potato family), including *Nicotiana* spp. (tobacco).

9.2 Toxic Agent and Mechanism

Nicotinic alkaloids can be found in a variety of alkaloid groups, such as diterpenoids (found in *Delphinium* spp.), piperidines (found in *Conium* spp.) and pyridines (found in *Nicotiana* spp.) (Pfister *et al*., 2001). Nicotinic receptors are pentameric ligand-gated cation channels, with many subtypes, that are activated by acetylcholine (Schmitt, 2000). They are found in the central nervous system, parasympathetic and sympathetic peripheral nervous systems and at neuromuscular junctions. Depending on the ligand-binding characteristics and the specific binding conditions, nicotinic receptors can transition between closed, open and desensitized states, leading to suppression, excitation or nonreactivity of affected central and peripheral neurological or neuromuscular pathways and functions (Giniatullin *et al*., 2005). Nicotine is the classic nicotinic alkaloid. It binds to nicotinic receptor subtypes relatively indiscriminately and tends to induce initial stimulation followed by nonreactivity in affected pathways. Many nicotinic alkaloids derived from plants share this characteristic to some extent, but different nicotinic alkaloids differ in receptor binding characteristics (Dobelis *et al*., 1999).

9.3 Risk Factors

The most problematic and widespread risk factor associated with nicotinic alkaloids is chronic exposure to tobacco smoke and other tobacco products, which is generally considered to be one of the most important preventable health risks in modern society. This is due, in part, to the tremendous addictive potential of nicotine (Bierut *et al*., 2008). Acute toxicity is, however, much less common and is usually associated with accidental exposure following misidentification of nicotinic-alkaloid-containing plants (Durand *et al*., 2008). The infamy of some plants, such as *Conium maculatum* (poison hemlock) that was used in the execution of Socrates, unfortunately contributes to their use in criminal poisoning (Trestrail, 2007).

9.4 Toxicity Syndrome

The acute effects of nicotinic alkaloids are characterized by initial stimulation, followed by loss of reactivity and

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function in nicotinic pathways in the central and peripheral nervous systems, and at neuromuscular junctions. Typical symptoms include nausea and vomiting, salivation, diaphoresis, trembling, dyskinesia, weakness, bradycardia followed by tachycardia, hypertension, increased respiration rate, urination, convulsions, paralysis, coma and death (Nelson *et al*., 2006; Vetter, 2004).

9.5 Management

Early decontamination, including stomach lavage and activated charcoal, may be effective in reducing toxic effects (Vetter, 2004). Treatment is symptomatic and should be targeted at correcting serious vital sign abnormalities, such as countering hypertension with diltiazem or nitroprusside. Seizures can be treated with intravenous benzodiazepines. Ventilatory support may be necessary in cases of respiratory muscle weakness or paralysis (Nelson *et al*., 2006).

10 PYRROLIZIDINE ALKALOIDS

10.1 Plants

Pyrrolizidine alkaloid toxicity is associated with a wide variety of plants including members of the Asteraceae (aster) family, including *Callilepis* spp. (ox-eye daisy) and *Packera* spp. (ragwort; formerly known as *Senecio* spp.); Boraginaceae (borage) family, including *Echium* spp. (viper's bugloss), *Heliotropium* spp. (heliotrope) and *Symphytum* spp. (comfrey); Fabaceae (bean) family, including *Crotalaria* spp. (rattlebox), *Sesbania* spp. (riverhemp); Lamiaceae (mint) family, including *Teucrium* spp. (germander); and Zygophylaceae (creosote-bush) family, including *Larrea* spp. (creosote bush). Many other plant families also have members that produce pyrrolizidine alkaloids and, although they are not as often associated with poisoning, can be potentially toxic, including the Apocynaceae (dogbane) family, Celastraceae (bittersweet) family, Convolvulaceae (morning-glory) family, Proteaceae (protea) family, Orchidaceae (orchid) family and Ranunculaceae (buttercup) family.

10.2 Toxic Agent and Mechanism

Pyrrolizidine alkaloids and related N-oxides are not directly toxic, but are metabolized by microsomal enzymes to pyrroles, which are dehydro- forms of the alkaloid, in a process that occurs mostly in the liver. Pyrroles are powerful alkylating agents leading to the formation of DNA adducts and crosslinking of proteins, amino acids and glutathione. Exposure is associated with various genotoxic effects including tumorogenicity, mutagenicity and teratogenicity (Fu *et al*., 2004), but a clear link between human cancer and pyrrolizidine alkaloid exposure has not been made (Prakash *et al*., 1999). The most prominent acute lesions occur in the liver, where high doses can cause centrilobular necrosis. Acute endothelial injury can also occur in the pulmonary vasculature in animals associated with the ingestion of *Crotalaria* spp. (Knight and Walter, 2001), but similar lesions have not been described in human pyrrolizidine alkaloid poisoning (Nelson *et al*., 2006). Chronic exposure leads to nonthrombotic veno-occlusive liver disease and, eventually, liver cirrhosis (Stickel and Seitz, 2000).

10.3 Risk Factors

The use of pyrrolizidine-alkaloid-containing plants in herbal medicines and dietary supplements is common in many parts of the world. It is one of the most important health risks associated with the unregulated use of herbal products (Stickel *et al*., 2000; Sheikh *et al*., 1997; Seeff, 2007). Inclusion of pyrrolizidine-alkaloid-containing plants as contaminants in foodstuffs, such as flour, is a potentially massive source of exposure (Prakash *et al*., 1999). Pyrrolizidine alkaloids are excreted through milk (Panter and James, 1990), which may be a potential source of exposure when milk-producing animals consume pyrrolizidine-alkaloid-containing plants and infants may be exposed through mother's milk. Lactation may partially protect lactating mothers, while exposing vulnerable infants (Schoental, 1968). Pyrrolizidine alkaloid exposure in pregnant women may lead to foetal poisoning (Rasenack *et al*., 2003). A particularly tragic example of the risks associated with inappropriate use of pyrrolizidine-alkaloid-containing herbal medicines is the lethal poisoning of young children due to toxic *Packera* spp. in South Africa (Steenkamp *et al*., 2000). The collection of plant material by nonexperts for sale in markets, and the difficulty of differentiating between toxic and nontoxic *Packera* spp., contribute to the problem.

10.4 Toxicity Syndrome

The major target organ in pyrrolizidine alkaloid poisoning is the liver. Hepatic degeneration and necrosis is mostly centrilobular, but panlobular necrosis is possible at massive exposure levels. Chronic liver lesions include fibrotic and cirrhotic changes. The clinical presentation depends on the level and duration of exposure. Massive, acute exposure leads to gastrointestinal

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symptoms, abdominal pain, hepatosplenomegaly and icterus (Nelson *et al*., 2006). Biochemical indicators such as aspartate ammotransferase (AST) and bilirubin levels are consistent with liver failure (Nelson *et al*., 2006). Chronic exposure can lead to cumulative effects, including cirrhosis, ascites and, potentially, liver carcinoma (Nelson *et al*., 2006; Prakash *et al*., 1999).

10.5 Management

There are no specific treatments available. Spontaneous repair of liver damage may occur, depending on the level of injury. Severe liver damage or cirrhosis may require liver transplant (Nelson *et al*., 2006).

11 TOXALBUMINS

11.1 Plants

Toxalbumin-containing plants include species of the Cucurbitaceae family (*Momordica*), the Fabaceae family (*Abrus*, *Robinia*), the Euphorbiaceae family (*Hura*, *Jatropha*, *Ricinus*) and the Visacaceae family (*Phoradendron*). The most infamous example of a toxalbumin-producing plant is *Ricinus communis* (castorbean), because it is the source of one of the most potent toxins known, ricin, which has been used for assassination and is of concern as a potential weapon of terrorism. The number of species containing similar toxalbumins shows, however, that toxalbumins are produced by a fairly large number of plant species.

11.2 Toxic Agent and Mechanism

The toxalbumins in plants that cause most concern are members of a large group of glycoproteins, called lectins, that have the ability to specifically bind or crosslink carbohydrates. They may be loosely classified into high-potency lectins, such as ricin (produced by *Ricinus communis*), abrin (produced by *Abrus precatorius*) and curcin (produced by *Jatropha curcas*), and low-potency lectins (present in most undercooked beans). The toxalbumins are typically water soluble and not present in oil extracts, such as castor oil, in significant concentrations. They denature under high temperature and are therefore wet-heat labile. Due to their large size and polar characteristics, the toxalbumins are poorly absorbed from the GIT and the parenteral lethal dose is typically much smaller than the oral lethal dose. The toxalbumins consists of two distinct chains, called the A-chain and the B-chain. The toxic effects are due to the inhibition of protein synthesis through irreversible inactivation of ribosomal subunits by the A-chain, while the B-chain is necessary for toxalbumin binding to glycolipids and glycoproteins on the cell surface, followed by entry into the cell by endocytosis (Doan, 2004). Human poisoning with low-potency lectins has not been well described, but it has been suggested that acute gastrointestinal distress following the ingestion of inadequately cooked legumes is due to inhibition of plasma-membrane repair (Miyake *et al*., 2007).

11.3 Risk Factors

Ricinus communis (castorbean) is a common weed in many parts of the world. Some varieties are also occasionally used as decorative garden plants. The seeds are quite attractive and may be of interest to children coming in contact with the plant. Although the seeds contain hazardous concentrations of ricin, its release requires mastication or maceration. All plant parts, including leaves and roots, may create a hazard when used in traditional medicines (Audi *et al*., 2005). An increase in the production of *Jatropha curcas* (physic nut) for use as a biofuel may create increased risk of poisoning, especially in children who are often interested in the attractive seeds and occasionally ingest seeds out of curiosity (Kulkarni *et al*., 2005; Menezes *et al*., 2006). A similar risk occurs due to the use of seeds from *Abrus precatorius* (precatory bean), which are particularly attractive (bright red with a black patch on one end), to make jewellery.

11.4 Toxicity Syndrome

Oral exposure is the most relevant route of exposure for unintentional poisoning by toxalbumins. Signs typically appear 2–4 hours, and occasionally as much as 10 hours, after ingestion and may include nausea, abdominal cramps, heartburn, vomiting, diarrhoea, hypotension, dehydration and hypovolemic shock. Haematemesis and melaena are possible in severe cases. Hepatotoxic and renal effects have been recorded, but are not typical. Flulike symptoms, including fatigue, headache and muscle pain may also occur. Laboratory findings may include leukocytosis, elevated transaminases and creatinine kinase, hyperbilirubinemia, renal insufficiency and anaemia (Audi *et al*., 2005; Kulkarni *et al*., 2005). Although possible, lethal poisoning with oral toxalbumins is uncommon and appears to follow severe damage to the gastrointestinal mucosa that allows increased toxalbumin absorption followed by effects on the liver, pancreas, muscle and other tissues. Acute exposure to high concentrations of low-potency lectins, such as those found in

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undercooked beans, is associated with nausea, vomiting and diarrhoea (Miyake *et al*., 2007).

11.5 Management

Treatment is mainly supportive and symptomatic and could include intravenous fluids, electrolyte correction and vasopressive treatment for hypotension. Gastric evacuation is considered to be of limited value, but can be considered if ingestion occurred within an hour or less. Activated charcoal may be of benefit if the patient is not vomiting (Audi *et al*., 2005).

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