MEDICAL BOTANY

PLANTS AFFECTING MAN'S HEALTH

WALTER H. LEWIS
Professor of Biology, Washington University
Senior Botanist, Missouri Botanical Garden

MEMORY P. F. ELVIN-LEWIS
Associate Professor
and Chairman of Dental Microbiology
Washington University
St. Louis, Missouri

A WILEY-INTERSCIENCE PUBLICATION

JOHN WILEY & Sons, New York • London • Sydney • Toronto

hyposensitization may be attempted preseasonally, ensuring that blocking antibodies are at their highest titer during the provocative period, since treatment during the symptomatic period (coseasonal) is less satisfactory. For allergies that occur throughout the year, such as those elicited with fungal spores, it may be necessary to maintain treatment year-round.

Anaphylactic Shock

Systemic anaphylaxis, a rare event in man, is the most severe of all allergic reactions. Typically, it can occur after an inciting dose has been given intravenously to a hypersensitive individual, but it has also been noted after oral, subcutaneous, or intramuscular administration. It is characterized by sudden vasomotor collapse leading to shock, paroxysmal bronchoconstriction, and, if treatment is not undertaken immediately, death. Most cases have been associated with serum therapy (serum sickness), penicillin therapy, and insect stings (especially the wasp, bee, and hornet). However, the following case history underlines the danger of chamomile tea ingestion by an individual known to have ragweed and *Chrysanthemum* atopic disease and other allergies.[4]

Within minutes of drinking a few sips of chamomile tea, the 35-year-old woman developed abdominal cramps, thickness of the tongue, and a tight sensation in the throat. This was followed by angioedema of the lips and eyes, diffuse pruritus, and a full sensation in the ears. There was no vomiting, diarrhea, sneezing, or wheezing. Fortunately, diphenhydramine was administered immediately and a steroid shortly thereafter. The symptoms cleared gradually over the next few hours and disappeared overnight. A subsequent scratch test with chamomile tea produced a large wheal and flare reaction with pseudopod formation. Similar reactions were also elicited among other ragweed patients, although none gave a history of chamomile tea ingestion. This suggests that allergens are shared among members of the family of which ragweed and *Chrysanthemum* are a part.

Prevention is empirical, but atopic individuals should be aware of the increased risk and should avoid agents having known anaphylactic potential, such as penicillin or chamomile tea.

Allergic Rhinitis (Hay Fever)[5]

Characteristic symptoms of hay fever, induced following exposure of the nasal mucosa to the allergen through inhalation, include profuse watery nasal discharge with sneezing, frequently accompanied by redness, irritated and watery eyes, and headache.

The inciting allergens are often found in windborne plant structures called aeroallergens. The spores from fungi and even certain algae may persist through the year, especially under warm humid conditions; but particularly in temperate regions, wind-pollinated plants elicit symptoms during certain flowering periods (Table 3-1). In North America there are three peaks in the pattern of seasonal rhinitis: the first occurs in the spring when trees shed their pollen; the second, during the summer months, involves pollen from many grasses as well as late flowering trees and weeds; and the last peak, in the autumn, is typified by weed and secondarily by grass pollen grains. Ragweed pollen (*Ambrosia*) predominates during this time and is the most allergenic pollen found in North America.

In tropical areas both perennial and seasonal patterns can also be observed with this disorder. Fungal spores and grass pollen are common aeroallergens,

Table 3-1 Aeroall
Asthma, and/or Hy

ALGAE
Chlorella, Chlor
FUNGI
Phycomycetes: Mu
Absidia, Cunnin
pus, Syncephala
Phycomycetes: Pe
Plasmopara (dow
Ascomycetes
Yeast, *Saccharor*
Powdery Mildew
Perithecial fungi
Ascostromatic fu
Basidiomycetes: T
Bullera, Sporobo
Basidiomycetes: U
Puccinia, Uromy
Basidiomycetes: U
Tilletia, Ustilago
Deuteromycetes (I
CRYPTOCOCCACI
Cryptococcus, Rho
DEMATIACEAE. *A*
(Hormodendrum),
ium, Nigrospora, P
Stemphylium
MONILIACEAE. *A*
chum, Gliocladiun
cilomyces, Penicill
choderma, Trichot
SPHAERIOIDACEA
TUBERCULARIACE
GYMNOSPERMS
Ginkgo biloba (g
Juniperus mexica
giniana (red ced
pole pine),[b] *Thuj*
dar);[b] for others
cisco area, see
ANGIOSPERMS: D
ACERACEAE (Mapl
ple)
AMARANTHACEAE
(water hemp), *Am*
weed)
APIACEAE (Carrot)
sley),[a,c] *Heracleum*
ASTERACEAE (Aste
AMBROSIEAE (

Table 3-1 Aeroallergens (Largely North American) Causing Allergic Rhinitis, Bronchial Asthma, and/or Hypersensitivity Pneumonitis

ALGAE
Chlorella, Chlorococcum
FUNGI
Phycomycetes: Mucorales
Absidia, Cunninghamella, Mucor, Rhizopus, Syncephalastrum
Phycomycetes: Peronsporales
Plasmopara (downy mildew)
Ascomycetes
Yeast. *Saccharomyces*
Powdery Mildew. *Erysiphe*
Perithecial fungi. *Chaetomium*
Ascostromatic fungi. *Pleospora*
Basidiomycetes: Tremellales (jelly fungi)
Bullera, Sporobolomyces
Basidiomycetes: Uredinales (rusts)
Puccinia, Uromyces
Basidiomycetes: Ustilaginales (smuts)
Tilletia, Ustilago
Deuteromycetes (FUNGI IMPERFECTI)
CRYPTOCOCCACEAE (false yeast). *Candida, Cryptococcus, Rhodotorula, Torulopsis*
DEMATIACEAE. *Alternaria, Cladosporium (Hormodendrum), Curvularia, Helminthosporium, Nigrospora, Pullularia, Spondylocladium, Stemphylium*
MONILIACEAE. *Aspergillus, Botrytis, Geotrichum, Gliocladium, Monilia, Mycogone, Paecilomyces, Penicillium, Sporotrichum, Trichoderma, Trichothecium, Verticillium*
SPHAERIOIDACEAE. *Phoma*
TUBERCULARIACEAE. *Epicoccum, Fusarium*
GYMNOSPERMS
Ginkgo biloba (ginkgo or maidenhair tree),[a] *Juniperus mexicana* (mountain cedar), *J. virginiana* (red cedar),[a] *Pinus contorta* (lodgepole pine),[b] *Thuja plicata* (western red cedar);[b] for others implicated in the San Francisco area, see Yoo[6]
ANGIOSPERMS: DICOTYLEDONS
ACERACEAE (Maple). *Acer* (box elder, maple)
AMARANTHACEAE (Amaranth). *Acnida* (water hemp), *Amaranthus* (amaranth, pigweed)
APIACEAE (Carrot). *Anthriscus* (hedge parsley),[a,c] *Heracleum* (hogweed)[a,c]
ASTERACEAE (Aster or Composite)
AMBROSIEAE (Ragweed tribe). *Ambrosia* (ragweed), *Dicoria, Hymenoclea* (greasebush), *Iva* (marsh elder, poverty weed), *Xanthium* (cocklebur)
ANTHEMIDEAE (Mayweed tribe). *Artemisia* (mugwort, sagebrush, wormwood), *Chrysanthemum* (ox-eye daisy)[c]
ASTEREAE (Aster tribe). *Aster,*[c] *Callistephus* (China aster),[c] *Solidago* (goldenrod)[c]
CICHORIEAE (Chicory tribe). *Taraxacum* (dandelion)[c]
BETULACEAE (Birch). *Alnus* (alder), *Betula* (birch), *Carpinus* (American hornbeam or blue beech), *Corylus* (hazelnut, filbert), *Ostrya* (hop hornbeam or ironwood)
BRASSICACEAE (Mustard). *Sinapsis* (charlock)[c]
CANNABACEAE (Hemp). *Cannabis* (marihuana), *Humulus* (hop)
CARICACEAE. *Carica papaya* (papaya)[b,c]
CASUARINACEAE (Casuarina). *Casuarina*
CHENOPODIACEAE (Goosefoot). *Allenrolfia* (burrow weed),[a] *Atriplex* (orach, saltbush, wing scale), *Bassia* (smotherweed), *Beta* (sugar beet),[a] *Chenopodium* (goosefoot, lamb's quarters), *Dondia* (sea blite), *Eurotia* (white or winter sage), *Kochia* (burning bush or tumbleweed), *Salsola* (Russian thistle or saltwort), *Sarcobatus* (greasewood)
EUPHORBIACEAE (Spurge). *Mercurialis* (Mercury)
FABACEAE (Pea). *Acacia* (acacia), *Prosopis* (mesquite)
FAGACEAE (Beech). *Fagus* (beech), *Quercus* (oak)
HAMAMELIDACEAE. *Liquidambar* (sweet gum)[a]
JUGLANDACEAE (Walnut). *Carya* (hickory, pecan), *Juglans* (butternut, walnut)
LAMIACEAE (Mint). *Leonotis nepetaefolia* (hollowstalk)[c]
MORACEAE (Mulberry). *Broussonetia* (paper mulberry), *Maclura* (Osage orange), *Morus* (Mulberry)
MYRICACEAE (Sweet Gale). *Comptonia* (sweet fern), *Myrica* (wax myrtle)
MYRTACEAE (Myrtle). *Eucalyptus* (gum tree)[a]
OLEACEAE (Olive). *Fraxinus* (ash), *Ligustrum* (privet), *Olea* (olive), *Syringa* (lilac)[a]

Table 3-1 (Continued)

PLANTAGINACEAE (Plantain). *Plantago*
PLATANACEAE (Plane Tree). *Platanus* (sycamore or plane tree)
POLYGONACEAE (Knotweed). *Fagopyrum* (buckwheat),[b,d] *Rheum* (rhubarb), *Rumex* (dock, sorrel)
RANUNCULACEAE (Buttercup). *Ranunculus*[a,c]
ROSACEAE (Rose). *Rosa*,[c] *Spiraea*[a,c]
SALICACEAE (Willow). *Populus* (aspen or poplar), *Salix* (willow)
SCROPHULARIACEAE (Figwort). *Leucophyllum* (canizo),[c] *Verbascum* (Mullein)[c]
SIMAROUBACEAE (Quassia). *Ailanthus* (tree-of-heaven)
TILIACEAE (Linden). *Tilia* (basswood, linden)
ULMACEAE (Elm). *Celtis* (hackberry), *Ulmus* (elm)
URTICACEAE (Nettle). *Parietaria* (pellitory-of-the-wall), *Urtica* (Nettle)

ANGIOSPERMS: MONOCOTYLEDONS

ARECACEAE (Palm). *Phoenix dactylifera* (date palm)
CYPERACEAE (Sedge). *Carex* (sedge),[a] *Eriophorum* (cottongrass)[a]
JUNCACEAE (Rush). *Juncus* (rush),[a] *Luzula* (wood rush)[a]
POACEAE (Grass). *Agropyron* (western wheat), *Agrostis* (redtop), *Anthoxanthum* (sweet vernal), *Avena* (oats), *Bouteloua* (blue grama or mesquite grass), *Cynodon* (Bermuda), *Dactylis* (orchard), *Digitaria* (crab), *Distichlis* (salt), *Festuca* (fescue), *Holcus* (velvet), *Koeleria* (crested hair), *Lolium* (ray or rye), *Phleum* (timothy), *Poa* (blue, June), *Secale* (rye), *Sorghum* (Johnson), *Zea* (corn)
TYPHACEAE (Cattail). *Typha*

[a] Suspected of causing an allergic reaction.
[b] Especially causing bronchial asthma.
[c] May cause an allergic reaction following accidental contact with the flowers, or if the sensitized individual is adjacent to plants that are typically entomophylous.
[d] Buckwheat flour as inhalant or ingestant allergen.

whereas those from weeds and wind-pollinated trees are of secondary importance. However the determination of aeroallergens in the more equatorial zones requires further study.

Although the majority of plants that induce allergic rhinitis are wind pollinated, a number of plants that are typically pollinated by animals (insects, birds, bats) have also been implicated. For example, old-fashioned roses, which are infrequently found in gardens today, are often heavily scented and their anthers are exposed by the loose and open form of the floral bud. Thus their attractiveness frequently used to lead to sensitization through inhalation of the pollen, and the term rose-fever or rose-cold was used to describe plant-associated rhinitis. Cultivated roses today rarely have much perfume, and the majority have a tight cone-shaped floral bud; thus few people sniff roses, and even fewer are exposed to the pollen from the hidden anthers. For other typically entomophilous plants implicated in allergic rhinitis and asthma, see Table 3-1, footnote c.

POLLEN AND THEIR ALLERGENS

The morphological diversity of windborne pollen varies from smooth-walled grains having a single pore, as found among the grasses, to the very spiny grains of ragweed, and the multiporate apertures typical of pigweed. Size and shape also vary. These features, as well as their wall structure, are related to dispersal mechanisms and their significance as aeroallergens.[7]

The majority of allergens are found in the walls of pollen and spores, but their purpose is not to elicit allergy; rather, they act as recognition proteins to stimulate the growth of the sperm-containing pollen tubes on specific "female" parts of

the flower. Thes
centrated below
intine or inner wal
rigid, outer wall c
cropores or ever
water soluble, anc
the "female" part
mucosa of man,
released within a f

Some of these
isolated only rece
fraction designate
allergenic proteir
sia). Others inclu
and Ra5. Among t
allergens have als
as allergens A anc
pratense) and al
allergens in rye (*L*
number of activ
isolated from al
However, the
allergens remain

SPORE AND POLLI

Many kinds of fu
are responsible f
3-1).[7] The most
gens are found
particularly the f
Moniliaceae, whi
tous genera as *A*
dosporium, Aspe
Of these, *Altern*
allergenic subst
greatest number
in the Midweste
though they pro
of windborne p
rarely elicit aller
windborne polle
common incitor
most troublesom
are the oaks (*Qu*
and elms (*Ulmu*
elder (*Acer*) pc
shown to have t
genicity among t

Table 3-2 Higher Plants of Allergic Significance in Continental United States[a]

Geographic Area	Trees	Grasses	Weeds	Major Pollen
Northeastern. New England, New York, New Jersey, Pennsylvania	Birch, elm, maple, oak, poplar	Annual blue, June, orchard, sweet vernal, timothy	Short and giant ragweed, plantain	Ragweeds, grasses
Middle Atlantic. Delaware, Maryland, Washington D.C.	Birch, hickory, maple, oak, paper mulberry, sycamore	Orchard, timothy	Short and giant ragweed, plantain	Ragweeds, orchard grass
Virginias and Carolinas	Elm, maple, oak, pecan, red cedar	Annual blue, Bermuda, June, orchard	Short ragweed, sorrel, dock	Short ragweed, Bermuda grass, pecan
Southern. Florida and Georgia to eastern Texas, including Texas, Arkansas, and southern Missouri	Birch, cottonwood, elm, oak, paper mulberry, pecan, poplar, privet, red cedar	Bermuda, orchard, timothy	Giant and short ragweed, pigweed, Russian thistle, water hemp	Bermuda grass, pecan, ragweeds
North Central. Ohio and Kentucky to northern Missouri, Iowa, Wisconsin, and Michigan	Ash, cottonwood, elm, maple, oak	June, orchard, timothy	Short ragweed	Short ragweed
Plains and prairies. Minnesota, Dakotas, eastern Montana, Nebraska, Kansas	Elm, oak	Bermuda, bluegrass, orchard, redtop, timothy	Giant, short and western ragweeds, Russian thistle	Ragweeds, Russian thistle
Rocky Mountains. Idaho, western Montana, Wyoming, Colorado, Utah	Birch, box elder, cottonwood, Rocky Mountain cedar	Fescue, June, orchard, redtop, timothy	Ragweed, sagebrush, Russian thistle	Russian thistle, sagebrush
Pacific Northwest. Washington, Oregon, Nevada, northern California	Acacia, alder, box elder, birch, cottonwood, oak, walnut	Bluegrass, fescue, oats, orchard, redtop, timothy, velvet, western rye	Dock, pigweed, Russian thistle, saltbrush, sagebrush, sorrel	
Southwest. western Texas, Nevada, New Mexico, Arizona	Cottonwood, mountain cedar, mulberry, olive	Bermuda, Johnson	Amaranth, canyon ragweed, Russian thistle, saltbush	Amaranth, Bermuda grass, goosefoot, mountain cedar
Southern California	Elm, oak, olive, walnut	Bermuda, salt grass	Dock, lamb's quarters, pigweed, Russian thistle, sage, saltbush, sea blite	Bermuda grass, saltgrass

[a] Adopted from MB Rhyne.[14]

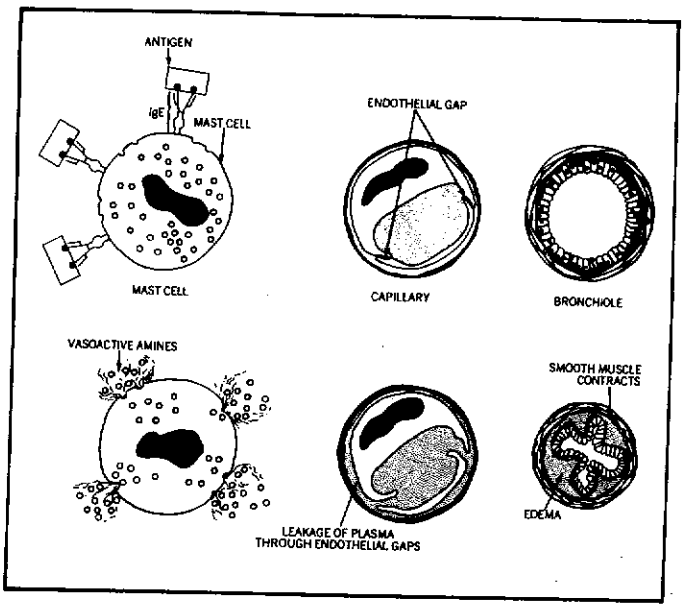

Figure 3-7 The IgE mediated release and action of vasoactive amines. IgE attaches to the surface of mast cell membranes by its Fc fragment. After combining with antigen, vasoactive amines are released from mast cell granules. This increases permeability through endothelial gaps and causes general contraction of smooth muscle, specifically around bronchioles. (From *Scope® Monograph on Immunology*, p. 46, fig 47, 1972, by permission of the Upjohn Company, Kalamazoo, Michigan.)

processes they elicit. Unlike extrinsic asthma antigens cannot be demonstrated and thus skin testing is of no value. The separation of purely extrinsic from intrinsic asthma can be diagnostically difficult whenever allergic phenomena are combined with infectious factors.

Possibly another IgE-mediated, Type I disease is the coffeebean and castorbean workers disease that is characterized by rhinitis, asthma, and dermatitis following inhalation of the hapten, chlorogenic acid. As it is widespread in plants and is concentrated in coffeebeans and castorbeans, chlorogenic acid may act more as a universal allergen than was first suspected.

HYPERSENSITIVITY PNEUMONITIS (TYPE III)

Another type of allergic respiratory condition, known as hypersensitivity pneumonitis or extrinsic allergic alveolitis, is often associated with specific professions. In these instances, animal, vegetable or bacterial enzyme material may induce the disease. For example, inhalation of *Thermoactinomyces vulgaris* or fungal spores of *Microsporum faeni*, which can contaminate hay, moldy sugar cane, or mushroom compost, have been causally related to farmer's (thresher's) lung, bagassosis, and mushroomworker's lung. In a similar way, *Cryptostroma corticale* has been associated with maple bark disease of woodworkers, *Penicillium caseii* to cheeseworker's disease, *Aspergillus clavatus* and *A. fumigatus* to brewer's lung disease, and *Graphium* and *Aureobasidium pullulans* to sequoiosis. By inhalation of the enzyme of *Bacillus subtilis*, those who work with detergents may also develop an allergic pneumonitis. Diseases produced by inhalation of airborne algae such as *Gloeocapsa* and *Chlorella*, are of more general incidence, however. Wood and paper mill workers may also develop

bronchial asthma through sawdust inhalation of the Gymnosperms, redwood (*Sequoia sempervirens*), western red cedar (*Thuja plicata*), cedar of Lebanon (*Cedrus libani*), and the Angiosperms, iroko or African oak (*Chlorophora excelsa*), Nicaragua rosewood (*Dalbergia retusa*), and other exotic woods. The immunopathology suggests that a mixture of many types of immune or allergic reactions may be involved in extrinsic allergic alveolitis and thus is classified as Type III.[17]

It is also possible that symptoms similar to those of allergic respiratory illness may be elicited by inhalation of airborne leaf hairs. Such a series of cases was recently reported among gardeners who had tended saplings of Oriental sycamores or the tree of Hippocrates (*Platanus orientalis*) at a medical school campus. It is interesting that Dioscorides centuries ago had noted watery eyes, sneezing, an irritating sensation in the nasal passages, soreness of the throat, an irritating dry cough, and other similar symptoms.[19]

THERAPY

A regimen of environmental control and hyposensitization is normally prescribed for pollinosis. Currently, three basic drugs have preempted ephedrine for use in the control of asthmatic attacks: epinephrine (adrenalin) and its congeners administered by aerosol, the methylxanthines administered intravenously for acute attacks and orally for chronic asthma, and the steroids (cortisone) for severe and intractable states, in combination with other drugs mentioned. In prophylaxis, particularly where hyposensitization fails, cromolyn sodium is used; this new compound, obtained from the seeds of *Ammi visnaga* (Apiaceae), is believed to affect the release of vasoactive substances and therefore, through a regimen of frequent inhalation, acts to prevent or modify the asthma.[20] This plant, known as khella from its native Mediterranean region, has a long history of use as an antiasthmatic among the Arab peoples, who also believe it is useful in the treatment of angina pectoris.

Although other plants used in domestic medicine to treat asthma have rarely been studied, the recent Indian research using the leaves of *Tylophora indica* (Asclepiadaceae) furnishes an interesting exception.[21] It is claimed that complete to moderate relief of nasobronchial allergic symptoms can be maintained up to one week after ingestion of but a few leaves of the plant. Typical of members of this family, *T. indica* is, however, very toxic and also has blistering or vesicant properties.

Ingestant Allergy[22]

Symptoms from ingesting a potential allergen can vary from urticaria to vomiting, diarrhea, and intestinal wall edema. It is sometimes difficult to differentiate between true atopy and toxicity, since clinical symptoms can be initiated by interaction of substances in foods with several different mediating systems. Therefore the appearance of hives (urticaria) after consumption of strawberries and citrus fruits can be traced to direct chemical mast cell degranulation; those of coeliac disease with intolerance to gluten (gliadin in wheat); and gastrointestinal upset associated with milk are traceable to inherited disaccharidase (lactase) deficiencies. Furthermore, several foodstuffs, particularly shellfish and mushrooms, contain notorious poisons. In susceptible persons, moreover, ricin (a phytotoxin from peanuts and castor beans), gossypol, aflatoxins, histamine, or tyramine (in cheese or yeast products) may also produce symptoms. It is also possible that certain nonallergenic components in food can trigger built-in labilities of mediator systems or can ac-

tivate the complement system (C1 and C3: see Glossary) to generate anaphylatoxin-like agents.

Likewise, physiological age may also have a bearing on an individual's ability to absorb or reject certain allergens. Many food allergies of childhood are altered as the digestive system matures. Among cereals, for example, skin test reactions with rice indicate that there is a lower degree of reactivity among the few children affected; the opposite is true among adults, and higher reactivity involving greater frequency is typical.[23] Any ingestant may prove to have an allergic potential; skin testing, the usual method of determining such susceptibility, may not accurately reflect the true allergic state. Rather, susceptibility is better determined by demonstrating symptoms after deliberate feeding tests. Therapy related to the ingestant is used thereafter. Other techniques include using the rectal mucosa as a shock organ or feeding the test ingestant in dilute form and observing changes in the intestinal tract by X-ray.

Among the active allergens isolated from food, there is good evidence that tomato allergens fall into the same category of active glycoproteins described for inhalant allergens, as do the ovomucoids of egg white, whereas allergens of fish are simple amines.

The major symptom of ingestant hypersensitivity is urticaria, in which wheals and erythematous areas of the skin cause intense pruritus and discomfort. Local edema (angioedema) sometimes accompanies urticaria, and this condition may be life threatening if it affects the mucosa of the pharynx or larynx, since this may result in severe respiratory obstruction.

Atopic dermatitis, a common infant and childhood affliction, is often the first indicator of allergic predisposition. This infantile or atopic eczema may be clinically present as a persistent, pruritic dermatitis that may be papular, exudative, or lichenified, involving the head, neck, and flexor aspects of the trunk and extremities. Most provoking allergens are difficult to identify, varying from animal epidermal allergens (hair) to various foods in the diet.

THERAPY

Whenever it is possible to identify the allergen, avoidance is the best therapy. Otherwise, ephedrine is administered orally, and topical steroids are applied if skin lesions are severe. Antihistamines are useful when pruritus complicates atopic dermatosis or if there is urticaria.

When angioedema is a complicating factor, epinephrine is most useful and can be used concurrently with intravenous antihistamine and steroids for severe cases that involve the larynx.

Dermatitis[24]

IRRITANT DERMATITIS

Plants can mediate inflammatory reactions of the skin, which mimic in many ways the "wheal and erythematous flare" of immediate hypersensitivity, or the more severe reactions associated with the delayed response. In some instances this effect is attributable to the nature of the plant itself, that is, spines, thorns, bristles, and hairs causing mechanical injury. Moreover, the needle-sharp calcium oxalate crystals found in the outer layers of many *Narcissus* species and hyacinth bulbs can elicit the formation of wheals (bulb fingers), a symptom suggestive of histamine release. However most forms of irriation are related to specific substances produced by plants and the mechanism for the adverse reaction is usually unclear.

Of the many plants that transfer their toxins by means of stinging hairs, the nettles (*Urtica dioica* and *Laportea cana-*

densis) contain histamin
found in bladders within
severe reaction is elici
species of Urticaceae,
which is found in tropic
material in its spinelil
considerable pain follow
lasting for several day
spurge nettle, *Cnidos*
(Euphorbiaceae), can eli
tion and itching followi
caustic irritant. Perhaps
reaction of all comes
pruriens (Fabaceae), whc
covering the seed pods
irritating proteolytic
mucunain. Poisoning ca
after the pods have d
herbarium collections. H
mate in adaptation is
Gurania guaransenia (
which in addition to
hairs, harbors a butte
similar devices.

The sap of other pla
and corrosive, results in
tory reactions, including
skin on contact. Many c
tropical, although a nu
cultivated (Table 3-3).

A characteristic of se
ritant plant families i
yellowish latex, usually
the plant. Although so
ing plants are harmless
either irritant or conta
as a general precaution
avoided. Apart from de
to those who prune or
varieties, is the eye dam
that can result from co
eye and the caustic sap.

Several of these irri
been characterized.
Brassicaceae contain
coside is harmless if di
converted into an irrit
the presence of water:
product of another glu

densis) contain histaminelike substances found in bladders within the leaf. A more severe reaction is elicited by another species of Urticaceae, *Urera baccifera*, which is found in tropical America. The material in its spinelike hairs causes considerable pain followed by numbness lasting for several days. Similarly, the spurge nettle, *Cnidoscolus stimulosis* (Euphorbiaceae), can elicit painful irritation and itching following transfer of a caustic irritant. Perhaps the most painful reaction of all comes from *Mucuna pruriens* (Fabaceae), whose barbed spines covering the seed pods contain a highly irritating proteolytic enzyme called mucunain. Poisoning can take place long after the pods have dried, even from herbarium collections. However, the ultimate in adaptation is exemplified by *Gurania guaransenia* (Cucurbitaceae), which in addition to its own stinging hairs, harbors a butterfly larva having similar devices.

The sap of other plants, itself caustic and corrosive, results in severe inflammatory reactions, including blistering of the skin on contact. Many of these plants are tropical, although a number are widely cultivated (Table 3-3).

A characteristic of several of these irritant plant families is their milky or yellowish latex, usually found throughout the plant. Although some latex-possessing plants are harmless, a majority cause either irritant or contact dermatitis, and as a general precaution they all should be avoided. Apart from dermatitis, a hazard to those who prune or tend horticultural varieties, is the eye damage and blindness that can result from contact between the eye and the caustic sap.

Several of these irritant factors have been characterized. Members of the Brassicaceae contain sinigrin; this glucoside is harmless if dried, but it can be converted into an irritant mustard oil in the presence of water. A decomposition product of another glucoside, anemonin, has been isolated from the buttercup (*Ranunculus*) and produces blisters on the face and around the lips of children who may chew the leaves or stems of injured plants. Furthermore, the pineapple (*Ananas comosus*, Bromeliaceae) possesses a proteolytic enzyme, bromelain, which causes separation of the superficial layers of the skin and increases skin and capillary permeability in a manner not unlike that found in the allergic wheal and flare reaction.

PHOTODERMATITIS

Photosensitization contact dermatitis is often caused by plants containing photosensitizing compounds related to furocoumarin.[25] After exposure to the appropriate furocoumarin in the plant, followed by exposure to ultraviolet radiation of a wavelength greater than 3200 Å (usually sunlight), the characteristic sunburnlike rash develops. For example, contact with *Phebalium argentium* (Rutaceae) leaves produces an erythematous blush within 24 hours and a blister by 48 hours. After healing, a white atrophic-looking area remains surrounded by a ring of dark brown pigment, leaving a recognizable area on the skin for years. Phototoxic reactions also occur in patients on sulfonamide therapy as well as in up to 40% of individuals that have received large doses of the tetracycline, declomycin.

Not all plant products known to be photosensitizing have been categorized as either phototoxic or photoallergic, although those containing the furocoumarins are considered phototoxic. Phototoxic reactions occur in most individuals by activation of such substances as the furocoumarins by photons, resulting in free radical formation that leads, by means of photochemical reactions, to cell damage, characteristic erythema, and bulla formation. Most of these compounds are tricyclic resonating aromatic

Table 3-3 Plants Primarily Responsible for Irritant Dermatitis

ANNONACEAE
Annona (blindness from juice of crushed seeds)
APOCYNACEAE
Plumeria,[a] corrosive juice often milky or yellowish
ARACEAE (calcium oxalate crystals and/or irritant, acrid sap)
Alocasia (giant elephant's ear), *Arisaema* (jack-in-the-pulpit), *Arum* (lords-and-ladies), *Caladium, Colocasia, Dieffenbachia* (dumbcane), *Monstera, Philodendron, Xanthosoma* (elephant's ear)
ARALIACEAE
Aralia (devil's walking stick), irritant hairs
BORAGINACEAE
Cynoglossum (hound's tonque), irritant hairs
BRASSICACEAE (irritant oils)[a]
Brassica
BROMELIACEAE
Ananas (pineapple), proteolytic enzyme
CAMPANULACEAE
Isotoma, milky latex
CAPPARIDACEAE
Crataeva, blistering sap
CARICACEAE
Carica (papaya)[b], latex
ELAEOCARPACEAE
Sloanea, irritant bristles
EUPHORBIACEAE (irritant hairs)
Cnidoscolus (spurge nettle), *Dalechampia, Jatropha, Tragia*
FABACEAE
Acacia (bull horn), thorns harboring stinging ants, *Mucuna* (cowitch), proteolytic enzyme from hairs
HYDROPHYLLACEAE
Wigandia, irritant hairs
LAMIACEAE
Leonotis (hollowstalk), leaf
LILIACEAE
Allium (garlic)[a], juice blistering, *Hyacinthus* (hyacinth), calcium oxalate crystals, *Narcissus* (daffodil, jonquil, narcissus), calcium oxalate crystals
LOASACEAE
Gronovia (pica-pica), stinging hairs, *Loasa,* stinging hairs
MORACEAE
Cecropia, harboring stinging ants, *Maclura* (Osage orange)[a], milky latex
MORINGACEAE
Moringa, crushed leaves
PAPAVERACEAE (sap, often yellowish)
Chelidonium (celandine poppy),[a] *Dicentra* (bleeding heart),[a] *Sanguinaria* (bloodroot)[a]
POACEAE (irritant bristles)
Bambusa vulgaris, Guadua
POLYGONACEAE (crushed leaves and stems)
Polygonum (smartweed), *Rumex* (dock)[a]
RANUNCULACEAE (sap)
Ranunculus (buttercup)
SAPOTACEAE (milky sap)
Calocarpum, Manilkara
SOLANACEAE (irritant spines)
Capsicum frutescens (bird or wild pepper)
Solanum (buffalo bur, horse nettle)
STERCULIACEAE (irritant hairs in fruit)
Sterculia (Panama tree)
THYMELAEACEAE (sap)
Daphne, Dirca (leatherwood)
URTICACEAE (stinging hairs or spines with caustic irritant)
Fleurya, Hesperocnide (western stinging nettle), *Laportea* (wood nettle), *Urera, Urtica* (stinging nettle)
VITACEAE
Cissus, juice of fruit

[a] Reaction is probably, in part, contact dermatitis.
[b] Used in meat tenderizing.

compounds that are not particularly reactive and have a molecular weight of about 200–500.

In genetically predisposed individuals, photoreactivation of the photosensitizing molecule of photoallergen causes the formation of a new substance, a photohapten. The conjugation of the photohapten with suitable proteins in the skin produces a complete photoantigen that elicits spongiosis and intradermal vesicle formation characteristic of allergic contact dermatitis (see Delayed Hypersensitivity in the following section).

This group is characterized by a halogenated phenol, coupled with another halogenated aromatic ring that is sometimes also hydroxylated. Photoallergy differs from phototoxicity reaction in several respects. Not only are these reactions rarer, the amount required to elicit the response is smaller, as well. Often the same substance can produce ordinary contact allergic dermatitis in the absence of light, and cross-sensitization between immunologically related substances has been demonstrated. Flareups can also occur at unexposed sites distant from the area of initial contact. In all cases, an incubation period is required before photoallergy is elicited. Ragweed oleoresin is a known plant photoallergen.

Not many plant families contain species with these photosensitizing compounds. In man they include the Fabaceae, Moraceae, Clusiaceae, Chenopodiaceae, Rosaceae, Ranunculaceae, and the Liverwort genus *Frullania*, but the compounds are most widespread in the families Apiaceae and Rutaceae (Table 3-4).[26] Photosensitivity reactions in animals are caused by a host of other plants including many grasses (Bermuda grass, oats, sorghum), legumes (alfalfa, alsike clover), and others.[27]

Table 3-4 Higher Plants that Provoke Photodermatitis in Man

Family and Species	Vernacular Name
APIACEAE	
Ammi majus	Artrillal
Anethum graveolens	Dill
Angelica spp.	Angelica
Apium graveolens	Celery
Daucus carota	Carrot
Foeniculum vulgare	Fennel
Heracleum spp.	Giant hogweed, cow parsnip
Pastinaca sativa	Parsnip
Peucedanum spp.	Masterwort
CLUSIACEAE. *Hypericum* spp.	St. John's wort
BRASSICACEAE. *Brassica* spp.	Mustard
FABACEAE. *Psoralea corylifolia*	Bavachi
CHENOPODIACEAE. *Chenopodium* spp.	Goosefoot
MORACEAE. *Ficus carica*	Fig
RANUNCULACEAE. *Ranunculus* spp.	Buttercup
ROSACEAE. *Agrimonia eupatoria*	Agrimony
RUTACEAE	
Dictamnus albus	Gas plant
Citrus spp.	Bergamot, lime, sour orange
Phebalium argenteum	
Ruta graveolens	Common rue

oats, Sorghum, legumes

CELLULAR—MEDIATED (DELAYED TYPE) HYPERSENSITIVITY (TYPE IV)

Delayed hypersensitivity may take days or weeks to develop; often prolonged contact with an antigen is necessary, and the reaction depends on the formation of specifically modified lymphocytes from the thymus-dependent series (T cells). Through specific receptors or other mechanisms, these cells are capable of responding specifically to antigens deposited at a local site and also of mobilizing nonsensitized phagocytic cells to localize there and participate with them in tissue destruction. Unlike immediate hypersensitivity, a reaction is not apparent for 12–24 hours, when inflammation and necrosis appear in the affected area.

To test for contact hypersensitivity, the candidate allergen is usually applied as a patch to the unbroken skin and observed for 24 hours for characteristic changes. The results of attempts to provoke

tolerance by deliberate desensitization through administration of repeated injection of antigen are often short-lived and frequently precipitate severe allergic reactions.

Substances of plant origin or chemicals including heavy metals can act as haptens to mediate a delayed hypersensitivity response after prolonged or repeated contact with the skin. Sensitization is dependent on attachment of the chemical to the structural proteins of the skin, which results in a change of the skin proteins. Alone or through release of substances from epidermal cells, this type of antigenic alteration can stimulate a specific inflammatory response that produces, after 24–48 hours, symptoms of pruritis, burning or stinging, erythematous macules, papules, vesicles, exudation, and crusting.

The sensitizing substances of most plants are found in the oleoresin fraction, which includes volatile oils, resins, and balsams (Table 3-5). Occasionally, water glycosides and other aqueous fractions may be the sensitizing materials.

The most dangerous examples are members of the Anacardiaceae, which are widespread throughout North America and Asia. It has been estimated that at least 70% of the population of the United States would acquire *Toxicodendron* dermatitis on casual exposure to poison oak, poison ivy, or poison sumac. Prolonged exposure would probably render even more of the population sensitive. These plants also have been known to elicit severe reactions in the oral cavity and gastrointestinal tract if ingested, and in the respiratory tract, if inhaled. The active principle is an oleoresin (urushiol), which

Table 3-5 Plants Causing Contact Dermatitis

Chemical Classification	Primary Component	Family and Species	Comments
VOLATILE (ESSENTIAL) OILS			
Hydrocarbons			
Terpenes			
Acyclic	Myrcene	CANNABACEAE	
		Humulus lupulus (hops)	Lupulin (glandular hairs)
Monocyclic	Limonene	APIACEAE	
		Anethum graveolens (dill)	
		Apium graveolens (celery)	
		Carum carvi (caraway)	Also ketone carvone
		RUTACEAE	
		Citrus spp. (peels of bitter orange, lemon, lime; bergamot)	Neroli oil, orange flower oil; also terpene alcohols and aldehydes
	Phellandrene	BURSERACEAE	
		Canarium luzonicum (elemi oil)	
		LAMIACEAE	
		Mentha spicata (spearmint)	Also limonene, pinene, ketone, and alcohols
		LAURACEAE	
		Cinnamomum zeylanicum (cinnamon)	

Table 3-5 (Continue

Chemical Classification
Dicyclic
Sesquiterpenes
Alcohols (acyclic, terpene, and sesquiterpene alcohols)
Aldehydes
Ketones

Table 3-5 (Continued)

Chemical Classification	Primary Component	Family and Species	Comments
		PINACEAE *Abies balsamea* (balsam fir)	Canada balsam oil
Dicyclic	Pinene	PINACEAE *Pinus* spp. (pine) and other Gymnosperms	Chief component of turpentine oil
Sesquiterpenes	Cadinene Selinene Zingiberene		
Alcohols (acyclic, terpene, and sesquiterpene alcohols)	Geraniol	GERANIACEAE *Pelargonium odoratissimum*	
	Linalool	BURSERACEAE *Bursera aloexylon*	Linaloe
		APIACEAE *Coriandrum sativum*	Coriander oil
	Citronellol	MYRTACEAE *Eucalyptus citriodora* (lemon-scented gum)	
		ROSACEAE *Rosa alba, R. centifolia, R. damascena, R. gallica*	Rose oil
		GERANIACEAE *Pelargonium odoratissimum, P. radula*	Geranium oil
	Borneol	ZINGIBERACEAE *Elettaria cardamomum*	Cardamon seed
	Santalol (sesquiterpene)	SANTALACEAE *Santalum album* (sandalwood)	
Aldehydes	Citral (geranial)	POACEAE *Cymbopogon nardus*	Citronella oil
	Citronellal	*C. nardus*	Citronella oil
Ketones	Camphor	ASTERACEAE *Blumea balsamifera* (Ngai camphor), *Chrysanthemum parthenium* (feverfew)	
		DIPTEROCARPACEAE *Dryobalanops aromatica* (Borneo camphor)	Borneol
		LAURACEAE *Cinnamomum camphora*	Camphor
	Carvone	LAMIACEAE *Mentha spicata, M. cardiaca* (spearmints)	Spearmint oil also contains terpenes, alcohol
		APIACEAE *Carum carvi*	Caraway oil also contains terpene limonene
	Irone	IRIDACEAE *Iris germanica, I. pallida*	Orris oil

Table 3-5 (Continued)

Chemical Classification	Primary Component	Family and Species	Comments
	Pulegone	LAMIACEAE *Hedeoma pulegioides*	Pennyroyal oil
	Thujone	ASTERACEAE *Artemisia absinthium* (wormwood)	Absinthe oil
		Tanacetum vulgare (tansy)	Many essential oils isolated
Phenols	Anethole	APIACEAE *Foeniculum vulgare*	Fennel oil, also contains ketones and terpenes
	Eugenol	MYRTACEAE *Eugenia caryophyllus*	Clove oil
	Safrole	LAURACEAE *Sassafras albidum*	Sassafras oil (80% safrole) suspected of contact dermatitis
	Thymol	LAMIACEAE *Thymus vulgaris*	Thyme oil also includes terpenes and alcohols
Oxides	Ascaridol	CHENOPODIACEAE *Chenopodium ambrosioides* var. *anthelminticum* (wormseed)	Chenopodium oil suspected of contact dermatitis
	Cineole (eucalyptol)	MYRTACEAE *Eucalyptus globulus*	Eucalyptus oil
		Melaleuca leucadendron	Cajuput oil
		LAMIACEAE *Rosmarinus officinalis*	Rosemary oil
Lactones (many sesquiterpenes)		LIVERWORT *Frullania nisquallensis*	Perhaps also due to usnic acid
		ASTERACEAE (tribes Anthemideae, Helenieae, Heliantheae) *Ambrosia* (ragweed) *Anthemis* (chamomile) *Arctium* (burdock) *Artemisia* (mugwort, sagebrush, wormwood) *Chrysanthemum* *Cynara* (artichoke) *Eupatorium* (boneset) *Gaillardia* *Helenium* (sneezeweed) *Tagetes* (marigold) *Xanthium* (cocklebur)	
Quinones	Primin	PRIMULACEAE *Primula obconica* (primrose)	Glandular hairs, the head containing the irritant primin
	Thymoquinone	CUPRESSACEAE *Libocedrus decurrens* (California incense cedar)	

Table 3-5 (Continued

Chemical Classification
RESINS AND RESIN COMBINATIONS
Oleoresins
OLEORESINS (pollen
matitis)
Balsams

[a] For the monogra

Table 3-5 (Continued)

Chemical Classification	Primary Component	Family and Species	Comments
RESINS AND RESIN COMBINATIONS			
Oleoresins	Urushiol (containing 3-pentadecylcatechol)	ANACARDIACEAE *Anacardium melanorrhoea* (rengas tree), *A. occidentale* (cashew) *Comocladia dodonaea* (Christmas bush) *Mangifera indica* (mango) *Metopium toxiferum* (coral sumac, poison wood) *Schinus molle* (Brazil pepper-tree), *S. terebinthifolius* *Toxicodendron diversilobium* (western poison oak), *T. radicans* (poison ivy), *T. rydbergii* (Rydberg's poison ivy), *T. toxicarium* (eastern poison oak), *T. vernis* (poison sumac)[a]	
	Capsaicin	SOLANACEAE *Capsicum frutescens* (capsicum or Cayenne pepper)	
	Asafoetida	APIACEAE *Feula* spp.	Gum asafetida
OLEORESINS (pollen dermatitis)		*Acer* (box elder, maple) *Ambrosia* (ragweed) *Erigeron* (mare's tail) *Fraxinus* (ash) *Iva* (Marsh elder) *Mangifera* (mango) *Populus* (poplar) *Ulmus* (elm) *Xanthium* (cocklebur)	
Balsams	Benzoin (benzoresin)	STYRACACEAE *Styrax benzoin* and other spp.	Friar's balsam; also benzoic, cinnamic, and balsamic acids
	Cinnamein	FABACEAE *Myroxylon pereirae* (Peruvian balsam)	Also resin esters, vanillin (aldehyde), etc.
	Resin esters	*M. balsamum* (Tolu balsam)	
	Storesin	HAMAMELIDACEAE *Liquidambar orientalis* (Oriental sweet gum)	Levant storax
		L. styraciflua (American sweet gum)	Cinnamic acid, cinnamein, resin esters

[a] For the monographic treatment of *Toxicodendron*, see Gillis.[28]