

Irritant Contact Dermatitis from Plants

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Irritant contact dermatitis (ICD) from plants is a very common phenomenon as potentially irritant plants and plant products are commonly found in the everyday environment, including the home, garden, workplace, and recreational setting. It is therefore essential to have a basic understanding of the various plant-derived physical and chemical irritants. ICD from plants is commonly divided into mechanical irritant contact dermatitis (MICD) and chemical irritant contact dermatitis (CICD). The common mechanical plant irritants include thorns, spines, glochids, trichomes, and sharp-edged leaves. Many chemical irritants have yet to be elucidated, but known culprits include calcium oxalate, protoanemonin, isothiocyanates, bromelain, diterpene esters, alkaloids, and other chemical irritants such as naphthoquinone and acids. This review details the major plant contributors to MICD and CICD, along with their respective irritants. The clinical presentations seen in ICD (versus other plant dermatoses) will also be described, along with diagnostic considerations and exposure data. We also review mechanisms for the development of ICD and current treatments for ICD from plants.

SKIN REACTIONS DUE to plants are common, as plants are ubiquitous and exhibit a number of physical and chemical properties that may result in harm. Four major types of cutaneous reactions following exposure to plant or plant-derived products have been described: irritant contact dermatitis, contact urticaria, allergic contact dermatitis, and phytophotodermatitis (Table 1). The term “irritant contact dermatitis” (ICD) is used to describe a cutaneous inflammatory response to physical or chemical injury. Although inflammatory and immunologic mediators may be activated, generally only innate immune response mechanisms are involved, along with an absence of memory T-cell function or antigen-specific immunoglobulins.^{1,2}

ICD is very common, accounting for approximately 80% of all contact dermatitis reactions and the majority of occupational and plant dermatoses.^{3,4} Plant-related ICD, as with ICD in general, has many diverse presentations. Irritant reactions to plants may produce a wide range of clinical findings. Mild chronic eczematous dermatitis may occur owing to irritant hairs on some plants. Severe acute toxic reactions with necrosis may be seen following exposure to potent alkaloids from plant sap.

Unlike in the case of allergic contact dermatitis, anyone exposed to a cutaneous irritant can potentially be affected. Irritation and its severity depends on the barrier function integrity of the individual’s skin, the potency and amount

of irritant to which one is exposed, and the duration of irritant exposure.

ICD can be subcategorized based on the nature of the irritant. Chemical irritants are responsible for chemical ICD (CICD), and physical irritants result in mechanical ICD (MICD) via mechanical trauma or microtrauma.⁵ There is, however, frequent overlap, and a presentation of plant-induced ICD may be secondary to more than one factor. An example is reactions to *Narcissus* bulbs: physical microtrauma from handling *Narcissus* bulbs may enhance the cutaneous penetration and effects of chemical irritant calcium oxalate crystals.⁶

The potential of various features of a single plant to contribute to a case of ICD makes the study of ICD from plants especially challenging. Further complicating the clinical picture are the facts that irritant skin damage by plants can render individuals more susceptible to allergic sensitization, and that many allergenic chemicals are also irritants by nature.⁷

Because of these features, the study of ICD from plants is challenging. We review the major plant contributors to MICD and CICD, along with their respective irritants. The clinical presentations seen in ICD (vs other plant dermatoses) will also be described, along with diagnostic considerations and exposure data. We also review mechanisms for the development of ICD and current treatments of ICD from plants.

Mechanical Irritant Contact Dermatitis

MICD is reportedly the most common plant dermatosis.⁸ Mechanical irritation is frequently the result of physical

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Table 1. Cutaneous Reactions to Plants

Reaction Type	Onset	Duration	Characteristics
Irritant contact dermatitis	Minutes to hours	Hours to days	Irritant reaction, which may potentially occur in any exposed individual. Does not represent an “allergy.” Polymorphous appearance, including pruritus, erythema, edema, vesicles, or necrosis. Usually restricted to areas of skin contact.
Contact urticaria, (nonimmunologic)	Seconds to minutes	Minutes to hours	Toxin-mediated. Immediate reaction, with urticaria, erythema, edema, pruritus.
Contact urticaria (immunologic)	Minutes to 1 hour	Hours to 1 day	IgE-mediated release of vasoactive mediators (including histamine). May be associated with atopic patients. Often worse with each subsequent exposure. Urticaria, erythema, edema, pruritus, classic “wheal and flare.”
Allergic contact dermatitis	24–48 h	4–10 d	Classic type IV delayed-type hypersensitivity reaction. Usually pruritic, with a polymorphous appearance, which may include erythema, edema, vesiculation. Begins at areas of contact but may spread outward. Often worse with each subsequent exposure.
Phytophotodermatitis	> 8–48 h	Days to years	Nonimmunologic. Due to photosensitizing agents (commonly psoralens and angelicins) in the plant. Reaction is typically erythematous with linear streaks. May be vesiculobullous. Frequent persistent hyperpigmentation of affected areas.

Adapted from Lovell CR²; McGovern TW, Barkley TM⁹; Crosby DG.³²
IgE = immunoglobulin E.

trauma caused by direct contact of the skin with the irritant. The mechanical irritant is usually anatomically sharp and can scratch, impale, or lacerate the skin, inducing wounds and excoriations. The resultant MICD can be papular or vesicular and may be pruritic. Implicated parts of plants include leaves, stems, and germinating organs such as the flowers or bulbs. Sharp-edged leaves and leaf hooks such as those seen on the leaves of holly trees (family Aquifoliaceae) (Fig 1), agave plants (family Agavaceae) (Fig 2), and yucca plants (family Agavaceae) may damage the skin. Thorns are a well-known hazard of many varieties of plants. Widely cultivated decorative plants such as roses (family Rosaceae) (Fig 3) and bougainvilleas (family Nyctaginaceae) are classic examples. Spines and glochids are also a well-known hazard of cacti, such as *Opuntia* (family Cactaceae) (Fig 4). Stem and leaf hairs like those on comfrey and forget-me-not (family Boraginaceae) and on *Bidens* and cardoons (family Asteraceae) may also be irritants. Even barely visible irritant fibers located on a plant can be problematic, as are those on rose hips (family Rosaceae) and on tulip bulbs (family Liliaceae)^{1,8} (Table 2). Hairs, bristles, and barbs are often referred to collectively as trichomes or glochids.

Hairs (Trichomes) and Hooks

Penetration of the skin by hairs (trichomes), spines, and thorns can produce a papular irritant eruption. Many plants bear trichomes on their stems or leaves. Examples include plants in the Boraginaceae family, including the borage plant, which is often used as an herb in cooking. The borage plant contains many coarse stiff trichomes that



Figure 1. Sharp-edged leaves of the American holly tree.



Figure 2. Sharp-edged leaves of the agave plant.

can elicit an MICD when the plant is handled.⁹ Other irritant members of the borage family with similar trichomes include the herb comfrey (*Symphytum* spp) and the flowering plant forget-me-not (*Myosotis* spp).



Figure 3. Thorns on the stem of a rose plant.



Figure 4. Prominent spines on the pad of a prickly pear cactus plant.

Cleavers (*Galium aparine* in the Rubiaceae family), also known as catchweed or stickyweed, is a common weed native to North America and Eurasia and famous for its ability to adhere to other objects, due to numerous trichomes. Some cleavers have pronounced hooked tips that resemble those on Velcro.¹⁰

Hooks occur on a number of other plants, such as some tropical palms and bindi (*Soliva pterosperma*), an Australian weed. Spearlike “awns,” which are bristlelike fibers on a head of grain, are present on cereal grasses, including barley (*Hordeum vulgare*). These must often be separated manually from the grain and can produce an eruption of pruritus and erythema on the hands.² Dogwood trees (*Cornus* spp) have T-shaped trichomes that can independently cause erythema and pruritus on contact.¹¹ Tulip bulbs may also result in MICD. Coarse dry fibers on the outer layer of tulip bulbs, termed “tecta,” are notorious for causing skin damage. These tecta, along with chemical irritants and allergens (including calcium oxalate and tulipalin A, respectively) in the sap contribute to the common occupational dermatosis of “tulip fingers.”⁴

Table 2. Common Plants Causing Mechanical Irritant Contact Dermatitis

Family	Common Name	Genus and Species	Irritant
Agavaceae	Agave	<i>Agave</i> spp	Pointed leaves with spines along edges
	Yucca	<i>Yucca</i> spp	Sword-shaped leaves
Amaranthaceae	Tumbleweed	<i>Salsola</i> spp	Sharp bracts
Aquifoliaceae	Holly	<i>Ilex</i> spp	Spiky leaves and thorns on stems
Araliaceae	Common ivy	<i>Hedera helix</i>	Stellate hairs
Asteraceae	Cardoon	<i>Cynara cardunculus</i>	Stalk hairs
	Stickseeds or tickseeds	<i>Bidens</i> spp	Barbed burrs, seeds
	Bindi or bindi weed	<i>Soliva pterosperma</i>	Barbed seeds
	Various thistles	<i>Carduus, Cirsium</i> spp	Trichomes on leaves and stems, thorns on stems, spikes on flowers
Berberidaceae	Prickly lettuce	<i>Lactuca serriola</i>	Glochids, pointed leaves
	Barberry, pepperidge bush	<i>Berberis</i> spp	Spines
Boraginaceae	Borage	<i>Borago</i> spp	Sharp stiff leaf and stem hairs
	Forget-me-not	<i>Myosotis</i> spp	Sharp stiff leaf and stem hairs
	Comfrey	<i>Symphytum</i> spp	Sharp stiff leaf and stem hairs
	Lungwort	<i>Pulmonaria officinalis</i>	Sharp stiff leaf and stem hairs, sharp-tipped leaves
Cactaceae	Various cacti	<i>Opuntia</i> spp	Spines and glochids
	Prickly pear	<i>Opuntia</i> spp	Spines and glochids
Cornaceae	Dogwood	<i>Cornus</i> spp	T-shaped trichomes
Lilaceae	Tulip	<i>Tulipa</i> spp	Course fibers on tecta
Moraceae	Fig	<i>Ficus</i> spp	Abrasive bristles
	Mulberry	<i>Morus</i> spp	Abrasive bristles
Poaceae	Barley	<i>Hordeum vulgare</i>	Pointed awns attached to grains
	Grasses	Numerous genera	Sharp leaf edges, fine hairs, and prickly spikes
Rosaceae	Rose	<i>Rosa</i> spp	Thorns
	Firethorn	<i>Pyracantha</i> spp	Thorns, serrated leaves
	Rosehip, dog rose	<i>Rosa canina</i>	Hairs
	Blackthorn	<i>Prunus spinosus</i>	Thorns
Rubiaceae	Cleavers (stickyweed)	<i>Galium aparine</i>	Trichomes, some with hooked tip
Scrophulariaceae	Flannel-plant (wooly mullein)	<i>Verbascum thapsus</i>	Wooly hairs
Urticaceae	Stinging nettle	<i>Urtica</i> spp	Trichomes; may be mixed picture with contact urticaria
	Wood nettle	<i>Laportea</i> spp	Trichomes; may be mixed picture with contact urticaria

Adapted from Lovell CR²; McGovern TW, Barkley TM⁹; Crosby DG³²; Powell RF, Smith EB⁷⁷; Quattrocchi U.⁷⁸

Spines, Glochids and Thorns

Cacti (family Cactaceae), which are among the most infamous mechanical irritant plants, have large prominent spines that cause reactions mimicking scabies or dermatitis from fiberglass. Interestingly, the smaller and nearly invisible barbed hairs (glochids) on these cacti are capable of causing cutaneous reactions that are more dramatic than those caused by the large cacti spines. The polka-dot cactus (*Opuntia microdasys*), for example, is common in homes and gardens and bears clusters of 100 to 200

glochids on each pad. These glochids grow in tufts on the areola of cactus pads and possess self-retaining barbs that make removal difficult. Implantation of these spines and glochids is an occupational hazard for growers.⁹

The prickly pear cactus (*Opuntia* spp) is native to Central America but is widely cultivated in temperate areas. The cacti are large and form bushes and have thus been used in Africa and the Middle East as “burglar-proofing” fences.⁹ The cacti are also cultivated for their edible fruit. In addition to the readily apparent spines, (see Fig 4), both the pad and the fruit of *Opuntia* bear tufts of

shorter hooked glochids, which cause mechanical cutaneous injury.¹² The glochids may also be transferred to clothing and then to any part of the skin, including the genitalia, and interdigitally.^{13,14} The oral mucosa and hard palate may be affected during consumption of the fruit. This eruption, like other cactus-induced MICD reactions, can closely resemble scabies and is colloquially referred to as “sabra dermatitis.” The fruits are usually shaved prior to being sold (Fig 5), but they can still cause irritation.²

Other plants known for their spines include *Serenoa repens* (family Arecaceae), a North American plant commonly known as saw palmetto (Fig 6). This palm gets its common name from the fine sharp spines on its stems that result in a saw-toothed appearance (Fig 7).



Figure 5. Prickly pear cactus fruit shaved and ready to be sold for consumption.



Figure 6. Saw palmetto.

Granulomas

Beyond the initial MICD elicited by the aforementioned mechanical irritants, these spines, glochids, and trichomes are also known for resulting in foreign body granulomas when lodged in the dermis. The glochids of the cholla cactus (*Opuntia lingularis*) and spines of *Opuntia acanthocarpa* cause immediate pain after penetrating the skin, followed by erythema and swelling. If the spines remain in situ and are not excised, granulomas may develop over the course of months and persist indefinitely.⁸

Thorns and wood splinters may also induce deep granulomas.^{15,16} A series of five cases of granulomatous synovitis and inflammatory monoarthritis due to plant thorn penetration has been reported; surgical removal of the thorns resulted in a return to normal joint function in each case.¹⁷

Secondary Infections

An often overlooked comorbidity of mechanical dermatitis from plants is the introduction of infectious organisms into the skin and subcutaneous tissue. Bacteria such as *Clostridium tetani* may be introduced by spines and thorns. *Staphylococcus aureus* can be commonly found on blackthorns (*Prunus spinosa*), which are used by some species of birds to impale their prey. Blackthorns are commonly used in hedgerows, and the brittle jagged tips of the thorns increase the ease of inoculation.¹⁸ *Sporothrix schenckii* infection, a deep fungal infection, may result in a nodular eruption at the site of inoculation, followed by involvement along the draining lymphatics (Fig 8). Inoculation



Figure 7. The saw-toothed appearance of a stem of the saw palmetto plant.

may occur following contact with rose thorns, sphagnum moss, some grasses, and cornstalks.¹⁹ Atypical mycobacteria may also be transmitted following mechanical plant injury. Examples include *Mycobacterium kansasii* transmitted through contact with blackberry bushes, *Mycobacterium marinum* transmitted by cactus spines, and *Mycobacterium ulcerans* transmitted by tropical vegetation.^{9,20} Last, vegetable fragments and barley awns have been noted to carry various *Actinomyces* species.²

Chemical Irritant Contact Dermatitis

The many thousands of plant species and their numerous chemical products make the study of CICD from plants appear daunting. The vast majority of CICD reactions, however, are caused by one of seven basic irritant groups: calcium oxalate, protoanemonin, isothiocyanates, diterpene esters, bromelain, and alkaloids. These are dissolved or suspended in the latex sap of the plant or housed in specific organelles such as stems, leaves, and bulbs (Table 3).

Calcium Oxalate

Found in many genera of plants, calcium oxalate is a water-insoluble salt that forms bundles of needlelike crystals called raphides. Contact with moisture causes plant cells to eject the raphides, which can then come into contact with skin or mucosal surfaces. Irritancy is mechanical in part and due to the anatomically sharp structure of the crystals themselves. The crystals are believed to be more irritant when longer than 180 μm .²¹ The raphides of calcium oxalate have been classified historically as a chemical irritant mainly because they allow



Figure 8. Patient with sporotrichosis of the hand following a penetrating injury from a rose thorn, with subsequent spread to the draining lymphatics of the arm.

the penetration of other plant chemical toxins (including proteases, saponins, and other chemicals) that may not normally breach the skin on contact. They also enhance the penetration of known skin irritants, including many alkaloids from daffodil bulbs, bromelain in pineapples, and saponins in *Dieffenbachia*.

The most frequently cited example of calcium oxalate-induced CICD is that of *Dieffenbachia* spp, commonly used as decorative plants.^{1,2,9} CICD caused by flower bulbs is usually less severe but much more common and economically more significant.² Bulbs, including those of tulips, daffodils, and hyacinths, may contain a high concentration of calcium oxalate. Bulb dermatitis is most prominently an occupational hazard of florists, gardeners, bulb planters, and the individuals who cut the flowers.¹ The reactions are localized to those areas in greatest contact with the bulbs, typically the fingertips, hands, and forearms. However, if dust containing calcium oxalate crystals from the bulbs penetrates clothing, the eruption can become more generalized and extensive.

Dieffenbachia

Innocuous-appearing houseplants may result in severe ICD, and some should therefore be treated as poisonous, especially in regard to children and pets. Members of the Araceae family, *Dieffenbachia* plants are popular as decorative plants in homes and offices. The leaves and the fruit of the plant are notorious for causing severe local effects. Contact can result in ejection of the raphides, penetration into the skin, and induction of histamine release from mast cells. Saponins, cyanogenic glycosides, proteolytic enzymes, and alkaloids likely contribute to the vesicant properties of the plant. The resultant dermatitis can be marked by pruritus and erythema along with vesicular and bullous eruptions that may include the palmar surfaces of the hands.²² If the plant is eaten, stomatitis, hoarseness, and aphonia can ensue, along with edema and erosions following the path of the plant along the gastrointestinal tract; thus, the plant is also known as “dumb cane.”² Ingestion of another group of common houseplants in the Araceae family, *Philodendron* spp, may also result in similar symptoms due to the presence of calcium oxalate, including proteases, saponins, and other chemicals.

It is also noteworthy that splashes of plant tissue juice or the transfer of raphides from the hands to the eyes cause immediate severe pain, lacrimation, and blepharospasm as large numbers of calcium oxalate crystals penetrate the cornea.²²

Table 3. Common Plants Causing Chemical Irritant Contact Dermatitis

Family	Common Name	Genus and Species	Irritant or Toxin
Agavaceae	Agave, century plant	<i>Agave</i> spp	Calcium oxalate, saponins
Alliaceae	Garlic	<i>Allium sativum</i>	Thiocyanates
	Chive	<i>Allium schoenoprasum</i>	Thiocyanates
	Onion	<i>Allium cepa</i>	Thiocyanates
Amaryllidaceae	Daffodil	<i>Narcissus</i> spp	Calcium oxalate, alkaloids
Araceae	Dumb cane	<i>Dieffenbachia</i> spp	Calcium oxalate, saponins
	Philodendron	<i>Philodendron</i> spp	Calcium oxalate
Asteraceae	Daisy	<i>Aster</i> spp	Calcium oxalate
Brassicaceae	Black mustard	<i>Brassica nigra</i>	Thiocyanates
	Radish	<i>Raphanus sativus</i>	Thiocyanates
	Wasabi	<i>Wasabia japonica</i>	Thiocyanates
	Horseradish	<i>Armoracia rusticana</i>	Thiocyanates
Bromeliaceae	Pineapple	<i>Ananas comosus</i>	Bromelain, calcium oxalate
Cactaceae	Old man cactus	<i>Cephalocereus senilis</i>	Calcium oxalate
Capparaceae	Caper	<i>Capparis spinosa</i>	Thiocyanates
Euphorbiaceae	Spurge family	Many genera	Diterpene esters (some with thiocyanates)
	Croton	<i>Croton</i> spp	Diterpene esters
	Manchineel tree	<i>Hippomane mancinella</i>	Diterpene esters
	Poinsettia	<i>Euphorbia pulcherrima</i>	Diterpene esters
	Spotted spurge, petty spurge, snow-on-the-mountain	<i>Euphorbia</i> spp	Diterpene esters
	Pencilbush	<i>Euphorbia tricualli</i>	Diterpene esters
	Castor bean plant	<i>Ricinus communis</i>	Diterpene esters, ricin
	Candelabra cactus	<i>Euphorbia lactea</i>	Diterpene esters
Hyacinthaceae	Hyacinth	<i>Hyacinthus</i> spp	Calcium oxalate
Juglandaceae	Walnut tree	<i>Juglans</i> spp	Juglone
Salicaceae	Osier, willow	<i>Salix viminalis</i>	Salicylic acid
Liliaceae	Tulip	<i>Tulipa</i> spp	Calcium oxalate, tulipalin A (allergen)
Ranunculaceae	Buttercup family	Many genera	Protoanemonin
	Buttercup	<i>Ranunculus</i> spp	Protoanemonin
	Christmas rose, hellebore	<i>Helleborus niger</i>	Protoanemonin
	Prairie crocus	<i>Pulsatilla</i> spp	Protoanemonin
	Clematis, old man's beard	<i>Clematis vitalba</i>	Protoanemonin
	Ceratocephalus	<i>Ceratocephalus falcatus</i>	Protoanemonin
Solanaceae	Chili pepper	<i>Capsicum</i> spp	Capsaicin
	Tobacco	<i>Nicotiana tabacum</i>	Nicotine
Thymelaeaceae	Winter daphne, February daphne	<i>Daphne</i> spp	Daphnane (diterpene ester)

Adapted from Lovell CR²; McGovern TW, Barkley TM⁹; Mascarenhas R et al²⁵; Karaca S et al²⁷; Polat M et al²⁹; Oztas P et al³⁰; Metin A et al³¹; Crosby DG³²; Quattrocchi U.⁷⁸

Tulips and “Tulip Fingers”

The sap of the tulip (family Liliaceae) contains the well-characterized allergen tulipalin A. The individual tulip bulbs contain a tough outer tectum that can fragment and impale the skin, resulting in mechanical irritant injury. Tulip bulbs also have some calcium oxalate raphides. The

combined effect of irritant and allergic contact dermatitis from tulips results in “tulip fingers.” Contact can be extensive for those who handle the bulbs for peeling, those who sort the bulbs and prepare them for shipping, or those who cut or pick the flowers.⁴

The clinical presentation of tulip fingers may range from fissured and hyperkeratotic fingertips, pulpitis,

paronychia, and nail changes, to an extensive eczema, sometimes with pustules on the fingers or even the entire hand. Additionally, the eczema may secondarily spread to the face, the neck, the arms, or the anogenital region.

Daffodils and “Daffodil Itch”

Contact with the stems and bulbs of daffodils (*Narcissus* spp) causes the dermatosis known as daffodil itch or lily rash. This is probably the most common contact dermatitis reaction among florists.² It is endemic among those who cut, bunch, and pack daffodils. The mucus from the hollow stems and the sap from the bulbs contain abundant calcium oxalate raphides. Contact with the mucus or sap can result in daffodil itch, the most severe presentation being among individuals who pick the flowers. Features of the rash are generally mild and include xerosis, scaling, fissures, and erythema affecting areas that have been in direct contact with the mucus or sap of the plant, most frequently the fingertips, hands, and forearms.⁴ Additionally, transfer of the raphides (such as when the hands touch the face) can result in more extensive dermatitis.

It is believed that, along with the calcium oxalate raphides, alkaloids in the sap and mucus of the daffodil may contribute to the rash (see the discussion of alkaloids, below). Unlike cases of tulip fingers, which can have a large allergic component, most cases of daffodil itch are primarily an ICD. The rash, unlike that in tulip fingers, is often self-limiting because of the mildness of the dermatitis and the brevity of the daffodil picking season. After going to great lengths to observe the work habits of daffodil pickers and handlers, Julian and Bowers documented the variations in the presentation of daffodil itch.²³

Hyacinths

Hyacinths (*Hyacinthus* spp) can elicit a CICD that closely resembles daffodil itch and occurs via a similar mechanism. The outer tectum of the hyacinth bulb can be broken into particles that cause mechanical trauma to the skin. Additionally, up to 6% of the hyacinth bulb is composed of calcium oxalate crystals. Handling the bulbs causes the tecta to break into small sharp particles, simultaneously releasing calcium oxalate crystals. These particles can readily become airborne, making contact with body regions other than the hands.⁴

Agave

Agave spp are laden with calcium oxalate raphides and saponins. A single droplet (0.03 mL) of juice extracted

from the leaves of the agave plant is reported to contain hundreds of calcium oxalate raphides, each as long as 500 μm .²⁴ These crystals and saponins are the presumptive source of the marked pruritus and stinging associated with exposure to the agave plant.³ The plant is indigenous to North America, and the fruit of some species (including *Agave tequilana*) is used in the production of tequila. On agave plantations and in tequila distilleries, CICD related to agave is more routinely seen.

Other Plants

Raphides are present in various amounts in other genera of plants. Some cacti, such as *Cephalocereus senilis*, contain up to 85% calcium oxalate by dry weight.² CICD from plants in the Asteraceae family (which includes daisies and carnations) has been reported, and calcium oxalate is a putative culprit.²⁵

Protoanemonin

Protoanemonin is a chemical irritant found almost exclusively among various members of the Ranunculaceae (buttercup) family. Upon maceration or bruising of plant tissue, ranunculin (a glycoside) is hydrolyzed into protoanemonin, which is a volatile unsaturated lactone of γ -hydroxyvinylacrylic acid.²⁶ While the mechanism of protoanemonin irritancy is not completely understood, protoanemonin has been shown to combine with sulfhydryl groups in the skin and disrupt disulfide bonds, resulting in subepidermal dysjunction and bulla formation.²⁷

Crushing of the plant leaves results in the production and release of protoanemonin, which can subsequently cause an irritating odor, conjunctival irritation, and irritation of the nasal airway. Transient contact of freshly crushed leaves with the skin results in warmth, burning, and irritation; sustained contact results in erythema, edema, vesiculation, blistering, ulceration, and residual hyperpigmentation.²⁸ Linear streaks are a hallmark of exposure to protoanemonin from field buttercups (*Ranunculus* spp), potentially contributing to a misdiagnosis of phytophotodermatitis.^{2,9} Only freshly macerated leaves are involved in irritant reactions because protoanemonin rapidly and spontaneously polymerizes into anemonin, which is not a skin irritant.

Specifically among *Ranunculus* spp, *Ranunculus ill-yriscus* is a ubiquitous weed commonly used in South America and the Middle East for medicinal purposes.

CICD reactions have been well documented in the literature.^{29,30}

Apart from *Ranunculus*, irritant members of the family Ranunculaceae include several genera of decorative flowering plants, including *Anemone*, *Clematis*, and *Helleborus*. A notable genus is *Pulsatilla*, which includes the European pasqueflower (*Pulsatilla vulgaris*) and the American prairie crocus (*Pulsatilla patens*), a common species on the dry prairies of Minnesota. The leaves, in particular, induce bullous irritant reactions.² Also noteworthy within the family is *Ceratocephalus falcatus*, a ubiquitous weed in the Middle East, known for causing second-degree burns.^{27,31} This weed, like many members of the Ranunculaceae family, is often used as an herbal medicine.

Mustard Oils (Isothiocyanates)

Isothiocyanates are the principal irritant constituents of the mustard oils found in many members of Brassicaceae (previously Cruciferae), the mustard family. Mustard oils are not found in intact plants but are instead generated upon injury to the plants. Glucosides (glucosinolates), which serve as precursors to isothiocyanates are found in all parts of the plants but especially in the seeds. The oil-generating reaction is catalyzed by an enzyme, myrosinase, which is released upon damage to the plant. The product in the reaction is isothiocyanate.^{26,32}

Isothiocyanates react readily with the amino-groups of proteins on human skin and mucosal surfaces. Interestingly, the spicy taste of plants in the Brassicaceae family is due to the irritant isothiocyanates.³³ The skin's reaction is generally an immediate and short-lived burning, erythema, and urticaria, which is especially prominent among food handlers and those who cook. The eyes are particularly sensitive; thus, mustard oil was used as a component of tear gas in warfare.³²

Mustard oils are well known for their pungent odor and for centuries have been used for cooking and for their medicinal properties. The isothiocyanate components of mustard oils have recently gained attention because of their potential for inhibiting carcinogenesis.

Along with mustards, members of the Brassicaceae family include cabbage, cauliflower, and radish. Horseradish (*Armoracia rusticana*) and wasabi (Japanese horseradish, *Wasabia japonica*) contain extremely reactive isothiocyanates and are accordingly especially potent irritants.²⁶

Plants from other families that produce similar oils include mignonettes (Resedaceae), papaya (Caricaceae), spurges (Euphorbiaceae), nasturtiums (Tropaeolaceae),

pokeweed (Phytolaccaceae), plantains (Plantaginaceae), and capers (Capparaceae). Numerous accounts appear in the literature regarding the glucosides and isothiocyanates of Capparaceae and their erythema-inducing and vesicant properties on the skin.³⁴

Diterpene Esters

Phorbol, daphnane, and diterpene are chemical irritants collectively known as diterpene esters. They are among the most irritant of plant-derived chemicals.³² Most commonly associated with these irritant esters are the spurges (family Euphorbiaceae), a very large, ubiquitous, and varied family that encompasses more than 8,000 species in 300 genera.³⁵ One commonality that is largely preserved within this diverse family is the corrosive irritant latex produced by almost all of its member plants. The primary active agents in the latex (or sap) are believed to be diterpene esters. In fact, almost 90% of the species of Euphorbiaceae screened for inflammatory capability have been shown to have activity in this regard.^{36,37} Besides their corrosive properties, diterpene esters are also believed to play a role in tumorigenesis, specifically by activation of intracellular protein kinase C.³⁸

Because of the irritant esters within their latex, euphorbs are among the most aggressively irritant plants. The skin and eyes are particularly susceptible, and presentations include pain, erythema, edema, blistering, conjunctivitis, and even blindness.^{2,39} If the leaves or fruits of euphorbs are consumed, bloody diarrhea and vomiting may ensue. These gastrointestinal manifestations are believed to be the basis of the common name given to euphorbs: "spurge."⁹

Plants of the genus *Euphorbia* bear special mention because every species is believed to have irritant properties in some form. Poinsettias (*Euphorbia pulcherrima*) are a prominent member of this group, given their popularity as decorative plants. They contain minimally irritant latex and generally cause a mild CICD reaction. Other common members of *Euphorbia* include the spotted spurge (*Euphorbia maculata*), the petty spurge (*Euphorbia peplus*), and snow-on-the-mountain (*Euphorbia marginata*), all of which are weeds that can cause irritation when pulled or handled with bare hands.^{32,33}

Perhaps the most notorious and formidable member of the Euphorbiaceae family is the manchineel tree, or beach tree (*Hippomane mancinella*). The tree is commonly found coastally in Central America, the Caribbean, and the southern regions of Florida. The tree produces a sweet-smelling fruit that can cause severe oral pain, mucosal

edema, and blistering if consumed, as well as vomiting and hemorrhagic diarrhea if swallowed.⁴⁰ Any part of the tree can cause cutaneous irritation from direct contact; the hands, face, and genitalia are common sites of irritation. Even the dried wood of the tree is toxic and cannot be cut or burned without risk of irritation. More widespread but also coastally located, the pencilbush (*Euphorbia triculalli*) produces copious amounts of milky latex that can cause severe dermatitis and even temporary blindness.³²

Most euphorbs in the United States are shrubs such as Texas croton (*Croton texensis*), a species that produces immediate skin blisters from phorbol esters in the leaves, stems, and seeds. About 45 species of croton are found in the United States. They may occasionally be seen as decorative garden plants, but most species can be found proliferating across prairie land because cattle do not willingly eat them.^{32,41}

An economically important euphorb is the castor bean plant (*Ricinus communis*), from which castor oil is extracted. The oil is used in the production of soap, detergents, paints, dyes, and lubricants. Of note, the seeds of the plant are poisonous because they contain ricin, a chemical that inhibits protein synthesis and that has the potential for use in biological warfare. Castor oil is itself a contact irritant because it is extracted from the beans of the plant, which contain a sap laden with diterpene esters.³⁷

Closely related to the euphorbs are plants in the family Thymelaeaceae, which includes species of daphne, including *Daphne odora* (winter daphne) and *Daphne mezereum* (February daphne). They produce daphnane, an ester considered to be among the most irritant of all plant chemicals.³² Most daphnes are evergreen shrubs that bear creamy sweet-smelling flower clusters that are lethal to eat and produce a CICA similar to that caused by the euphorbs.

Bromelain

Bromelain is a plant-derived collection of enzymes originally extracted from the pineapple plant (*Ananas comosus* of the family Bromeliaceae). The enzymes include proteases, phosphatases, and peroxidase. Because of its enzymatic activity, bromelain has been used by the food and beverage industries for the tenderizing and processing of meat and for the clarification of beer during brewing.⁴²

The proteolytic activity of bromelain is purported to be the source of cutaneous irritation. It is thought that calcium oxalate raphides in the pineapple plant cause microabrasions, allowing bromelain to exert its proteolytic

effect on dermal blood vessels.⁹ It is therefore not surprising that pineapple workers often develop fissures and fingerprint loss on their hands.

Capsaicin and Other Alkaloids

Capsaicin (8-methyl-N-vanillyl-6-nonenamide) is an alkaloid derived from members of the Solanaceae family, including chili peppers (*Capsicum* spp) (Fig 9). In humans, capsaicin binds to vanilloid receptors on sensory neurons, which can also be stimulated by heat and pain. The neuronal activation results in the sensation of heat. As only nerves are affected, capsaicin elicits a dose-related cutaneous burning and erythema without any overt blistering.⁴³ Other local effects include smooth-muscle stimulation, glandular secretion, and vasodilation.⁹ By these same actions, capsaicin contributes to the pungency of chili peppers.³²

Irritation from chili peppers has been reported in the literature as “Hunan hand syndrome” or “chili burns.”⁴³ It is reported to frequently present among those who



Figure 9. Chili pepper plant.

handle chili peppers, including cooks and workers who handle large batches for processing.

The alkaloids as a chemical group are very diverse and include many of the commonly known bioactive compounds derived from plants, such as ephedrine, morphine, and quinolones. Colchicine, for example, is a cytotoxic alkaloid used in the treatment of various malignancies and is derived from the autumn crocus (*Colchicum autumnale*). Nicotine is presumed to be the active irritating component of the tobacco plant, which has been reported to cause cutaneous irritation among workers on tobacco plantations.⁴⁴

Not all alkaloids are innately cutaneous irritants, but they can often irritate the skin upon breaching the skin barrier. For example, at least 15 alkaloids have been isolated from daffodils, some of which (including homolycorin, lycorin, and masonin) are believed to contribute to the ICD caused by the plant's calcium oxalate raphides.^{4,23}

Other Plants and Chemical Irritants

Garlic

Garlic, onions, and chives are all members of the *Allium* genus within the Alliaceae family. With regard to garlic, allergic cutaneous reactions are more typical.³³ However, clinical presentations have also been reported that more closely resemble an irritant picture, suggesting that garlic may cause a mixed allergic and irritant dermatitis.⁴⁵ Workers in the food industry, such as cooks, are most frequently affected.⁴⁶ Generally, the dermatitis involves the fingertips of the first three fingers of the nondominant hand, which hold the garlic in place for chopping.

The possible chemical irritants in garlic have not been well characterized, but it is believed that many of the bulbs of plants in this genus may contain the previously discussed irritant isothiocyanates.

Garlic has been used as an herbal remedy, and irritation from the topical application of crushed garlic to intact skin has been well documented (Fig 10). Cases of individuals with erosions, ruptured hemorrhagic bullae, and second-degree burns have been documented.^{29,47,48}

Juglone

Juglone is an aromatic naphthoquinone found in the leaves, roots, and bark of many members of the Juglandaceae family, particularly walnut trees (*Juglans*



Figure 10. Patient with severe irritant contact dermatitis that occurred after the application of raw garlic as home therapy for a tinea corporis lesion on the lateral thigh. (Photograph courtesy of Dr. Blanca Ochoa)

spp). It has been documented to cause an ICD as well as hyperpigmentation of the skin.⁴⁹ The hyperpigmentation is not postinflammatory but rather occurs via chromophore groups, similar in mechanism to henna.⁵⁰ The pigmenting properties of juglone has resulted in the juice of fresh walnut husks being used in dyes and tanning products.

Woods and Trees

ICD from woods is more common than allergic contact dermatitis from woods, and almost any wood has the potential to be a mechanical irritant when its dust comes in contact with the skin.⁵¹ Trees are constituents of many of the culprit plant families previously discussed, and their irritant chemicals include various alkaloids and diterpene esters. These irritating compounds occur in many woods commonly found throughout the United States. Pine and spruce trees are well-documented sources of ICD among woodcutters, carpenters, and builders.¹

Acids

Acids (citric, acetic, formic, malic, salicylic, and oxalic) make up a group of chemical irritants that deserve brief mention.^{1,52} The cutaneous irritant properties of salicylic acid (from the salix tree, *Salix* spp) are used in the treatment of many dermatologic conditions such as acne. The vegetable rhubarb comes from the stalk of the rhubarb plant (*Rheum rhubarbarum* of the family Polygonaceae).

Whereas the stalk is commonly consumed, the leaves contain oxalic acid and are toxic when consumed.⁵⁰

Clinical Considerations

Risk Factors and High-Risk Populations

It is generally accepted that because of the nature of chemical and mechanical irritants, the primary factors determining the level of irritation to a particular irritant are the length of exposure, the concentration or amount of irritant in contact, and the integrity of the normal skin barrier function. Modjtahedi and Maibach found that ethnicity does not appear to play a role in risk stratification for ICD.⁵³ Similarly, while it was previously thought that females have a higher risk of developing ICD in the occupational setting, this assertion has since been disputed.^{54,55}

Individuals at risk tend to be those who may come into frequent contact with plant irritants. Therefore, many cases of ICD from plants can be viewed as occupational dermatoses.³³ ICD is the most common presentation of occupational skin disease and is extremely common among florists, farmers, grocers, and outdoor workers.^{7,55} For example, hand dermatitis from plants can affect up to 30% of all florists in a given year.⁹

Other documented occupational risk factors for ICD from plants include humid or wet working conditions, perspiration, the relative expertise of the florist or worker, and the technique used to cut and handle the plants.^{2,4,8,23}

Clinical Presentation

As discussed, the clinical appearance of ICD from plants is quite polymorphous. The general rule is that any part of the body in direct contact with the plant irritant can be affected. Typical examples are the fingers, hands, wrists, forearms, and face. Irritants can be transferred from fomites and already exposed skin areas to those parts normally protected by clothing or not in direct contact with plants. Such secondarily affected regions commonly include the axilla, eyes, buttocks, and genitalia. The presentation of individuals with dermatitis on these secondarily affected areas makes the diagnosis of ICD particularly challenging.

Acute forms of ICD can occur within a few hours of contact and include erythema, edema, papules, and vesicles. Chronic ICD from plants following repeated exposure to the irritant presents commonly with xerosis,

hyperkeratosis, and fissures.⁸ While already varied in presentation, ICD may be particularly difficult to diagnose when patients present with more striking manifestations such as superficial necrosis, hemorrhagic bullae, and ulcerations.^{5,8,39} The clinical picture of ICD may be further complicated by the presence of systemic findings, such as when the plant or plant product is consumed or inhaled.^{4,32}

Histologically, ICD lesions vary from mild keratinocyte degeneration with spongiosis to epidermal necrosis with ulceration. Typically, there are superficial changes that involve disruption of the corneal layer as well as some intraepidermal necrosis. Plant irritants may also result in exocytosis of lymphocytes or neutrophils. Even the histologic patterns of karyorrhexis and perivascular neutrophilic infiltrate with leukocytoclastic vasculitis have been noted in the lesions of patients with ICD from plants.³

In contrast to allergic contact dermatitis (ACD), the exocytosis and spongiosis seen in ICD is accompanied by prominent epidermal hyperproliferation.⁵⁶ Generally, structural changes in the stratum corneum, karyorrhexis, pyknosis, and the presence of superficial vesicles with neutrophilic infiltrate are all more characteristic of an ICD reaction than an ACD reaction.⁵⁷ However, there are no histologic features that absolutely distinguish between ICD and ACD.

Diagnosis of ICD

In spite of its ubiquity, ICD may be a difficult diagnosis to make. Distinguishing it from other plant dermatoses (ACD in particular) can be challenging. ICD is quite frequently a diagnosis of exclusion.⁵⁵

A good history is essential in evaluating ICD from an irritant plant. Lovell states that, in addition to ascertaining the patient's occupation, it is necessary to acquire a "mental picture" of how the patient works with plants, which parts of the plant come into contact with the skin, and the extent to which such contact occurs.⁶ Other important information includes the onset of first symptoms, the initial site of onset, sites of subsequent spread, improvement or worsening when the patient returns to work, and whether others have experienced similar symptoms in the workplace.²

Patch testing, while crucial in ruling out an allergic reaction, may often be misleading in cases of irritant plant reactions.² Irritant plants often cause false-positive patch-test results.²¹ A major caution for dermatologists is that patch testing must never be performed with an unidenti-

fied plant. As our review highlights, a number of plants have mechanical or chemical irritant potential, which would only be intensified in a closed patch test. Negative patch-test results are mainly of value in ruling out an ACD reaction and keeping open the possibility of ICD.⁵⁸

Tissue histology may be helpful in distinguishing ACD from ICD, but there is frequent histologic overlap in features.⁵⁷ Benezra and colleagues described the presence of trichome remnants seen under polarized light from a biopsy specimen, which can aid in the diagnosis of MICD from a plant.⁸ Furthermore, Mascarenhas and colleagues reported that, if the suspected culprit plant sap or tissue is available, mechanical irritants such as calcium oxalate raphides may be visible under magnification.²⁵

By clinical appearance alone, ICD and ACD may be very similar and difficult to distinguish. Like ICD, ACD can present in many different forms; the most common and easily identifiable form is an erythematous edematous eruption at sites of allergen contact. ICD tends to develop on the day of contact with the irritant. ACD generally intensifies between 24 and 48 hours after exposure, but persons who have been previously sensitized to an allergen may develop symptoms more rapidly.⁵⁸ Pruritus is also not a distinguishing feature as both types of reactions have been documented to be extremely pruritic^{6,59} (see Table 1).

New techniques that may have the potential to aid in distinguishing between ACD and ICD include reflectance confocal microscopy, transepidermal water loss measurements, fluorescence excitation spectroscopy *in vivo*, and a novel “behind-the-knee” irritant test.^{56,60}

Determining the Culprit Plant and Irritant

Once the diagnosis of ICD has been made, further investigation into the culprit plant and its constituent chemicals responsible for the irritation is challenging. Often the plant is not available for evaluation or identification. For situations in which the plant is available, Avalos and Maibach documented a systematic methodology for preserving the plant and its flowering parts for botanical identification and subsequent literature search.¹ Of note, a Web-based botanical dermatology database is available, along with numerous books documenting irritant plants.^{1,34,61}

In many cases, the structure or name of the individual plant irritant is unknown. This is partly due to the complexity of the identification process, which includes preparation of the plant extract, isolation and purification of the active molecules, and identification of the structure of the compound. These steps involve liquid, gas, or high-

performance chromatography and the combination of identification techniques such as mass spectrometry, infrared spectrometry, and nuclear magnetic resonance. Additionally, many plant irritants (including those discussed above) are short-lived and volatile, making isolation extremely difficult.¹

Immunologic Response in ICD

Although it does not elicit an antigen-specific immune response, ICD is nonetheless the result of inflammation arising from the release of proinflammatory cytokines.⁶² Cytokine release studies show that irritants are heterogeneous in both the individual cytokines released and the quantity of cytokines released. However, there is believed to be underlying commonality among all ICD reactions with regard to the mediators involved; these mediators include interleukin (IL)-1 α , IL-1 β , and tumor necrosis factor- α .^{58,63} Smith and colleagues reported that ICD may promote or enhance ACD because some of these mediators play a role in both ICD and ACD.⁶⁴

Treatment and Prevention

Treatment

Most of the conventional treatments used for general ICD are applicable to plant-induced ICD. In the setting of acute ICD, topical corticosteroids remain the mainstay of treatment.⁶⁵ Cool compresses made with Burow's solution (aluminum acetate in water), saline, or water have been shown to reduce vesiculation associated with acute ICD and are also thought to reduce inflammation.⁶⁶ Steroid-sparing agents such as tacrolimus may also be beneficial by virtue of suppressing the immune response and may be safer to use on areas where more potent topical steroids are contraindicated (eg, the face and genitals).⁶⁷

If the irritation is milder or subacute, lipid-rich moisturizers and barrier creams may be successful in treatment, possibly by helping restore barrier function to irritated skin and by increasing hydration.^{68,69} There is also evidence suggesting that topical skin lipid mixtures containing ceramide-3 can be effective for ICD.⁷⁰

Recent animal studies show success in the treatment of ICD with topically applied peroxisome proliferator activated receptor- α agonists (such as clofibrate or linoleic acid).⁷¹

If the irritation is more chronic, moisturizers, topical steroids, and steroid-sparing agents may be effective for

treatment. Chronic ICD has also been successfully treated with psoralen plus ultraviolet A and ultraviolet B light therapy, both of which reduce immune function and the inflammatory response.⁶⁷

If the dermatitis was caused specifically by calcium oxalate raphides, the symptoms may improve simply by aggressively irrigating the affected area to remove the crystals. The benefit of soap and water is equivocal in such instances.⁴ The severity of the dermatitis will dictate the aggressiveness of treatment. In severe cases of CICD caused by *Dieffenbachia* contact or consumption of an irritant, therapy with intravenous steroids, antacid mouthwash, and opioid analgesics may be necessary.⁹

Glochids, trichomes, and spines will often continue to cause irritation as long as they are embedded in the skin. Treatment therefore involves their removal from the skin. In one controlled study evaluating the removal of *Opuntia ficus-indica* glochids from rabbits, 95% of the implanted glochids were removed in large clumps with forceps, followed by the use of glue and gauze (the gauze was pulled off the skin after the glue dried).⁷²

As secondary infections have been associated with plant-based mechanical irritants, therapy also includes educating the patient on the need to monitor the area. Topical antibiotics are sometimes used as well.

Irritation to chili peppers is common among food workers and during household exposures, and home remedies include immersion in oils or cool tap water. In one study of elderly Hispanic women, cool tap water immersion provided some initial relief, but 75 minutes of immersion in vegetable oil (which binds to hydrophobic capsaicin) provided better long-term relief.⁷³

Prevention

The most important principle in the prevention of ICD is the avoidance of irritants. In the workplace, a good ventilation system and regular vacuum cleaning are important for the prevention of flower bulb dermatoses among florists and other plant workers.⁴ Gloves are similarly important as they may prevent initial contact with the irritant plant. Frequent application of barrier creams and moisturizers may help in the maintenance or replenishment of the skin barrier, which may prevent or delay irritation.⁷⁴ Berndt and colleagues found that the actual type of cream used was much less important than the frequency and regularity of application in order to prevent ICD.⁷⁴ Similarly, Loffler and Effendy found that education (such as training in the correct application of cream, and knowledge of irritants in the workplace) was

the most important measure in the prevention of ICD.⁷⁵ For those who handle plants in the setting of food preparation and production, the application of natural vegetable fats of high linoleic acid content (eg, palm plant fats) to the hands prior to the handling of irritant plants has shown significant protective potential.⁷⁶

Conclusion

Irritant contact dermatitis (ICD) from plants is a very common phenomenon and accounts for the vast majority of plant dermatoses. Potential irritant plants and plant products can be found almost anywhere people are found: in the home, garden, workplace, and recreational setting. It is therefore essential to have a basic understanding of the various plant-derived physical and chemical irritants in order to formulate a complete differential diagnosis when evaluating a case of apparent contact dermatitis.

The common mechanical plant irritants include thorns, spines, glochids, trichomes, and sharp-edged leaves. Many chemical irritants have yet to be elucidated, but known culprits include calcium oxalate, protoanemonin, isothiocyanates, bromelain, diterpene esters, alkaloids, and other chemical irritants such as naphthoquinone and acids.

Affected areas of the body include any parts that may directly make contact with the irritant in question. Most commonly, these are the fingers, hands, wrists, and face. Secondary spread to normally unexposed areas can complicate the clinical picture and make the diagnosis more challenging.

Confirming a diagnosis of plant-related ICD can be challenging because the various substances can irritate the skin in many different respects and to varying degrees. The frequent overlap of chemical ICD with mechanical ICD and of ICD with allergic contact dermatitis also contributes to the challenge in proper diagnosis. The presenting history, although important, may be inaccurate or incomplete, and current diagnostic tools are inadequate for confirming ICD. Other assays are on the horizon, and diagnostic techniques may improve as a better understanding of the mechanisms involved in ICD from plants is gained.

Although therapy most importantly involves the removal of the irritant, topical steroids and barrier creams are generally used as first-line therapeutic agents. The most effective preventive measures to date include avoidance and patient education.

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